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CONTENTS

ORAL PRESENTATION

CONTENTS

ORAL PRESENTATION

POSTER PRESENTATION

CONTENTS

POSTER PRESENTATION

CONTENTS

POSTER PRESENTATION

CONTENTS

POSTER PRESENTATION

CONTENTS

POSTER PRESENTATION

IAP-THAILAND
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Welcome to the 59th IAP-Thailand Annual Meeting, Bangkok, Thailand

Dear Colleagues,

On behalf of the organizing committee, I am very delighted to welcome all of you to join the 59th IAP-Thailand Annual Meeting, during November 6th-8th, 2019 at Swissotel Bangkok Ratchada.

In this congress, there will be several interesting topics on the updates and practical points in various fields of anatomic pathology presented by renowned international experts and local speakers, eg. Gynecopathology, Gastrointestinal Pathology, Genitourinary Pathology, Molecular Pathology, Hematopathology, Head and Neck Pathology, Breast Pathology, Dermatopathology, Thoracic Pathology, Cytopathology, Bone and Soft tissue Pathology, Neuropathology, Ophthalmic Pathology, and Digital Pathology. On top of these, there are also topics related to laboratory accreditation from College of American Pathologists (CAP), pre-lunch symposia, sponsor sessions, poster and oral presentations as well as SHOWTIME session in which participants will be able to present their interesting cases to audiences. There are more than 30 speakers, both international and local, participating in this congress with different topics being presented in 3 separate rooms.

In addition to academic activities, this year, we also address 100-year history of pathology in Thailand to celebrate the 100th anniversary of pathology in Thailand which started since Professor Aller G. Ellis established his pathology work in Thailand as the first chairman of pathology department at Siriraj Hospital in 1919.

I am certain that this would be a great opportunity for you to update your knowledge on diagnostic pathology along with getting the chance to enjoy this lively capital and meet with other colleagues from different countries. I do hope that the 59th IAP-Thailand Annual Meeting at Bangkok this year will be one of the most memorable experiences in your life.

Somboon Keelawat, MD.
President, IAP-Thailand

Prevalence of *KRAS* and *NRAS* gene mutation in Thai patients with colorectal cancers

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Abstract

Background:
EGFR monoclonal antibody such as cetuximab and panitumumab are effective against *KRAS/NRAS* wild type colorectal cancers (CRCs).*KRAS/NRAS* mutation test is therefore mandatory to select patients eligible for the targeted treatment. The purpose of this study was to determine the prevalence of *KRAS/NRAS* mutation in Thai patients with CRC.

Materials and Methods:
CRC specimens of Thai patients submitted to Chulalongkorn GenePro Center during 2015-2018 were retrospectively analyzed. *KRAS* and *NRAS* was determined, using mass array technique (ColoCarta® or HS iPLEX®).

Result:
Of the 445 CRC samples tested in the study period, 205 cases (46%) carried *RAS* mutations, 193(43.4%) with *KRAS* and 12 (2.7%) with *NRAS* mutations. For *KRAS*, mutations were most frequently found in codon 12 (145 cases, 75.1%), followed by codon 13 (32 cases, 16.6%), codon 61 (8 cases, 4.1%), codon 146 (5 cases, 2.6%), and codon 117 (3 cases, 1.6%). 106 mutants were men (55%) and 87 were women (45%);with age range <50 years,12.4%; 50-59 years, 27.5%;60-69 years, 35.7%; and ≥70 years(24.4%).For the 12 *NRAS*-mutant cases, 9 and 3 were located in codon 12(75%) and codon 61(25%), respectively.10 mutant cases were men (83.3%) and 2 were women (16.7%); with age range <50 years, 16.7%; 50-59 years,16.7%; 60-69 years, 25%; and ≥70 years, 41.6%.

Conclusion:
Prevalence of *KRAS*(43.4%)/*NRAS*(2.7%) mutation (46%in total) in Thai patients with colorectal cancers is within the range of that reported from other parts of the world(33.6% to 39.6% for *KRAS* and 2 to 5.7% for *NRAS*).

Prevalence of *BRAF* and *PIK3CA* Mutations in Thai Patients with Colorectal Cancers

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Abstract

Background:
Mutations in *BRAF* and *PIK3CA* genes have been shown to lower response rate of EGFR monoclonal antibody in *RAS*-wildtype colorectal cancers (CRCs). Prevalence of *BRAF* mutations has rarely been studied in Thai patients while *PIK3CA* mutation has not yet been determined.

Materials and Methods:
A retrospective descriptive study was performed at Chulalongkorn GenePRO Center. Cases during 2015-2018 were retrieved for analysis. Detection of *BRAF* and *PIK3CA* mutations was performed by Mass Array technique (ColoCarta® or HS iPLEX® platform).

Result:
445 cases were identified, and there were 12(3%) patients with *BRAF* and 32(7%) patients with *PIK3CA* mutations. Of 241 *KRAS/NRAS*-wildtype cases, *BRAF* mutation was found in 10, *PIK3CA* in 14, and combined *BRAF* and *PIK3CA* mutations in 2 cases. Concurrent mutations were detected, 15 cases with *KRAS* and *PIK3CA* mutations, 1 with *NRAS* and *PIK3CA* mutations, and 2 with *PIK3CA* and *BRAF* mutations. All *BRAF* mutations were detected in exon 15, V600E(11) and D594G(1). Of the 32 *PIK3CA*-mutant cases, 26(81.2%) were found in exon 9 (E542K, 12 cases; and E545K, 14 cases); 5(15.6%) in exon 20 (H1047K); and 1(3.2%) with double mutations in exon 9 and 20 (E545K and H1047R).

Conclusion:
Prevalence of *BRAF*(3%) and *PIK3CA*(7%) mutations in Thai CRC patients is within the range previously reported (1.8-7.1% for *BRAF* and 5.5-13% for *PIK3CA*). Although *BRAF*/*PIK3CA* mutation test is not currently recommended, mutations in these genes have been shown to lower response rate for anti-EGFR and may be worth routinely testing in our patients.

Mineral oil as a safe and cheap substitute for xylene in tissue processing

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Abstract

Background:
In spite of its toxicity xylene, an aromatic benzene with NFAP of 2, 3, 0, is widely used as a clearing agent in tissue processing. Mineral oil, an aliphatic petroleum hydrocarbon, is less toxic and safe with NFAP of 0, 1,0 and four times cheaper than xylene. The objective of this study was to assess the suitability of mineral oil to replace xylene in tissue processing.

Materials and Methods:
A total of 100 pairs of different types of tissue were sampled from various organs excluding biopsies. One set of tissue was processed using xylene and the other with mineral oil. Tissue block preparation, microtomy sectioning, slides preparation and routine H & E staining were performed under same conditions for both sets of tissue. Four microtomy characteristics, 5 microscopic physical and 4 staining characteristics were blindly assessed using standard independent 3 tire scoring systems. Sign test and paired T test were used for comparison with significance level at 0.05.

Result:
The microtomy characteristics of mineral oil processed tissue were similar to that of xylene processed tissue with a significantly better result in the ribboning in mineral oil processed tissue. Three out of 4 microscopic staining characteristics in mineral oil processed tissues were superior. All 4 microscopic physical characteristics assessed were better in xylene processed tissue.

Conclusion:
Mineral oil may be a substituted for xylene in tissue processing, provided that relevant measures are taken to improve the physical quality of microscopic characteristics.

Pathologic diagnosis of Patients with Mucinous Appendiceal Tumor and peritoneal disease in Siriraj Hospital

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Abstract

Background:
Mucinous neoplasm is the most common tumor of appendix. Previously the nomenclature, classification and staging system for this tumor have not been consensus. Until recently, the diagnostic criteria for tumor classification and staging system have been accepted. Siriraj Hospital is a referral hospital. We experience a certain number of cases and we are one of a few centers that could perform definitive surgery including hyperthermic intraperitoneal chemotherapy (HIPEC) recommended for advanced stage tumor.

Materials and Methods:
The aim of this study is to evaluate and correlate clinical presentation, surgical treatment, pathologic diagnosis, tumor staging and clinical outcome. We retrospectively reviewed clinical data and surgical pathology of the appendiceal mucinous neoplasm from January 2009 to April 2018.

Result:
This study included 85 patients with appendiceal mucinous neoplasm with female preponderance (M/F: 3/8). Median age is 61 years. Most patients (38.8%) presented with increased abdominal size. Pathologic diagnosis included low-grade appendiceal mucinous neoplasm (LAMN) (76.4%), mucinous adenocarcinoma (21.2%) and high-grade appendiceal mucinous neoplasm (HAMN) (2.4%). Most common gross surgical finding was ruptured appendix with intraabdominal metastasis (52, 61.2 %). Omentum is the most site of tumor spreading. Extra-appendiceal spreading of LAMN increased 5-year recurrence from 11.1% to 53.9%. Patients received HIPEC had advanced stage and higher rate of 5-year recurrence.

Conclusion:
This study demonstrates clinical and pathologic characteristics for mucinous appendiceal neoplasm and also correlation between clinical outcome, treatment and pathologic diagnosis.

Accuracy of image analysis program using artificial intelligence algorithm to evaluate signet ring cells in pathological images

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Abstract

Background:
Currently, the workload of pathologists is very high when compared the number of patients' specimens to the number of pathologists worldwide. This potentially increases in the risk of errors, which may be caused by fatigue from excessive work. Therefore, there is an idea to use computer and image analysis software to help in pathological diagnosis. We proposed an image analysis model with artificial intelligence (AI) by choosing the signet ring cell carcinoma as a model in this experimental study.

Materials and Methods:
H&E slides of 15 signet ring cell carcinoma cases from any organs, diagnosed by experience pathologists, were scanned to digital files using digital slide scanner (Aperio ScanScope XT). Images in the target areas were captured at 400x magnification by Aperio ImageScope software, and then upload for training in AI cloud platform (customvision.ai, Microsoft Azure). The protocol we selected was an object detection. The training results were evaluated on test images with different thresholds.

Result:
The probability threshold at 50% can predict signet ring cells with 68% sensitivity and 90% specificity. When increased probability threshold to 90%, the sensitivity decreased to 52% with specificity increased to 97%.

Conclusion:
Computer vision and artificial intelligence could be able to analyze signet ring cells in the pathological images with high accuracy comparing with the standard diagnosis by pathologists.

Accuracy of Aspergillus Immunohistochemistry for Diagnosis of Aspergillosis in Formalin-Fixed Paraffin-Embedded Samples

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Abstract

Background:
Histopathological diagnosis *of Aspergillus spp.* is challenging since the fungus is morphologically overlapping with other fungal organisms. Aspergillus antibody for immunohistochemistry (IHC) is commercially available but its accuracy needs verification. This study was aimed to evaluate the sensitivity and specificity of aspergillus IHC, using polymerase chain reaction (PCR) and sequencing as the gold standard.

Materials and Methods:
Formalin-fixed paraffin-embedded (FFPE) surgical specimens containing filamentous fungi were retrieved from the archives of the Department of Pathology, Faculty of Medicine, Chulalongkorn University, during 2017 to 2018. IHC was performed by standard indirect method, using a rabbit polyclonal antibody to Aspergillus (ABCAM, UK). Immunoreactivity was scored as negative, 1+, 2+, and 3+; and only 2+ and 3+ cases were considered positive. DNA was extracted from the FFPE samples, amplified, and sequenced to identify the fungal species.

Result:
81 specimens were enrolled in the study. The sensitivity and specificity of aspergillosis IHC were 98% and 54%, respectively. Of the 11 non-aspergillosis cases verified by PCR, 5 were positive with Aspergillus stain. The antibody showed cross reactivity with *Mucorales spp.* (3 cases), *Scedosporium spp.* (1 case), and *Fusarium spp.* (1 case) in our cohort.

Conclusion:
Aspergillus immunostain has acceptable sensitivity but limited specificity to be used in routine pathological diagnosis. In the absence of culture, molecular method is a more appropriate diagnostic tool.

Applicability of a novel anti-lipoarabinomannan monoclonal antibody (anti-LAM mAb) for detection of Mycobacterium tuberculosis on formalin-fixed paraffin-embedded (FFPE) tissue

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Abstract

Background:
Tuberculosis (TB) is one of the major public health problems in Thailand. However, identification of Mycobacterial organisms may not be easy. Culture is considered the gold standard diagnostic test but it takes several weeks for the result. Ziehl-Neelson (ZN) is another method which requires quite simple technique but has poor sensitivity. In this study, we evaluate a novel anti-LAM mAb immunohistochemistry for detection of TB in FFPE specimens which, so far, has not been studied in Thailand.

Materials and Methods:
A diagnostic test study was conducted using 110 FFPE specimens, including cases with and without histomorphologic features of TB, were collected from the database of KCMH. All samples were stained with anti-LAM mAb, provided by one of the authors (EY). Interpretation of the staining was made by 3 pathologists (MP, SK, SS) focusing at 1 hotspot under 40x. Two criteria were used to determine TB cases. The gold standard tests for diagnosis of TB in this study were culture and/or PCR.

Result:
The number of dots stained by anti-LAM mAb correlated well with gold standard tests. Specificity increased with number of detected dots. According to the ROC curve, the best cut-off point was determined to be >5 dots. With culture as the gold standard, anti-LAM mAb had sensitivity of 16.1%, specificity of 90.3%, PPV of 62.5% and NPV of 51.9%. Using culture and/or PCR as the gold standard, anti-LAM mAb had sensitivity of 18.6%, specificity of 100%, PPV of 100% and NPV of 12.7%. The results were rather comparable with ZN, by which, when culture was used as the gold standard, sensitivity was 17.4%, specificity was 92.9%, PPV was 80% and NPV was 40.6% and when culture and/or PCR as the gold standard, sensitivity was 16.3%, specificity was 100%, PPV was 100% and NPV was 7.7%.

Conclusion:
This study indicated that anti-LAM mAb can served as another ancillary tool that may increase chance to identify Mycobacterial organisms in addition to ZN. We suggested the minimum of 5 dots/HPF as the cut-off value in order to achieve the best diagnostic ability.

EVALUATING THE P53 AS DIAGNOSTIC MARKER BY USING LIQUID BASED CERVICAL SAMPLE IN CERVICAL CARCINOGENESIS

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Abstract

Background:

p53 is known as the guardian genome and tumour suppressor gene as it involved in the induction of cell cycles and preventing mutation by activating cellular apoptosis. P53 mutation is observed in numerous types of malignancies such as in ovary, lungs, breast, colorectal, uterus and cervical cancer. Cervical cancer is one of the most common cancer in the female population. According to the Malaysian National Cancer Registry 2007-2011, the prevalence of cervical cancer among other female cancer in Malaysia was observed at 7.7%. The association between the Human Papillomavirus (HPV) infection and cervical cancer is well established. The emergence of the HPV negative squamous lesion could hamper the high-risk HPV (hrHPV) detection in Pap smear. Instead of looking into the HPV protein, we explored the expression of p53 in various stages of cervical carcinogenesis and determine the utility of p53 as potential diagnostic marker for cervical cancer.

Materials and Methods:

This is a cross-sectional study using left over samples of routine liquid based cytology (LBP) from Ministry of Health facilities in Johor Bahru, Johor and Kota Bharu, Kelantan from May 2016 to May 2018. All the LBP samples were selected according to cervical carcinogenesis; negative for intraepithelial malignancy (NILM), low grade squamous intraepithelial lesion (LSIL), high grade squamous intraepithelial lesion (HSIL) and squamous cell carcinoma (SCC) and fulfilled the inclusion and exclusion criterion. Each LBP smear underwent cytopathological examination by respective resident pathologists and certified medical laboratory technicians, results were classified according The Bethesda System (TBS) 2014. The selected left over samples were converted to cell blocks and were subjected for p53 IHC staining. The nuclear expression of p53 IHC stain was assessed and quantified by usingHisto-score (H-Score). The cytological diagnosis was not known during the interpretation of the IHC

Result:

The p53 IHC scores obtained showed an increase in p53 expression in more severe cervical dysplasia and SCC and showed good sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). The statistical analysis between the mean p53 IHC score with cervical carcinogenesis categories were done using analysis of variance (ANOVA) which showed statistically significant result, p value <0.05. Post-hoc test (Tukey) among the cervical carcinogenesis categories showed statistically significant results, p value <0.05.

Conclusion:

Our findings suggest that p53 can be used as a diagnostic tool to differentiate normal cervical pap smear samples from the sample that has undergone different stages of cervical carcinogenesis. p53 also manage to stratify each category of cervical carcinogenesis. The cell blocks are also providing an excellent ancillary test for routine cervical pap smears.

Histopathologic features of orchiectomy specimens from patients with clinical diagnosis of testicular regression syndrome

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Abstract

Background:
Testicular regression syndrome (TRS) is a congenital condition in which no macroscopically normal testicular tissue can be identified following exploration for a clinically impalpable testis. Owing to variable incidence of seminiferous tubules (STs) and viable germ cells (GCs) reported in different studies and inconclusive future malignancy risk, optimal management of testicular remnant in TRS is controversial. This study aims to ascertain the incidence of STs and GCs, and to characterize histopathologic features of testicular remnants resected from TRS cases.

Materials and Methods:
A search of the histopathology database between 2006 to 2018 was made to identify cases with diagnosis of TRS. Histopathologic findings were reviewed with particular regard to presence or absence of testicular structures, fibrosis, calcification, hemosiderin-laden macrophages, paratesticular and spermatic cord structures.

Result:
A total of 34 specimens were identified. Patient age ranged from birth to 11.4 years (mean 4 years; median 2.2 years). Locations included inguinal (70.6%), scrotal (20.6%), and intraabdominal (8.8%). The average size was 0.7 cm. STs were identified in 11/34 (32.4%); 2/11 contained viable GCs. None showed GCNIS. Presence of STs was not associated with location or patient age. Other histopathologic findings included fibrosis (91.2%), calcification (41.2%), and hemosiderin-laden macrophages (38.2%). Calcification and hemosiderin-laden macrophages were likely to be present in younger age. Vas deferens and epididymis were observed in >50%.

Conclusion:
The incidence of STs and GCs in testicular remnants resected from TRS cases was 32.4% and 5.9%. There was no association between presence of STs and location or patient age. Fibrosis was noted in > 90% of specimens.

Histopathologic findings of cutaneous involvement by extranodal NK/T-cell lymphoma, nasal-type

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Abstract

Background:
Background: Cutaneous involvement by extranodal NK/T cell lymphoma, nasal-type (ENKTL) is common but the histopathologic findings have not been reported. Objectives: To study histopathologic findings of cutaneous involvement by ENKTL, either primary or secondary.

Materials and Methods:
Retrospective review of H&E and immunostained slides of cutaneous involvement by ENKTL from 2006 to 2018 and one year survival rate of the patients.

Result:
Total of 22 cases were recruited (secondary 12 cases, undetermined 5 cases and unknown primary 5 cases). The lymphoma cells varied from medium to large in size. Tumor necrosis was found in12 cases while angioinvasion was found in 13 cases. The histopathologic patterns included subcutaneous panniculitis-like lymphoma (6 cases), dermal nodular (4 cases), mixed dermal and subcutaneous nodular(4 cases), subcutaneous nodular (3 cases), interface dermatitis-like (3 cases), mycosis fungoides-like (1case), and granulomatous panniculitis (1 case). The median follow-up was 18.3 months and the 1-yearoverall survival was 31.25%.

Conclusion:
There were various histopathologic patterns of cutaneous involvement by ENKTL, providing differential diagnosis for other cutaneous lymphomas, dermatitis, and infectious conditions. Thus, when encountered with abnormal medium or large-sized lymphoid cells in the skin lesions, complete studies are highly recommended to determine whether this is cutaneous involvement by ENKTL or not.

H3 K27M Mutation is Rare in Pilocytic/Pilomyxoid Astrocytomas

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Abstract

Background:
H3 K27M mutation in HIST1H3B (H3.1) or H3F3A (H3.3) genes was thought to be the hallmark of diffuse midline glioma with dismal prognosis (WHO 2016 grade IV). The mutation has, however, been reported in several cases of pilocytic astrocytoma, a circumscribed astrocytoma with excellent prognosis (WHO 2016 grade I). This study was aimed to survey the prevalence of H3 K27M mutation in pilocytic (PAs)/pilomyxoid astrocytoma (PMAs)..

Materials and Methods:
All PA/PMA samples diagnosed during 2008 to 2018 were retrieved from the pathology file at the Department of Pathology, Faculty of Medicine, Chulalongkorn University. H3 K27M immunohistochemistry (rabbit polyclonal #ABE419, EMD Millpore) was performed in all cases. Additional molecular analyses of H3.1, H3.3, KRAS, NRAS, and BRAF genes were carried out in all immunopositive cases.

Result:
61 patients with diagnosis of PA (60) and PMA (1) were identified. There were 36 male and 25 female patients, with age ranging from 1-79 year (mean = 20.16). Only one PA (1.64%) showed positive nuclear staining of H3 K27M. The positive case was an intramedullary thoracic cord tumor in a 50-year-old man. Further molecular studied confirmed the presence of the mutation in H3.3 gene. The tumor did not carry KRAS, NRAS, and BRAF mutations, and BRAF duplication test was negative. Not directly related to the tumor, the patient passed away 3 years after diagnosis.

Conclusion:
H3 K27M mutation is rare in pilocytic/pilomyxoid astrocytomas, and prognosis of the mutation in this setting is still unclear. In typical PA/PMA cases, performing H3 K27M stain may not be necessary.

Correlation of hepatic steatosis and fibrosis in chronic viral hepatitis B and C patients

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Abstract

Background:
Chronic hepatitis B (CHB) and C (CHC) are the important cause of chronic liver disease andcancer developmentin the patient with progressive fibrosis, which often associated with hepatic steatosis. The aims of this study are to evaluate the prevalence of hepatic steatosis in Thai CHB and CHCpatients and correlation with fibrosis staging.

Materials and Methods:
The liver biopsies of the CHB and CHC patients who diagnosed in Srinagarind hospital between 2016 and 2018. H&E with PAS and Masson trichrome staining were used to evaluation of the histology of fibrosis and steatosis and examined by the METAVIR and SAF scoring systems.

Result:
The mean age of the patient was 45 year-old (19-69). The CHC was detected in 96 patients (69.6%) and CHB was detected in 42 patients (30.4%). Liver biopsies showed steatosis in 73 patients (52.9%) which divided into; grade I 67.1%, grade II 19.2%, and grade III 13.7%. Fibrosis by METAVIR was evaluated; stage I in 51.4%, stage II in 34.8%, stage III in 5.8%, and stage IV in 8%. The SAF Steatosis grading was associated with METAVIR fibrosis staging, SAF activity score, and body mass index (p<0.05).

Conclusion:
Hepatic steatosis was mostly seen in of CHC and CHB patients. Steatosis grade appears to be related with fibrosis stage, BMI, and SAF activity score.

A CASE OF ADRENOCORTICAL CARCINOMA PRESENTING WITH CUSHINGOID FEATURES

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Abstract

Introduction:
Adrenocortical carcinoma is a rare neoplasm with an incidence of 0.02-0.2% of all malignancies. Majority of the tumors are functional which secrete cortisol and dehydroepiandrosterone sulfate (DHEA-S).

Case Report:
A 48 year old female patient presented with complaints of breathlessness, facial swelling and hypertension. Contrast enhanced CT showed a well defined lobulated heterogenously enhanced mass lesion of right suprarenal gland. Serum cortisol, urine cortisol and DHEA-S were elevated. Urine Vanillyl mandelic acid was normal. Total adrenalectomy was done. Gross examination revealed a circumscribed tumor measuring 10x8x7 cms. The cut surface showed tan yellow areas with necrosis. Microscopic examination showed an encapsulated tumour composed of diffuse sheets and focal large nests of pleomorphic tumor cells with enlarged oval vesicular nucleus with single prominent nucleolus and moderate amphophilic cytoplasm. Brisk mitoses (30/10 high power fields), areas of necrosis and foci of lymphovascular and capsular invasion were noted. Immunohistochemistry was performed and the tumor cells showed moderate cytoplasmic positivity for Inhibin. p53 was positive in scattered cells and Ki67 index was 8%. The diagnosis was high grade adrenocortical carcinoma.

Discussion:
Adrenocortical carcinoma is a rare neoplasm with poor prognosis The main differential diagnoses are adrenocortical adenoma, pheochromocytoma, and renal cell carcinoma. High mitotic rate, necrosis, lymphovascular and capsular invasion are features of adrenocortical carcinoma. Phaeochromocytoma shows Zellballen arrangement of tumor cells with chromogranin positivity. Renal cell carcinoma infiltrating adrenal gland shows positivity for cytokeratin.

Conclusion:
Adrenocortical carcinoma is a rare neoplasm. It is essential to differentiate it from adenoma by correlating with clinical, biochemical and histological features.

CLEAR CELL SARCOMA- A DIAGNOSTIC ENIGMA

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Abstract

Introduction:
Clear cell sarcomas are rare tumours accounting for 1% of the sarcomas. They are also referred to as malignant melanoma of soft tissue in view of their morphological resemblance. They arise from the neural crest cells in the soft tissue.

Case Report:
A 60 year old lady presented with fever and weight loss since one month. Systemic examination was normal. On investigation, the patient had isolated anaemia. Workup for pyrexia of unknown origin like blood cultures, tests for malaria and tropical infections were negative. Endoscopy ruled out gastrointestinal malignancy. Contrast enhanced computerised tomography of the thorax and abdomen was normal. Patient was discharged. Subsequent review after two weeks showed a hard mass in the left iliac fossa and inguinal region measuring 8x6x4cms. Fine needle aspiration showed numerous singly scattered pleomorphic tumour cells having prominent nucleoli. A possibility of poorly differentiated carcinoma was suggested. Biopsy showed grey brown tumour with necrosis. The microscopy showed nests of tumour cells with clear to eosinophilic cytoplasm, prominent nucleoli and extensive areas of necrosis. Human Melanoma Black-45 and S-100 showed positivity in the tumour cells suggestive of clear cell sarcoma of soft tissue.

Discussion:
Clear cell sarcomas have to be distinguished from other sarcomas. The 5 year survival in these patients is 67%. The prognosis is poor in patients with tumour size >5cms and in tumours showing necrosis.

Conclusion:
Clear cell sarcomas have always been a diagnostic challenge for the pathologist. Diagnosis requires a high index of suspicion, extensive study of morphology and aid of immunohistochemistry.

Impact of antiretroviral drugs on PD-L1 expression and copy number gains with clinical outcomes in HIV-positive and -negative locally advanced cervical cancers

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Abstract

Background:
Cervical cancer has become a leading cause of death in both HIV-infected and uninfected women. Many studies show that ART possesses anti-HPV and antitumour properties and may act as an anticancer agent in addition to improving functional immunity in HIV-positive individuals. However, no studies have examined the relationship between ART with clinical outcomes for patients with pre-existing invasive cervical cancer.

Materials and Methods:
We analysed 48 HIV-positive and 123 HIV-negative patients with locally advanced stages IB2-IVA cervical cancer between December 2008 and December 2016. Tumours were categorized based on immunoreactivity for PD-L1 and copy number alterations in the PD-L1 gene assessed by FISH.

Results:
ART-exposed patients displayed a lower prevalence of PD-L1 immunopositivity and PD-L1 amplification and polysomy than ART-naïve patients and HIV-negative patients. ART-exposed patients with PD-L1 -immunonegativity had better RFS than ART-naïve and HIV-negative patients with PD-L1 immunopositivity (p=0.041vs.p=0.030). Furthermore,ART-exposed patients with PD-L1 disomy had better LRR (p=0.039 vs . p= 0.007) , RFS(p<0.001vs.p=0.006), and CSS(p=0.021vs.p=0.025) than HIV-negative patients with PD-L1amplification and polysomy, and ART-exposed patients withPD-L1 disomy had better RFS(p<0.001) and CSS(p<0.001) than HIV-naïve patients withPD-L1 amplification and better LRR (p=0.028) than HIV-naïve patients with polysomy. In multivariate analysis, FIGO stage and PD-L1amplification were predictiveof worse RFS (HR,2.43;95%CI,1.37-4.30; p=0.002vs.HR,7.03;95%CI,2.79-17.74;p<0.001) and CSS(HR,11.47;95%CI,4.70-27.99;p<0.001vs.HR,4.05;95%CI,1.64-9.98;p=0.002). In contrast, only PD-L1 polysomy was predictive of worse LRR in multivariate analysis (HR,2.50;95%CI,1.11-5.63;p=0.027). HIV status was not associated with worse outcomes in Cox models.

Conclusion:
Our results indicate the possibility of ART for the treatment of cervical cancer in both HIV-infected and uninfected patients. Further research is warranted to elucidate these findings

Prognostic significance of PD-L1 protein expression and copy number gains in locally advanced cervical cancer

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Abstract

Background:
Although immune checkpoint inhibitors against programmed death-1 (PD-1) and its ligand (PD-L1) have demonstrated promising results in several solid malignancies including cervical cancer, there are some limitations to using PD-L1 immunohistochemical expression as a predictive biomarker for selecting patients who may benefit from such therapy.

Materials and Methods:
We investigated the PD-L1 gene copy number gains assessed by fluorescence in situ hybridization (FISH) and PD-L1 expression using immunohistochemistry in 123 patients with locally advanced cervical cancers between December 2008 and December 2016.

Results:
The prevalence of PD-L1 immunohistochemical expression was detected in 103/123(83%) cases. PD-L1 gene amplification and polysomy were detected in 7% and 40% of cases, respectively. PD-L1 gene amplification and polysomy were associated with positive PD-L1 immunostaining (score1+-3+) in 88% and 68% of cases, respectively. Clinically, PD-L1 immunopositivity was associated with parametrial invasion at diagnosis. In contrast, PD-L1 polysomy was associated with parametrial invasion and FIGO stage III-IV whereas PD-L1 amplification was associated with nodal metastasis. In multivariate analysis, PD-L1 amplification was predictive of worse RFS (HR, 5.68; 95%CI, 1.98-16.28; p = 0.001) whereas PD-L1 polysomy was predictive of worse LRR (HR, 4.13; 95%CI, 1.63-10.49; p = 0.003). PD-L1 immunohistochemical expression was not associated with worse outcomes in Cox models.

Conclusion:
Our results showed that an increase in PD-L1 gene copy number could be a novel prognostic and possible predictive biomarker for anti-PD-1/PD-L1therapy in locally advanced cervical cancer.

Status of PD-L1 protein expression and copy number gains in HIV-positive versus HIV-negative locally advanced cervical cancer

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Abstract

Background:
The programmed death-1/programmed death-ligand-1 (PD-1/PD-L1) immune regulatory axis has recently discovered as a potential new target for cancer therapy, including cervical cancer. However, the status of antitumor immunity represented by the expression of PD-L1 is still poorly understood in HIV-infected patients with cervical cancer.

Materials and Methods:
In this study, we analyzed HIV-positive (n=42) and HIV-negative (n=110) patients with locally advanced, stage IB2-IVA cervical squamous cell carcinomas between December 2008 and December 2016. Tumors were categorized based on immunoreactivity for PD-L1 and copy number alterations in PD-L1 gene (amplification, polysomy, disomy) assessed by FISH.

Results:
PD-L1 immunopositivity showed a lower prevalence in HIV-positive women when compared to HIV-negative women (p < 0.001) whereas PD-L1 copy number status showed nostatistically significant difference between HIV-positive and HIV-negative women. PD-L1 gene amplification and polysomy were associated with positive PD-L1 immunostaining (score1+-3+) in 92% and 70% of cases, respectively. For survival analysis, PD-L1 amplification was an independent predictor of worse recurrence-free survival (HR, 6.01; 95%CI, 2.44-14.81; p<0.001)and cancer-specific survival (HR, 3.60; 95%CI, 1.48-8.76; p=0.005) whereas PD-L1 polysomywas an independent predictor of locoregional recurrence (HR, 3.27; 95%CI, 1.27-8.40; p=0.014).Both HIV-positive patients and PD-L1 immunopositivity were not associated with worse outcomes in Cox model.

Conclusion:
Our findings indicate that utilization of PD-L1 immunohistochemistry should be reconsidered and exercised with caution in patients with HIV, whereas an increase in PDL1 gene copy number is more reliable and could be an alternative prognostic and possible predictive biomarker for antiPD1/PDL1 therapy, regardless of HIV status.

Collision of osteosarcoma, giant cell rich and benign phyllodes tumour of the breast: a case report

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Abstract

Introduction:
PT tumour accounts for less than 1% of primary breast tumours. PTs are classically classified into benign, borderline and malignant. The malignant PT may display several mesenchymal differentiation and these include liposarcomatous, osteosarcomatous or chondrosarcomatous differentiation.

Case Report:
We report a 60 year old woman with left breast primary breast osteosarcoma originating in a benign phyllodes tumour

Discussion and Conclusion:
Pure osteosarcomas of the breast should be distinguished from heterologous osteosarcomatous differentiation of a malignant phyllodes or metaplastic carcinoma. In some cases, osteosarcomatous differentiation may involve more than three quarters of the cellular stroma of malignant PT, and therefore extensive sampling, to identify the epithelial component, is deemed necessary to establish the correct diagnosis. Our case however showed concurrent presence of malignant transformation of a benign phyllodes tumour into a primary sarcoma of the breast. Thus, identifying any residual epithelial element is important in distinguishing malignant phyllodes tumour from a primary sarcoma of the breast.

Utility of Napsin A in primary lung carcinomas

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Abstract

Background:
Pulmonary cancer is the leading cause of cancer related mortality in Malaysia and worldwide. Identification of a specific and more sensitive marker is need to allow for more accurate diagnosis and subtyping of pulmonary carcinomas. The aim of this study was to evaluate the utility of Napsin A immunohistochemical stain in the diagnosis of primary lung carcinoma and its potential immunohistochemical marker for lung adenocarcinoma.

Materials and Methods:
One hundred and twenty three formalin-fixed paraffin-embedded cases of primary lung adenocarcinoma (n=46), lung squamous cell carcinoma (n=44) and lung small cell carcinoma (n=33) diagnosed from January 2013 to May 2018 were retrieved.

Results:
Napsin A expression was positive in all (46/46, 100%) cases of lung adenocarcinoma . None of the (0/44) lung squamous carcinoma and (0/33) cases of small cell carcinoma cases were positive for Napsin A. TTF-1 expression was positive in 44 of 46 cases of lung adenocarcinoma (95.7%), 1 in 44 cases of lung squamous carcinoma (2.1%) and 28 in 33 cases of lung small cell carcinoma (84.8%). Napsin A was more sensitive than TTF-1 for primary lung adenocarcinoma (100% vs 95.7%); P < .001) and the former was also more specific than TTF-1 for primary adenocarcinoma versus other primary lung carcinoma (100% vs 62.3%; P <.001).

Conclusion:
Napsin A is an excellent marker in distinguishing lung adenocarcinoma from squamous carcinoma and small cell carcinoma subtypes and shown to be more specific than TTF-1.

Osteosarcoma of the breast: a case report

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Abstract

Introduction:
Osteosarcoma of the breast is an extremely rare and aggressive tumor. Histopathalogy is undistinguished from the osseous osteosarcoma.

Case Report:
: A 53 years old Thai woman with right breast mass for1 year. No history of radiation. The breast examination showed 10 cm. ill define and firm mass. The mammography presented a lobulated, iso-to-hyperdense mass with containing a group of several coarse heterogenous calcification. The gross pathology for modified mastectomy showed well defined firm mass that was 9 cm in diameter and whitish tan appearance of the cut surfaces. Histopathology presented pleomorphic spindle, epithelioid and round cells tumor with some foci of osseous formation with osteoclast-like giant cells. The diagnosis was osteosarcoma of the breast. Theinvestigation for metastatic evaluation was negative.

Discussion:
Osteosarcoma of the breast is an extremely rare and difficult to be distinguished from metaplastic tumor from the breast neoplasm.However, both entities are extremely rare, aggressive behavior and have no current treatment guideline. Surgical resection with adequate margin and metastasis evaluation should be performed.

Conclusion:
The osteosarcoma of the breast is an extremely rare and aggressive tumor. After resection with appropriated margin. Further investigation for metastasis evaluation and close following up shouldbe performed.

The external compression of the displaced brachiocephalic trunk as a cause of tracheal stenosis: A case report

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Abstract

Introduction:
Congenital tracheal stenosis is a life-threatening disorder. The most common cause is malformed cartilage. The authors report a rare cause of tracheal stenosis by external compression by displaced right brachiocephalic artery.

Case Report:
A female neonate was born at 32 weeks gestation due to maternal preeclampsia with a birthweight of 1,532 g. At 3 weeks old, the baby developed critical dyspnea and desaturation. Then the resuscitation was performed. The endotracheal tube could not be inserted deeply to its usual position. The neonate still had desaturation and the symptom was worsen which raised the clinical suspicious for tracheal stenosis. The bronchoscope finding was confirmed tracheal stenosis at thoracic inlet level, about 8.5 cm from incisor. Sliding tracheoplasty was done. However, after surgery her clinical status was not improved and she passed away at 2 months of age from the complication of ventilator-associated pneumonia.

Discussion:
An autopsy reveals the brachiocephalic trunk displacement. It originated from aortic arch more distal in comparison to those of normal population, and then crossed the midline and externally compressed the trachea. It was able to cause pressure effect to the anterior tracheal wall leading to tracheal stenosis.

Conclusion:
The external compression to the trachea is a rare cause of tracheal stenosis. Besides intraluminal evaluation of the trachea, investigation of the surrounding structures, in particular great vessels, is essential to exclude other possible rare causes of tracheal stenosis.

A non-receptor tyrosine kinase, FYN, is decrease expression in clear cell of ovarian cancer in Northern Thailand

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Abstract

Background:
FYN is a non-receptor tyrosine kinase that may have a role in metastasis in several cancer type with a potential for targeted therapy. In ovarian cancer, FYN has been reported to be a hub of gene interaction network in the pathway of the cisplatin-resistance in ovarian carcinoma cell line. However, ovarian epithelial carcinoma represents a heterogenous group of tumors. Clear cell carcinoma (CCC) is a subtype of high-grade ovarian carcinoma with a propensity for chemoresistance. To our knowledge, information of FYN expression in ovarian clear cell carcinoma has not been reported.

Materials and Methods:
116 ovarian cancer tissue samples were evaluated for the FYN expression using quantitative real-time PCR method; including 29 CCC (including 2 mixed cell type), 50 non-CCC high-grade ovarian adenocarcinoma (including 42 high-grade serous type), 19 low-grade ovarian adenocarcinoma, and 18 metastatic carcinomas.

Results:
FYN was expressed in 44.8% of CCC, 90% of non-CCC high-grade adenocarcinoma, 68.4% of low-grade adenocarcinoma, and 55.6% of metastatic cancers. FYN expression levels in CCC were decreased by 1.3 to 3.11 folds compared to the other groups of tumors. The levels of FYN expression in CCC were significantly lower than the non-CCC high-grade adenocarcinoma ($p = 0.029$).

Conclusion:
Ovarian CCC has low FYN expression in comparison with other histologic types. FYN expression may not involve in the chemoresistance pathway of ovarian CCC.

Effects of preanalytical sample collection time and temperature on p210 BCR-ABL1 gene expression level in patients with chronic myeloid leukemia

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Abstract

Background:
Quantitative real-time quantitative polymerase chain reaction (RQ-PCR) for BCR-ABL1 plays a crucial in chronic myeloid leukemia (CML) response monitoring. Time and temperature are well-known factors negatively affecting RNA quality. This study aimed to determine whether transport time and temperature from blood collection to the laboratory have detrimental effects on BCR-ABL1 expression level.

Materials and Methods:
Blood samples (10 ml each) of CML patients with a white blood cell count > 100,000 cells per cubic millimeter were aliquoted, 2 ml were immediately RNA extracted for routine BCR-ABL1 RQ- PCR test and 6 tubes of 1.3 ml blood were kept at 4°C and room temperature (RT) for RNA extraction on days 2, 3 and 4. RNA from all 7 conditions of each cases were stored at -80°C before being simultaneously examined using a standard BCR-ABL1 RQ-PCR method.

Results:
Of 29 cases with BCR-ABL1 expression, ABL control gene were detected in all cases while BCR-ABL1 transcript were undetected in 3 cases (10.34%) after day1. Therefore, there were 26 cases included for data analysis, with an average BCR-ABL1/ABL expression level at day1 of 66.68% (min-max; 35.35%-90.14%). Compared with day1, BCR-ABL1/ABL expression levels were significantly changed in RNA samples of day2(4°C), day3(4°C), day4(4°C) and day3(RT), by -15.04%, -16.14%, -16.52% and -16.43%, respectively. When considering copy number using day1 as a reference, both BCR-ABL1 and ABL copy numbers were significantly lower in samples of day4(4°C) and all days 2-4 at RT. A significantly progressive decrease in copy number of both BCR-ABL1 and ABL genes was observed over time after day1 in RT samples (P=0.0009 and P=0.0001, respectively; repeated measures ANOVA).

Conclusion:
This study demonstrated that preanalytical transport time and temperature have significant effects on BCR-ABL1/ABL expression levels tested by a standard RQ-PCR method. Blood samples should be transported at 4°C and processed within 24 hours.

Epithelioid-cell myofibroblastoma of the breast: a case report of an uncommon benign mimicker of invasive mammary carcinoma

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Abstract

Introduction:
Myofibroblastoma (MFB) is a distinct benign stromal tumor of the breast with fibroblastic/myofibroblastic differentiation and a wide variety of cytomorphologic and architectural features. Epithelioid-cell MFB, a rare morphologic variant that predominantly comprising cells with epithelioid morphology, may closely mimic invasive carcinoma, particularly the lobular subtype

Case Report:
In this report, we describe the clinicopathologic features of a case of epithelioid-cell MFB of the breast in a 46-year-old woman who presented with a lump in right breast.

Conclusion:
This particular case emphasizes that epithelioid-cell MFB can be a diagnostic challenge when evaluating breast biopsies and resection specimens. Awareness of this entity is essential to avoid diagnostic error.

Primary leiomyosarcoma of the maxillary gingiva : A case report

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Abstract

Introduction:
Oral leiomyosarcoma is a rare malignancy of the head and neck malignant neoplasms.

Case Report:
We report a case of 44-year-old female with 4-week history of a soft tissue swelling. Intraoral examination revealed an asymptomatic mass in the left maxillary buccal gingiva, 2.4 x 3.0 cm in dimension, pink, firm, ulcerated, exophytic, involving the area of teeth 24-26. An incisional biopsy of the lesion was performed. Macroscopic examination of the specimen revealed one previously fixed piece, tan, soft, 2.1 x 1.8 x 1.8 cm in dimension. Histologic examination demonstrated malignant spindle cell proliferation. Immunohistochemical analysis of the tumor was done. The tumor cells showed a strongly diffuse positive for SMA and negative for Desmin, S100, ALK, CD68 and P63. The smooth muscle cell origin of the tumor cells was confirmed by Electron microscopic examination. All together findings, the final diagnosis of leiomyosarcoma was made. The patient was undergoing surgical removal of the mass. No recurrences or metastases were detectable at a 6-month follow-up.

Conclusion:
Leiomyosarcoma is rarely found in the oral cavity. The clinical presentation of the neoplasm may appear similar to those reactive lesions. Microscopic examination and immunohistochemical analysis of the specimen is required to make the final diagnosis of the leiomyosarcoma.

ACRODERMATITIS ENTEROPATHICA

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Abstract

Introduction:
Acrodermatitis enteropathica (AE) is a rare autosomal recessive disorder in zinc (Zn)-transporter proteins ZIP4. The incidence of AE is estimated to occur in 1 per 500,000 children. Zn deficiency results in classic triad of dermatitis (perioficial and acral), diarrhea, and alopecia.

Case Report:
We reported a case in infant boy, 8 years old, complained reddish peeling spots which appeared in some body areas. There was history of diarrhea. Physical examination found multiple erythematous macules with scales, erosions, and brown crusts at head, face, neck, buttock, groin, both hands and foot palms regions. There're alopecia, perionychia, scurvy, and poor nutritional status. Microscopic features showed psoriasiform hyperplasia, parakeratosis, orthokeratosis, pale keratinocyte, and spongiosis. Zinc serum test showed below normal value.

Discussion and Conclusion:
AE usually appears during infancy shortly after weaning. Some conditions leading to Zn deficiency among infant are low Zn level in nursing mother (low intake), preterm infant (low absorption), and baby which has been born from HIV infected mother. Based on clinical and histopathological findings, patient suspected as AE, but the histological features are difficult to distinguish from other nutritional disorders. Therefore, Zn serum level test is a mandatory to be performed. If there's decrease in Zn serum, Zn supplementation and lesion treatment should be addressed. Late management can cause fatal complications, meanwhile early AE responds dramatically to therapy. Preferable prognosis is achieved from proper management.

Histo-cyto correlation & risk of malignancy in AUS/FLUS Bethesda category; an audit of nine years thyroid cytology

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Abstract

Background:
The Bethesda system (TBS) for reporting thyroid cytology has brought standardized nomenclature & management guidelines. Atypia of undetermined significance/ Follicular lesion of undetermined significance (AUS/FLUS) in TBS not poses inter & intra-observer variability among pathologists, but is also source of physicians' dissatisfaction. The risk of malignancy in this category varies from 6-81%.

Materials and Methods:
Total 256 AUS/FLUS cases of 2342 thyroid FNACs were reported in our institution from 2010 till 2018. Only 104 cases with subsequent surgical resections were included in study.

Results:
Patients' age ranged from 15 to 71 years, mean age of 43.5 years. Majority (70.3%) of patients were female. AUS/FLUS accounted for 10.9% of thyroid FNACs. Seventy of 104 resection specimens (67.3%) were reported benign and 34 cases (32.7%) had malignant diagnosis. Of the benign category 30 (42.9%) were benign nodular hyperplasia followed by Hashimoto's thyroiditis (15.7%), adenomatous nodules (12.9%) & Follicular/Hurthle cell adenomas (25.7%). NIFTP was reported in 2.9% cases. In malignant category, Papillary thyroid carcinoma, conventional variant & Follicular variants accounted for 38.2% & 14.7% respectively. Follicular carcinoma was 2nd common malignancy (23.5%). Papillary micro carcinoma was seen in 8.8%. One case each of Poorly differentiated carcinoma, DLBCL, Mucoepidermoid carcinoma & paraganglioma was reported.

Conclusion:
The AUS/FLUS category of TBS poses a great diagnostic challenge. The wide range of reported risk of malignancy in literature reflects its difficult nature. The diagnosis should be restricted by using stringent cytological criteria in conjunction with clinical & radiological features.

Dedifferentiated & Undifferentiated Carcinoma of Endometrium: Uncommon Entities with Dismal Prognosis

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Abstract

Background:
Dedifferentiated and Undifferentiated carcinomas of endometrium are uncommon variants of endometrial carcinoma. Our aim is to study the clinicopathological features of Dediff &Undifferentiated carcinoma of endometrium, entities better described by WHO now.

Materials and Methods:
A total of eleven cases were retrieved from first January 2017 to first February 2019. Six cases were diagnosed on hysterectomy specimen while five were diagnosed on endometrial curretings.

Results:
Age ranges from 40-65 years. Mean age was 54. Seven cases were of undifferentiated carcinoma while four were dedifferentiated carcinoma. The mean size was 4 cm. All seven tumors in hysterectomy specimen involve more than half of the thickness of myometrium. The undifferentiated area is composed of round to spindly cells which exhibit marked degree of nuclear pleomorphism and hyperchromasia. The dedifferentiated carcinoma exhibits intermingling of low grade endometroid adenocarcinoma and high grade undifferentiated areas. The undiff.areas is usually cytokeratin and ER & PR negative. Low molecular weight cytokeratin and EMA are usually positive in undiff.areas. In dediff.ca. Extensive sampling is needed to look for low grade component. The undiff.areas is usually cytokeratin and ER & PR negative. Low molecular weight cytokeratin and EMA are usually positive in undifferentiated areas. In dedifferentiated carcinoma extensive sampling is needed to look for low grade component.A follow up was available in 10 out of 11 patients. Follow up period ranged from 1 month 24 months (mean 9.3 months). Four patients of undifferentiated carcinoma died of disease after 2-4 months of follow up (mean 3 months).Two of these patients developed brain metastases. One patient of undifferentiated carcinoma also developed colonic metastasis, but alive after 8 months of follow up.

Conclusion:
I. Dedifferentiated & Undifferentiated carcinomas of endometrium are uncommon variants with grave prognosis. It usually goes unrecognized due to lack of a characteristic morphologic spectrum.
II. Extensive sampling is needed to look for low grade areas in dedifferentiated carcinoma.
III. Undifferentiated carcinoma behaves more aggressively than dedifferentiated carcinoma, as all four patients in our study died of disease were of undifferentiated type.
IV. These entities need to be recognized and differentiated from other aggressive endometrial lesions because of its most adverse outcome therefore it is important for pathologist to be aware of these uncommon entities.

Concordance of pre-operative and post-operative diagnoses of endometrial epithelial malignancies

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Abstract

Background:
Diagnosis of a malignancy in endometrial biopsy(EB) is a common problem in histopathology practice. Histological type and grade of the endometrial carcinoma will determine whether limited or extensive surgery is required; and providing this information on limited tissue is a challenge.

Materials and Methods:
48 histopathology reports of endometrial malignancy resection specimens and their corresponding EBs during the period 2013-2017, received at the Department of Pathology, University of Kelaniya were retrieved. The diagnoses made on EBs were correlated with those of the hysterectomy specimens. The FIGO classification scheme was used for the histological typing and grading. The Pearson correlation coefficient was used to assess the concordance between pre-operative and post-operative diagnoses

Results:
The postoperative diagnoses were endometrioid-low grade(ELG)(72.9%,n=35), endometriod-high grade(EHG)(14.5%,n=7), serous(6.2%,n=3), and carcinosarcoma(6.2%,n=3).The diagnoses made preoperatively were adenocarcinoma(n=17), endometrioid adenocarcinoma(n=23), serous(n=1), carcinosarcoma(n=2) and atypical hyperplasia(AH)(n=2). Three were non-diagnostic. Thus the correlation of the pre and post-operative diagnoses was 0.88(P value is 0.009). Malignancy was accurately diagnosed in 43/48(89.5%). Histological subtyping had been performed in 26/43(60%) and 24/26(92.3%) had been correctly subtyped in EBs.(one upgraded to serous from EHG, one endometrioid diagnosed as carcinosarcoma and two AH diagnosed as ELG). 7/23(30.43%) endometrioid adenocarcinomas had been subtyped.

Conclusion:
A satisfactory concordance was achieved between the pre-operative and post-operative diagnoses of epithelial malignancies. However histological subtyping and grading of tumours on EB was suboptimal; mainly due to the perception of tumour heterogeneity and the lack of appreciation of its significance in patient management. Thus the importance of improving this aspect in reporting malignancies in EB is highlighted.

Concordance of pre-operative and post-operative diagnoses of endometrial epithelial malignancies

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Email: g.hiroshi@yahoo.com

Abstract

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Conclusion:
A satisfactory concordance was achieved between the pre-operative and post-operative diagnoses of epithelial malignancies. However histological subtyping and grading of tumours on EB was suboptimal; mainly due to the perception of tumour heterogeneity and the lack of appreciation of its significance in patient management. Thus the importance of improving this aspect in reporting malignancies in EB is highlighted.

Case Report: Mucinous carcinoma of breast, accidentally diagnosed in young female patient with fibroadenoma.

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Abstract

Introduction:

Mucinous carcinoma (MC) is a slow growing carcinoma and also known as gelatin/colloid carcinona. 0.5-3% of breast carcinoma an ussualy happen in older women. The characteristic is tumor cells floating in lakes the extracellular mucin. There are 2 tyoe : pure and mixed. Mucinous carcinoma has good prognostic because nodal metastasis is rare.

Case Report:

We report 32 years old woman with history lump in breast at upper lateral breast dextra about 2 year as big as duck's egg for 2, the size in not enlarge rapidly, she has no complain pain, no nipple discharge and no peau d'orange. Axillary node not enlarge. The surgeon suppose the lump as benign tumor as fibroadenoma mammae. Gross cutting we found area white dense and gelatinous. Microscopic feature is unifomely tumor cells floating in the lake extracellular mucin and fibroadenoma feature. We expertise as mucinous carcinoma.

Poorly Differentiated Endometrial Adenocarcinoma-Case Report

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Abstract

Introduction:

Endometrial carcinoma has a high morbidity in the advanced countries of Western Europe and the USA and also in Japan, where its morbidity has increased in recent years. In 1970, endometrial carcinoma constituted ~3% of total uterine cancers in Japan, but the ratio increased to ~40% in 1998. Therefore, it has become increasingly important to understand the oncogenic mechanisms and prognostic factors in endometrial cancer. It was previously reported that grade of differentiation is one of the critical prognostic factors in endometrial carcinoma (1–4). Creasman et al. (5) reported that the 5-year survival rate was 92.0% for G1 endometrial carcinoma cases and 86.9% and 74.0%, respectively, for G2 and G3 cases. This suggested a significantly poorer prognosis for carcinomas of lower differentiation grades. Delaloye et al. (6) investigated the rates of local recurrence, metastasis, disease-free survival and overall survival according to differentiation grade for stage I endometrial adenocarcinoma cases, and showed that the lower the grade was, the higher the metastasis rate was and the lower the disease-free survival rate and overall survival rate were. It has been suggested that there are two types of endometrial cancer based on oncogenic pathology. One type develops in women with signs of high-estrogen conditions such as obesity, hyperlipidemia, anovular bleeding, infertility, delayed menopause and proliferation of the ovarian stroma or endometrium. Another type develops in women without these signs. Many cases of the former type have the G1 or G2 differentiation grade with shallow muscle invasion, a high sensitivity to hormone therapy and a relatively favorable prognosis (7–9). The latter group, in many cases, has the G3 differentiation grade, with deep muscle invasion, high probability of lymph node metastasis, and shows a poor sensitivity to hormone therapy and a poor prognosis (8). Therefore, it is important to examine clinical characteristics of G3 endometrial carcinoma cases separately from highly differentiated cases. Endometrioid adenocarcinoma constitutes 70% of endometrial carcinomas (5), and those with other tissue types such as clear cell adenocarcinoma and serous adenocarcinoma show a significantly poorer prognosis compared with endometrioid adenocarcinoma (5,10)

Case Report:

We received a large specimen of a uterus with cervix with bilateral tubes and ovaries measuring 16x10x9 cms in total. Each of the ovaries measured 4x3x2.5 cms and both tubes measured approximately 6 cms in length. No external gross findings were observed. The sample was fixed in 10% neutral buffered formalin upon receipt. The specimen was cut open and grossly, no major finding was observed in the endometrium or cervix except for a small darkened grey brown area and a nabothian cust in the cervix. The ovaries on cut open position showed corpora alicanti. The fallopian tubes showed unremarkable features. The attending surgeon provided no clinical details except for bleeding p/v and no suspicion of malignancy was present. No other significant clinical history was relevant in this case. Sections were submitted from the endometrium, cervix, tubes and ovaries. Multiple sections of the material received show a poorly differentiated high grade malignant neoplasm of the endometrium composed of sheets of small round to oval cells with scant cytoplasm and dysplastic nuclei, separated by fibrous septae infiltrating the myometrium. All other surrounding tissues showed the following. Cervix showed non-specific inflammatory changes. Both tubes appeared microscopically normal and both ovaries showed corpus luteum. Immunohistochemistry was performed on the tumor and showed strong ER, PR positivity and EMA, Pan Ck were focally positive. IHC was performed using Dako antibodies.

Discussion:

This is an architecturally solid tumor with at least focal gland formation. The solid component is usually arranged in large nests, and it may also form trabeculae. Solid and gland-forming elements transition seamlessly within the tumor. The tumor cells in gland-forming areas are frequently columnar. There may be squamous and mucinous metaplasia, as well as secretory changes. The nuclear grade in both the solid and glandular components is usually 2 on a 3-point scale. Background hyperplasia is present in a minority of cases. International Federation of Gynecology and Obstetrics (FIGO) grade 3 EECs metastasize primarily to pelvic and para-aortic lymph nodes, pelvic tissues, and, occasionally, to abdominal organs and the lung. Extrauterine extension is generally correlated with deep myometrial invasion and lymphovascular invasion.

Grade 3 EEC has an overlap with type II EC in both clinical behavior and prognosis. They share the some etiologic factors. Some studies suggest that grade 3 ECC more closely resembles type II NEEC than grades 1 to 2 ECC, arguing for the inclusion of grade 3 ECC into type II cancers. Grade 3 EEC also shares similar molecular alterations with both low-grade EEC and serous carcinoma. In addition, some ECs exhibit overlapping features of type I and type II cancer. This includes endometrial adenocarcinoma "with ambiguous features" and undifferentiated adenocarcinoma. They have an aggressive behavior. (10)

Conclusion:

Further studies are warranted to correlate the clinical situation with the findings enlisted above to determine prognostic factors and proceed to treat accordingly. It is imperative to also ensure that although no clinical findings, gross findings or clinical suspicions prevail, rare tumors can still exist

Cytological diagnosis of malignant melanoma by fine-needle aspiration biopsy

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Abstract

Background:
Fine Needle Aspiration (FNA) plays a pivotal role in aiding pathologist to diagnose melanomas at earlier, more curable stages and a minimally invasive modality which can be utilized to determine metastatic lesions. The previously reported cytological features of melanoma were heterogeneous, such as the presence of elongated cytoplasm, plasmacytoid cells, or prominent nucleoli. However, not all melanomas contain these characteristic features. This study aims to determine the cytological features of melanoma to develop reliable criteria for an accurate FNA-based diagnosis

Materials and Methods:
A total of 26 FNA samples which stained positive for HMB45 were included in this study, stained by Papanicolaou stain. The samples were analyzed based on the presence of melanin pigment, elongated cytoplasm, plasmacytoid cells, discohesive cells and prominent nucleoli.

Results:
The result showed that the melanin pigment deposition, plasmacytoid cells, elongated cytoplasm, prominent nucleoli and discohesive cells were detected in 57.6%, 53.8%, 61.5%, 46.2% and 100% of the total samples, respectively. The cellular discohesiveness is the most prominent cytological features of melanoma in this study. However, this cellular characteristic will be limited by its lack of specificity in differentiating melanoma from other malignancy. The other cytological features which mention above were relatively evenly distributed among samples.

Conclusion:
There is no dominant cytological characteristic of melanoma which could be used as a definitive diagnostic criterion for FNA sample. However, the presence of plasmacytoid cells and elongated cytoplasm in FNA sample might be considered as a screening criteria for melanoma especially if there is no sign of melanin pigment deposition.

Subcutaneous Panniculitis-Like T-Cell Lymphoma : Pediatric Rare Case

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Abstract

Introduction:
Subcutaneous Panniculitis like T cell Lymphoma (SPTCL) is a cytotoxic T-cell lymphoma that preferentially infiltrates subcutaneous tissue that is rare in childhood. Its account for less than 1% of all non Hodgkin lymphomas.

Case Report:
We report 2 case of SPTCL in infancy with swelling of the face with no regional lymphadenopathy. Clinically diagnosed as lupus panniculitis. Histopathology showed a lobular panniculitis with individual adipocytes surrounded by atypical lymphocytes. Immunohistochemical evaluation of the atypical lymphocytes showed CD3 and CD8 immunoreactivity and CD 20, CD4 and CD56 negativity and high proliferation rate, confirmed as SPTCL.

Discussion:
The disease should be considered in the differential diagnosis of any atypical skin lesion involving subcutaneous fat

Conclusion:
Suitable deep skin biopsy and immunohistochemical staining are essential to differentiate between SPTCL and Lupus panniculitis.

BONE MARROW CHANGES IN RETROVIRAL INFECTION

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Abstract

Background:
Acquired Immune Deficiency Syndrome (AIDS) was first recognized as a new disease in 1981when increasing numbers of young homosexual men were afflicted with unusual opportunistic infections and rare malignancies. Hematological abnormalities "involving all the three lineages of blood cells" are commonly seen among HIV infected individuals. Bone marrow aspiration and biopsy of these patients show hypercellularity, dysplasia involving one or more hematopoietic cell lines, increased plasma cells and histiocytes, lymphoid aggregates, granulomas and lymphoma infiltration

Materials and Methods:
Retrospective study was done on 100 HIV positive patients at KMC, Manipal(Karnataka)India over a period of 2 years.Only those HIV positive patients whose bone marrow study was done were included in the study.Changes in both bone marrow aspirate and bone marrow biopsy and its correlation with CD4 counts was studied.

Results:
Bone marrow biopsy showed majority of the patients to have hypercellular marrow. Other findings in bone marrow biopsy included benign lymphoid follicle (18%), atypical lymphoid aggregates (11%), infiltration by abnormal cells (9%), granulomas (28%) and hemophagocytosis (39%). Bone marrow aspirate showed normal M: E ratio in majority of patients. All the patients showed dyspoiesis involving either of the 3 lineages. Majority of HIV infected patients (79%), irrespective of ART, showed CD4 counts <200/µL.

Conclusion:
The often striking marrow hyperplasia with concomitant peripheral cytopenias identifies the bone marrow as a frequently targeted organ system in Acquired immunodeficiency syndrome. The disparity between peripheral cytopenias and marrow hyperplasia suggests mechanisms of either ineffective hematopoiesis, abnormal release or increased peripheral destruction of blood cells.

PLEURAL MULTICYSTIC MESOTHELIAL PROLIFERATION IN A PATIENT WITH THORACIC ENDOMETRIOSIS. A CASE REPORT.

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Abstract

Introduction:
Pleural multicystic mesothelial proliferation (PMMP) is a rare condition of serosal, with unclear pathogenesis and controversy towards its reactive and neoplastic basis. It usually occur in women in their reproductive age.

Case Report:
A 41 years old women, who had history of pneumothorax with bullectomy 8 years ago, currently presented with cyclical chest pain and hemorrhagic pleural effusion. Pleuroscopy found dark red nodules and cyst on parietal pleura and diaphragm. First biopsy from parietal pleural showed PMMP. The second biopsy was taken from diaphragm after 6 months.
Pathological finding: The first specimen displayed multiple thin walled cyst, lined by cuboidal mesothelial which stained positive for Calretinin and WT1. The stromal is loose and show focal, strong "aggregated pattern" of nuclear positivity for ER and PR. And thus, endometriosis cannot be totally ruled out even in the absence of glands and hemosiderin laden macrophages. The second biopsy contained a few cluster of columnar epithelium with luminal space, together with aggregates of hemosiderin laden macrophages.
Management: VATS and Talc pleurodesis, endometrial ablation and diaphragm repair are done.

Discussion and Conclusion:
Pathological differential of PMMP includes a number of benign and malignant lesions that presented as cystic mass. Though it usually occurred in abdominal cavity as an asymptomatic mass, patient presented with hemothorax are also recorded in some literature. In this case, the PMMP is likely due to reactive process of endometriosis. Clinicopathologic correlation is thus essential

Clinicopathology profile of Hodgkin Lymphoma in Bandung City, Indonesia

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Abstract

Background:
Chemoresistant Hodgkin lymphoma is well-known as an aggressive disease which has conditions of very limited treatment options and a short period of survival. These conditions leads to poor prognostic to the patient among medical institutions. These study describes the patient profiling of Hodgkin lymphoma at local hospitals in Bandung City, Indonesia.

Materials and Methods:
Retrospective, observational study that was conducted at Hasan Sadikin general hospital, Advent hospital, and Santosa General Hosiptal in Bandung City. This study elaborates patient's medical records which has been taken between 2014 to 2019.

Results:
This study found 159 Hodgkin lymphoma cases between 2014 to 2019. By immunohistochemistry, The Classic Hodgkin lymphoma (CHL) is the most common type with 138 cases (87%). In CHL, the male:female ratio was 2:1 and mean age were 42-years old. The result confirm 47 cases out of 138 cases were reliable to be used for evaluating the responses of the corresponding therapy of ABVD (doxorubicin, bleomycin, vinblastine and darcarbacine) regimen. Twelve cases (25.5%) were chemoresistance. Furthermore, 83% patients which has the chemoresistance have High risk score of International Prognostic Score-7. Four of them were passed away in less than 3 years.

Conclusion:
This study clarifies the Hodgkin Lymphoma's patient are chemosensitive with ABVD regimen and needs further alternative solutions of medical treatment to increase the survival rate.

The role of intraoperative frozen section in the diagnosis of thyroid nodule: A review in single institution

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Abstract

Background:
The use of intraoperative frozen section (FS) in the diagnosis of thyroid nodules is currently not recommended along with increased accuracy of Fine needle aspiration cytology (FNAC) and molecular examination. In Indonesia, molecular examination for the diagnosis of thyroid nodules is currently not available and not all institutions have a high FNAC diagnostic value. This study aims to evaluate the usefulness of intraoperative FS, and compare with FNAC in the diagnosis of clinically suspected malignant thyroid nodule

Materials and Methods:
One hundred and ninety five clinically suspected malignant thyroid nodules were evaluated. FS were performed in all cases at RSUP Dr. Hasan Sadikin Bandung during 2014 - 2018. FS results were compared to histopathological results to determine the diagnostic value of FS and also compared it with the diagnostic value of FNAC in the same case. Only 82 of 195 cases had corresponding preoperative FNAC. Postoperative histopatological diagnosis were benign in 125 cases and malignant in 70 cases

Results:
In our study, the sensitivity, specificity and accuracy of FS in diagnosis of clinically suspected malignant thyroid nodules were consecutively 98.6%, 100% and 99.5%. While for FNACs were 36.4%, 97.9%, 73.2%. In our institution FS is superior compared to FNAB in the diagnosis of thyroid nodules. The reason of low sensitivity of FNAC in our institution was because the FNACs were performed without USG guiding.

Conclusion:
In our institution FS still plays an important role in the diagnosis of clinically suspected malignant thyroid nodules.

Unicentric Castleman's Disease in Central Nervous System : a Case Report

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Abstract

Introduction:

Castleman's disease (CD) is a heterogenous lymphoproliferative disorder, with focal or systemic lymph node involvement. There are two major pathologic variation of CD: (1) the hyaline-vascular variant and (2) the plasma-cell type. Unicentric CD of the hyaline vascular variant is the more common type of CD and usually affects a single lymph node or one group of lymph nodes. Multicentric CD affects more than one group of lymph nodes and can also work on other organs, such as lungs, kidneys, muscle, etc. Unicentric CD which located in central nervous system is very rare, but the number is increasing nowadays. Thus, it should be taken considered into the diagnosis of intracranial tumor.

Case Report :

We report a case of 49-year-old woman with chief complaints of dizziness and lose contacts for 2 years. Brain MRI showed extraaxial contrast enhancing tumor mass with dural tail located in left temporal lobe. The clinical and radiographical features of this patient are very concordant with meningioma. Microscopically showed diffuse lymphoid tissue. There are proliferation of lymphoid folicles, regressive germinal centres, concentric lymphocytes and onion skin appearance in mantle zone. Histopathology and immunohistochemistry results support the diagnosis of CD, hyaline vascular variant.

Spleen inflammatory pseudotumor-like follicular/fibroblastic dendritic cell sarcoma --- a case series and literature review

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Abstract

Background:
Inflammatory pseudotumor-like follicular/fibroblastic dendritic cell sarcoma (IPT-like FDCS) is a rare low grade malignant tumor. Due to its inflammatory background, this distinct entity was often diagnosed as inflammatory pseudotumor (IPT) or inflammatory myofibroblastic tumor (IMT) in the past. Recently, additional morphological patterns besides the typical IPT or IMT pattern were described. Here, we present a case series including two less common patterns.

Materials and Methods:
The clinical information, gross findings and histopathology of the 4 splenic IPT-like FDCS cases collected in our hospital from 2015 to 2019 were retrospectively analyzed. Histochemical stains, immunohistochemical stains and EBER in situ hybridization (ISH) were performed.

Results:
The collected cases included two males and two females and their ages ranged from 49 to 82. Clinically, the tumors were mostly incidental findings. Macroscopically, the splenic tumors were all well-defined masses. Microscopically, all cases were characterized by spindle tumor cells loosely dispersed in the prominent lymphoplasmacytic background. One of the challenging cases demonstrated extensive granulomatous inflammation and the other showed predominantly aggregates of vessels reminiscent of vascular lesions. All the neoplastic spindle tumor cells were positive for EBER ISH and immuno-reactive with smooth muscle actin and at least two follicular dendritic cell markers. Histochemical stains for the case with granulomas showed neither mycobacteria nor fungus.

Conclusion:
Splenic IPT-like FDCS often leads to misdiagnosis due to its rarity and features resembling many inflammatory diseases. The morphology is not limited to IPT pattern as its name implies. Therefore, EBER ISH is a requisite for the identification of IPT-like FDCS.

Hematologic response and bone marrow morphology in CML patients with different treatment regimens

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Abstract

Background:
The CML therapeutic landscape changed dramatically with the development of tyrosine kinase inhibitors (TKIs) that interfered with the interaction between the BCR-ABL1 oncoprotein and adenosine triphosphate (ATP), blocking cellular proliferation of the malignant clone. This "targeted" approach altered the natural history of CML, improving the 10-year survival rate from approximately 20% to 80–90%.

Materials and Methods:
This is a 4 year retrospective study including 84 diagnosed cases of CML with one year follow up. The clinical details were derived from the medical records and the laboratory parameters were derived from the lab information system. SSPS version 16 was used as the statistical device.

Results:
M:F ratio was 2:1.Median age of presentation was 45yrs. Amongst the 84 diagnosed CML cases only 34 (40%) received treatment in our institute.

Stage and treatment at diagnosis	First follow up (1 – 45 months)					
	CompleteHematologic Response	Chronic phase	Accelerated phase	Blast phase	Atypical CML	Inadequate for opinion
CML - CP on Imatinib (n = 22)	10 (45.5%)	4 (18.2%)	1 (4.5%)	4(18.2%)	-	3 (13.6%)
CML – AP on Imatinib (n = 3)	2 (66.7%)	-	-	-	-	1 (33.3%)
CML – CP on Hydroxyurea (n = 9)	-	4 (44.4%)	1 (11.1%)	1 (11.1%)	1(11.1%)	2 (22.2%)

The mean haemoglobin, total leukocyte count and platelet count were 10.4, 165.2 and 327.1 respectively at presentation while the mean haemoglobin, total leukocyte count and platelet count were 10.6, 56.7 and 201.5 respectively at first follow up.
The morphological changes observed in bone marrow aspirate in cases treated with Imatinib included normalization of cellularity, erythroid hyperplasia, reduction of megakaryocyte number, normalization of megakaryocyte morphology, absence of basophils and increase in marrow lymphocytes. On the other hand, the morphological changes noticed in bone marrow in cases treated with Hydroxyurea include decrease in bone marrow cellularity, regeneration of erythroid, reduction of megakaryocyte number and increase in fibrosis.

Conclusion:
Imatinib showed better response with normalization of bone marrow morphology as compared to cases on Hydroxyurea monotherapy but due to financial constraints Hydroxyurea still remains the treatment of choice for many patients in our institution

CLINICOPATHOLOGY PROFILE OF GIANT CELL TUMOR OF BONE IN BALI, 5 YEARS EXPERIENCE

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Abstract

Background:
Giant cell tumor (GCT) of bone is one of the rare primary bone tumors. Incidence of the GCT of bone is approximately 5% of all resected primary bone tumors. There are no data yet on the clinic-pathology profile of the GCT of Bone in Bali.

Materials and Methods:
This research is a descriptive study that collects GCT of bone data at Sanglah Hospital Denpasar-Bali based on pathology reports from the last five years

Results:
From 2013 to 2018, we found 44 cases GCT of bone, more frequently found in women than men (30 cases (68.2%) and 14 (31.8%) respectively), the most cases occurred in the second to fourth decade with a peak incidence in the fourth decade (14 cases (31.8%)), and the location of the most common tumors in the distal femur and distal radius were 13 cases (29.5%) respectively. This result is consistent with the literature where GCT is slightly more frequently found in women, occurring in the third and fourth decades and most often it affects the distal femur, distal radius, proximal tibia, and sacrum

Conclusion:
GCT of bone in Bali is more commonly found in women, the most common age in the 4th decade and most commonly affects the distal femur and distal radius. This data can be used to guide in establishing a diagnosis.

PRIMARY MEDIASTINAL YOLK SAC TUMOR IN CHILDREN
A Case report

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Abstract

Introduction:
Primary mediastinal yolk sac tumor is a rare malignant neoplasm. It is a sub type of germ cell tumor that can present extra gonadal mainly in structures of median line such as in mediastinum. It correspond about 10-20% of all mediastinal cancer, and more frequently occurred in children. Patients may present with dyspnea, chest pain, cough, fever, night sweats, and generalized weakness

Case Report:
We report a case of primary mediastinal yolk sac tumor of a 10-year-old boy. He was suffered from chest pain, cough and dyspnea. No specific history of malignancy was found in his family. The chest X-Ray and Thorax MSCT revealed a bulky anterior mediastinal mass that compressed right pulmonary lobe, main bronchus, trachea, heart and superior venae cava. The histopathology examination revealed the findings of yolk sac tumor, e.g. proliferation of primitive cells in reticular and solid pattern with Schiller Duval's bodies and hyaline globules among the necrosis area. The tumor was grow rapidly and highly aggressive. Patient was died after biopsied and had not been examined for the AFP and β –HCG.

Conclusion:
Based on clinical manifestation, imaging and histopathology findings, this case was concluded as a primary mediastinal yolk sac tumor

The correlation of *BRAF* V600 Mutational Status with histopathological characteristics in melanoma

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Abstract

Background:
The objective of the current study was to compare the BRAF mutational status with histopathological characteristics of melanoma.

Materials and Methods:
Altogether, 35 patients undergoing melanoma surgical treatment at Riga East University Hospital in 2012-2014 were retrospectively enrolled to the study. The study was approved by the Central ethical committee. The histopathological characteristics were assessed according to the current WHO and AJCC 8. edition guidelines. The melanoma BRAF mutation status was assessed by RT-PCR.

Results:
35 patients were enrolled in the study (10 were males and 25 were females). The mean age was 61.4 ± 10.2 The BRAF mutation was observed in 15 patients (42.0%). BRAF exon 15 c.1799T>A V600E mutation was observed in 14 patients (40.0%) and BRAF exon 15 c1801A>G V601E mutation was observed in one patient (2.0%).

Obtained results showed that BRAF mutation was observed predominantly in nodular melanoma (73.0%) and in superficial spreading melanoma (24.0%). 83% of BRAF mutation cases was found in the trunk. The significant correlation between BRAF mutational status and Breslow thickness was observed (Rho=+0.49; p=0.003). In addition, BRAF mutational status correlated with T stage (p=0.04). However, the correlation between BRAF mutational status and Clark level, ulceration, lymphovascular invasion, mitotic count, peritumoral lymphocytic infiltration was not found.

Conclusion:
Melanoma BRAF mutational status correlated with the tumour nodular type, high T stage and Breslow thickness. The BRAF mutation assessment for the potential personalized treatment should be based not only on clinical, but also on histopathological characteristics.

Prevalence of submandibular gland metastasis in oral squamous cell carcinoma

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Abstract

Background:
Present study aims to identify the prevalence of submandibular gland involvement with metastasis in oral squamous cell carcinoma (SCC) cases treated with wide excision and radical neck dissection in Pakistani population.

Materials and Methods:
All oral SCC wide excision with neck dissection cases reported by Histopathology section of Dow Diagnostic Research and Reference Laboratory (DDRRL), Dow University of Health Sciences (DUHS), Pakistan between 2017 – to date (May 2019) were retrieved and reviewed. Cancer case summary was recorded in specifically designed protocol. Data was analyzed in SPSS version 21.0. Chi-square test was used to test association between categorical variables.

Results:
Out of 121 cases, majority (73.5%) were males with male to female ratio 2.8: 1. A wide age range (20 – 84 years) with mean age 46 (± 13) years was noted. Most patients (35.5%) were > 50 years, but a large number of cases (n=17) was noted in younger (21 – 30 years) age group. Buccal mucosa (52.9%), followed by tongue (17.45%) were most frequently involved sites. Tumor showed remarkable predilection for left (55.4%) side involvement. A significant association was recorded between tumor size and tumor thickness ($P<0.001$), and also between tumor size and histological grade ($P=0.029$). Only one (out of 121) submandibular gland was involved by metastatic carcinoma.

Conclusion:
Present study highlights that submandibular gland involvement in oral SCC cases is negligible. Keeping in view our findings and those reported previously, we question the justification for excision of submandibular gland and urge for consideration of a gland-sparing neck dissection.

Polymorphism in proinflammatory and immune related genes in DLBCL susceptibility and overall survival in Arab population: A Case- Control Study.

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Abstract

Background:
(DLBCL) is the most common NHL. In this study we aim to explore the relationship between 5 selected proinflammatory and immune-mediated genes (TNF rs1800629G>A, rs161525G>A, rs1799964T>C, LTA rs1800683G>A, rs909253A>G, TNFAIP8 rs1042541C>T, LEPR rs1327118G>C, LEP rs2167270G>A) and the risk and overall survival in DLBCL patients in Jordanian Arab population

Materials and Methods:
A 125 patients whom diagnosed with DLBCL at KAUH from the period of 2013 to 2018 and 235 healthy cancer-free control subjects were included in the study. Genomic DNA was extracted from FFPE tissues. Genotyping of the genetic polymorphisms was conducted by using sequencing protocol.

Results:
Our study showed that no significant differences in the distribution of all studied polymorphisms of DLBCL between patients and controls except for TNF rs1800629G>A (p value 0.01) where the G allele harbors higher risk for DLBCL (GG and GA genotypes when compared with AA genotype) (p value 0.044). The TNF-a rs1799964 was the only SNP to show significant survival results. Subjects with the dominant model (TT genotype in comparison with the combined TT/TC genotype) had better overall survival (p=0.028).

Conclusion:
TNF rs1800629G>A polymorphism is associated with increased risk of DLBCL among Jordanian Arab population and the LEP rs2167270 G>A polymorphism is associated with decreased risk of DLBCL in the recessive mode models. The TNFa rs1799964 polymorphism shows better overall survival with the dominant model (TT genotype in comparison with the combined TT/TC genotype).

Concordance of cytomorphological features of Cervical Lymphadenitis suspected for Mycobacterium Tuberculosis on Fine Needle Aspiration biopsy with GeneXpert for Mycobacterium Tuberculosis on aspirated material

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Abstract

Background:
The objective of the study was to correlate different cytomorphological presentations of cervical lymphadenitis suspected for Mycobacterium Tuberculosis (MTB) on Fine Needle Aspiration Cytology (FNAC) with MTB detection by geneXpert on aspirated material.

Materials and Methods:
FNAs of a total 100 patients with cervical lymphadenitis suspected for MTB were included and the cytomorphologylogy was compared with geneXpert.Data was analyzed using SPSS version 23

Results:
A total of 100 cases were included. Male to female ratio was 1.12:1. Mean age was 31±15 years and maximum incidence of disease was seen in young patients. A total of 78 cases were positive for MTB while 22 cases were negative when compared with molecular analysis on aspirated material. Positivity for MTB by geneXpert was seen in 93% of cases with both caseous necrosis and granulomas,80% of cases with caseous necrosis only,80% of cases having granulomas along with neutrophilic abscess,70% of cases showing granulomas and 14% of cases with neutrophilic abscess.(p value <0.05). Sensitivity of FNAC was 97% and specificity was 54. PPV was 88% and NPV was 85%.

Conclusion:
MTB was detected by GeneXpert in a significant percentage of the FNAC samples included in our study. FNAC is a rapid, safe, easily available, minimally invasive, outpatient procedure and GeneXpert analysis can be performed on the aspirated material. This can aid the clinicians in timely initiation of ATT in our country where tuberculosis is rampant and advanced diagnostic facilities are not easily accessible.

Immunohistochemical Evalution of Leukemia Inhibitory Factor (LIF) as a Marker for Endometrial Receptivity in Women with Unexplained Infertility

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Abstract

Background:
The process of embryo implantation is considered the most critical step for achieving pregnancy. This process requires coordination of complex interactions between blastocyst and endometrium. Two factors are presently considered to be of prime importance for reproductive success: endometrial receptivity and oocyte quality , LIF is a cytokine that plays a role in embryonic implantation .The aim of this work is to assess leukemia inhibitory factor (LIF)expression for endometrial receptivity in women with unexplained infertility.

Materials and Methods:
This studyis a retrospective study conducted at Ain Shams University Maternity Hospital , on 140 patients divided into two equal groups: Group I (study group): women with unexplained infertility (inability to conceive inspite of regular marital life for at least 12 months). Group II (control group): matched women with infertility due to tubal factor, from outpatient Infertility Clinic. Ultrasound examination for endometrial thickness was performed. Histopathological examination: D&C biopsy was done for dating & exclusion of any pathological lesion in the endometrium. Immunohistochemical study for LIF was done and scored.

Results:
LIF staining intensity score was significantly lower in the unexplained infertility group during the secretory phase, compared to the tubal factor group. A cutoff value for LIF staining score of ≤1 predicted unexplained infertility with a sensitivity of 73.33% and specificity of 70.67%. A cutoff of ≤10 mm for endometrial thickness had the highest sensitivity of 100%, but lacked specificity (only 16%).

Conclusion:
LIF may be a predictor for unreceptive endometrium in cases of unexplained infertility especially if coupled with different ultrasonic parameters.

EBV analysis by EBER in situ hybridization in DIFFUSE LARGE B CELL LYMPHOMAS IN QUEEN ELIZABETH HOSPITAL BIRMINGHAM UNITED KINGDOM

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Abstract

Background:
EBV positive status in Diffuse large B cell lymphoma (DLBCL) has been shown to be significantly associated with more advanced stage, higher International Prognostic Index, presence of B symptoms, poorer outcome to clinical treatment and poorer overall survival and progression-free survival. High incidence of EBV+ DLBCL has been reported in the Asian countries. Little is known about the incidence and the clinicopathological characteristics of EBV+ DLBCL in the UK.

Materials and Methods:
Cases of 'High grade lymphomas' and 'DLBCL' over a 15 year period from 1996 to 2010 were retrieved. 300 cases were subjected to EBER in situ hybridization to detect EBV status. Cases were recorded as 'EBV-positive' if > 10% of tumour cells were positive. Immunohistochemistry for LMP1 and EBNA2 were performed to classify cases into one of three EBV latency types. All cases were also stained for CD10, BCL6 and MUM1 for subtyping.

Results:
14/300 (4.7%) of DLBCL patients were EBV positive with the mean age of 57 years. 12/14 (85.7%) of EBV+ DLBCL patients had B symptoms compared to the EBV- patients (p=0.009). All of the EBV+ patients were of non-GCB subtype (p=0.001). 8/14 (57.1%) patients showed EBV latency III pattern (EBER+,LMP1+, EBNA2+), 2 (14.3%) latency II (EBER+,LMP1+, EBNA2-) and 4 (28.6%) latency 1 (EBER+,LMP1-, EBNA2-).). EBV+patients had significantly shorter event free survival than their EBV- counterparts (p=0.033).

Conclusion:
EBV+ DLBCL patients have poorer prognosis however the incidence of EBV+DLBCL is low (1-4%) in the UK as compared to Asian countries (7-12%) with EBV latency 3 being the commonest. This study supports the notion that there is geographic variation of EBV positivity and ethnic predisposition to the development of EBV positive DLBCL.

EXPRESSION OF ANGPTL4 AND IGF-1 IN YOUNG BREAST CANCER IN RELATION TO MOLECULAR SUBTYPES

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Abstract

Background:
Invasive breast carcinoma (IBC) in young patient has been reported to be more aggressive. Angiopoietin-like protein 4 (ANGPTL4), a member of the angiopoietin family of proteins plays a critical role in cancer growth and progression that contributes to metastasis. Meanwhile, insulin growth factor-1 (IGF-1) is a potent mitogen that can stimulate breast cancer development and demonstrate increased metastatic potential. This study aimed to investigate the possible association of young IBC with the expression of IGF-1 and ANGPTL4.

Materials and Methods:
A cross sectional study was conducted using 75 archived formalin-fixed paraffin embedded tissue blocks of young breast cancer with age <45 years old. The molecular breast carcinoma subtype was classified into Luminal A, Luminal B, HER2, and triple negative based on surrogate marker of ER, PR and HER2. All samples were stained for ANGPTL4 and IGF-1 by immunohistochemistry method.

Results:
The age of patients ranged from 23-44 years old with mean age 37 (SD 5.48). Luminal A 28 (37.7%), were the highest molecular subtype in young IBC patient followed by triple negative 20(26.7%), Luminal B 15 (20%) and HER-2 12 (16%). Among 75 of young IBC patient, 51 (68%) of them are immunopositive for ANGPTL4. Meanwhile 67 (89.3%) showed positive expression towards IGF-1. Among the molecular subtype, 19 (37.3%) of Luminal A subtype were positive for ANGPTL4 followed by triple negative 14 (27.5%), Luminal B 10 (19.6%) and HER2 subtype 8 (15.7%). The expression of IGF-1 were also high in Luminal A 27 (40.3%) but lowest in HER2 10(14.9%). There was significant association (p=0.028) between IGF-1 and molecular subtype but not for ANGPTL4 (p=0.823)

Conclusion:
Luminal A was the highest subtype in young IBC and demonstrated highest expression toward ANGPT4 and IGF-1. There was a significant association of young IBC molecular subtype with IGF-1 expression that may add another therapeutic potential in young breast cancer.

Spectrum of histological features of Denosumab treated Giant Cell Tumor of Bone; a potential pitfall and diagnostic challenge for pathologists

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Abstract

Background:
Denosumab is RANKL inhibitor which is being used in the treatment of locally advanced, recurrent and metastatic cases of Giant Cell Tumor of Bone (GCTB). After Denosumab treatment, GCTB exhibit diverse morphological features which can pose diagnostic challenge.

Materials and Methods:
We retrieved and reviewed H&E stained microscopy glass slides of 30 GCTB cases with history of Denosumab treatment. These cases were treated at different institutes and diagnosed at our institute between January 2017 and July 2019. Morphologic features such as presence of residual giant cells, appearances of mononuclear and bony component, necrosis and stromal changes were assessed.

Results:
Microscopically, peripheral shell of reactive bone was observed in all cases. In 16 (53.3%) cases, there was complete elimination of MOGC. Necrosis was observed in 10 (33.3%) cases. Mononuclear cells were predominantly spindle shaped and arranged in fascicular and storiform pattern. Bony component manifested as trabeculae of woven bone with osteoblastic rimming and immature trabeculae of unmineralized osteoid with haphazardly present osteoblasts. Prominent stromal changes included cystic spaces, foamy macrophages, inflammatory infiltrate, Hemangiopericytoma-like (HPC-like) vessels, hyalinization, edematous areas and hemosiderin pigment deposition. The tumors showed areas which resembled other tumor such as Non-ossifying fibroma, Fibrous dysplasia, Osteoblastoma, Sclerosing epithelioid fibrosarcoma and osteosarcoma.

Conclusion:
Denosumab treatment induces a variety of changes in GCTB. Clinical history and knowledge of these features are necessary for excluding differential diagnoses and avoiding misdiagnoses.