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Diagnostic Surgical Pathology: the importance of Second Opinion in a Developing Country

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Abstract

Objective:
To review the cases sent to the section of histopathology, Aga Khan Universty (AKU) for second opinion and see whether there are significant differences in the original outside diagnosis and the subsequent diagnosis submitted by us.

Methods:
A retrospective study of all consecutive cases for second opinion in the form of paraffin blocks from 1st Novemver 2001 to 31st July 2002. The primary submitted diagnosis in each case was compared with the subsequent AKU diagnosis.

Results:
The study included a total of 381 cases. However, in 45 cases (11.81%), initial histopathological diagnosis was not provided. Out of the remaining 336 cases, there were differences between the original diagnosis and the subsequent AKU diagnosis in 120 cases (35.71%). Out of these 120 cases, immunohistochemistry was performed in 65 cases (54.16%) only.

Conclusion:
In a developing country like Pakistan, where few laboratories are equipped to function as modern histopathology units, second opinion on difficult cases is very important. Worldwide, the concept of second opinion in surgical pathology is well established (JPMA 54:306;2004).

Introduction

While the basic aim of the practice of surgical pathology is to provide accurate diagnosis, it is equally essential to prevent an erroneous diagnosis, which can result in serious errors in the treatment and prognosis of the patient. In Pakistan, surgical pathology is still evolving as a science and it is only now that clinicians are becoming aware of the importance of an accurate surgical pathology diagnosis for the treatment of their patients. In a developing country like Pakistan where most centers lack the facilities and expertise that are needed to function as modern surgical pathology units, the Section of Histopathology at the Aga Khan University Hospital is serving as the major referral center for diagnostic surgical pathology. While the overwhelming majority of surgical pathology cases which we report are those which are sent primarily to us, a new trend is being observed which is represented by cases that are sent to us for second opinion by clinicians and in some cases by the primary pathologists themselves. The purpose of this study is to review the cases sent to Section of Histopathology, Aga Khan University for second opinion and see whether there are significant differences in the original outside diagnosis and the subsequent diagnosis submitted by us.

Materials and Methods

All consecutive cases for second opinion in the form of paraffin blocks, which were received over a nine-month period i.e., from 1st November 2001 to 31st July 2002, were included in the study. The primary submitted diagnosis in each case was compared with the diagnosis submitted by us. The use of

immunohistochemistry in 54.16% cases was noted. It was assumed that the blocks we received for second opinion were the same ones on which the original diagnosis was submitted.

Results

Over the 9 month study period, a total of 381 cases were received for second opinion. In 336 cases (88.18%), the initial surgical pathology diagnosis was provided. In 45 cases (11.81%) initial surgical pathology diagnosis was not provided. In 204 out of 336 cases (60.71%) initial diagnosis

Table1. Commonest organ systems on which second opintion was sougt.

1	Lymph Nodes	72	21.42
2	Soft Tissues	65	19.34
3	GIT*	52	15.47
4	Bones and Joints	30	8.92
5	Breast	30	8.92
6	Female genital tract**	27	8.03
7	Head and Neck***	27	8.03

* Includes liver, gall bladder andbiliary tract, pancreas, and salivary glands. ** Includes vulva, vagina, cervix, endometrium, ovaries, and placenta. *** Includes jaws and oral cavity, nose, paranasal sinuses, nasopharynx, larynx, eyes and ocular adnexae.

Table2. Lymph nodes cases.

S. No.	Submitted Diagnosis	Second opinion Diagnosis
1	Chornic granulomatous inflammation with caseation necrosis. T.B	Peripheral T cell NHL (LCA, T positive)
2	Non Hodgin's Lymphoma	Reactive folicular Huperplasia.
3	Chornic granulmatous inflammation T.B.	Reactive lymphadenitis not T.B. nonspecific
4	Hodgkin's lymphoma mixed cellularity	Anaplastic large cell (kil) lymphoma
5	Non Hodgkin's lymphoma	Chronic Granulomatous inflammation T.B.
6	Non Hodgkin's lymphoma	Reactive lumphadenitis
7	D/DT cell NHL/Hodgkin's disease	Diffuse large cell NHL of B phenotype (LCA, B positive)
8	Hodgkin's lymphoma mixed cellularity	Diffuse large cell NHL of B phenotype (LCA, B positive)
9	Metastatic Carcinoma	Diffuse large cell NHL of B phenotype (LCA, B positive)
10	Hodgkin's lymphoma	Atypical lymphoid hyperplasia
11	Non Hodgkin's lymphoma	Non-specific reactive lymphadenitis
12	Follicular lymphoma	Reactive folicular hyperplasia
13	Reactive lymphadenitis	Diffuse large cell NHL of B phenotype (LCA, B positive)
14	D/D reactive lymphadenties Hodgkin's lymphoma	Diffuse large cell NHL of B phenotype (LCA, B positive)
15	Hodgkin's lymphoma	Non-specific reactive lymphadenitis

16	Non Hodgkin's lymphoma	Reactive follicular hyperplasia
17	Follicular lymphoma	Reactive follicular hyperplasia
18	Non Hodgkin's lymphoma	Reactive follicular hyperplasia
19	Chronic granulomatous inflammation T.B	Atypical lymphoid hyperplasia
20	Malignant undifferentiated neoplasm	Chronic granulomatous inflammation T.B
21	Non Hodgkin's lymhoma	Metastatic carcinoma (CK MNF, CAM 5.2 positive LCA negative)
22	Reactive lymhadenitis	Diffuse large cell NHL of B phenotype (LCA, B positive)

and AKU diagnosis were the same. In 120 cases (35.71%), AKU diagnosis was different from the initial diagnosis. In 12 cases, we could not give a diagnosis due to the presence of marked fixation/processing artifact. Immunohistochemistry was performed in 125 out of 336 cases (37.20%). Out of the 120 cases in which the initial diagnosis and AKU diagnosis were different, Immunohistochemistry was performed in 65 cases (54.16%). Table 1 lists the commonest organ systems on which second opinion was sought, while tables 2 to 10 list the cases with differences in diagnosis belonging to various organ systems.

Discussion

The Section of Histopathology at the Aga Khan University Hospital, Karachi is the largest center of histopathology in Pakistan. In 2001, over 28,000 cases of surgical pathology and over 14,000 cases of cytopathology were reported. The section has the services of six full time academic pathologists with diverse background along with ten to twelve fellows and residents. The section acts as the major referral center for histopathology in the country and specimens for primary diagnosis as well as second opinion are received from all over the country through laboratory collection points of the Aga Khan University Hospital located in all important cities and towns of the country. The section is equipped with the latest state of the art Immunohistochemistry and Molecular labs, and is playing a leading role in the development and advancement of diagnostic histopathology in the country. Pakistan being a developing country, there are very few laboratories, which can function as modern surgical pathology units. Facilities like Immunohistochemistry are restricted to a handful of centers in the entire country. Moreover, clinicians, especially in small towns and cities are only now becoming aware of the importance of an accurate surgical pathology diagnosis. With this increased awareness and recognition of surgical pathology as a major science, sensitivities of clinicians towards surgical pathology diagnosis are also increasing and more and more cases are being received by us in which a second opinion is sought.

Table3. Soft tissue eases.

S. No.	Submitted dianosis	Second opinion diagnosis
1	Fumngal linfection	Neurofiborma (S 100 protein positive)
2	Soft Tissue sarcoma	Diffiuse large cell NHL of B cell phenotype (LCA pan B positive)
3	Mailgnant peripheral nerve sheath tumor	Metastatic carcinorma (CK MNF and CAM 5.2 positive)
4	lipsarcoma	Malignant peripheral nerve sheath tumor, (Vimentin S 100 protein positive)
5	Lipoma	Ewing's sarcoma/ PNET (Vimentin, MIC 2 positive)
6	Hemangiopericytoma	Fibrosarcoma

7	Fibrosarcoma	Leiomyosarcoma (Vimentin, ASMA, Desmin positive)
8	Fibrosarcoma	Leiomyoma (Vimentin, ASMA positive)
9	Fibrosarcoma	Synovial sarcoma (CK MNF, CAM 5.2 EMA, Vimentin positive)
10	Malignant peripheral Nerve sheath tumor	Malignant Melanoma, (Vimentin, S100 protein, HMB 45 positive)
11	Small roung blue cell tumor DVD PNET/ Neuroblastoma	NHL, (LCA pan B positive)
12	Myxoid liposarcoma	Malignant peripheral nerve sheath tumor (Vimentin, S100 protein positive)
13	Liposarcoma	Malignant peripheral nerve sheath tumor (Vimentin, S100 protein positive)
14	Non Hodgkin's Lymphoma	Yolk Sac Tumor (CK MNF CAM 5.2, AFP positive)
15	Fibrosarcoma	Malignant peripheral nerve sheath tumor high grade (Vimentin, S100 protein positive)
16	Fibrosarcoma	Synovial sarcoma (CK MNF CAM 5.2, EMA, Vimentin positive)
17	Alveolar soft part sarcoma	Malignant Melanoma (Vimentin, ASMA positive)
18	Pleomorphic liposarcoma	Leiomyosarcoma, (Vimentin, ASMA positive)
20	Angiosarcoma	Diffuse large cell NHL of B phenotype (LCA, B positive)
21	Fibrosarcoma	Nodular fascitis
22	Malignant Melanoma	Nodular Tenosynow itis
23	Rhabdomysarcoma	Ewing' sarcoma/PNET (MIC 2 positive desmin negative)
24	Fibroma	Fibrosarcoma Grade II
25	Tuberculosis	Pilomatrixoma
26	Myxoid liposarcoma	Benign Adipose tissue
27	Metastatic amelanotic melanoma	Metastatic carcinoma CK MNF, AE 1 / AE3 positive
28	Angiosarcoma	Benign Fibrous histiocytoma (Vimentin, CD 68 positive)
29	Soft wissue sarcoma	Malignant melanoma (Vimentin, S100 protein, HMB 45 positive)

The concept of second opinion in surgical pathology is well established. The American Society of Clinical Pathologists (ASCP) has recognized second opinion as an important component of total quality assurance programs in diagnostic surgical pathology and cytopathology.1 The Association of Directors of Anatomic and Surgical Pathology has developed recommendations for consultations in surgical pathology.2 Numerous studies in literature have noted the usefulness and efficacy of second opinions in diagnostic surgical pathology.3-7 An analysis of our results shows that in 35.71% cases, the second opinion diagnosis submitted by us was different from the original submitted diagnosis. This is a significantly high figure. The results also show that the differences in diagnosis in most cases were major, having significant implications for the treatment and prognosis of the patient. It must always be kept in mind, however, that a difference between primary and secondary diagnosis does not prove that the latter is correct and studies in literature have demonstrated that diagnostic disagreements occur

between experts. 8 There is a great variation in the results from different studies looking at second opinions in diagnostic surgical pathology. Krontz et al.5 reported a 1.4% discrepancy rate for all organ systems while Abt et al.3 reported a 1.3% overall discrepancy rate. These are very low discrepancy rates. However, Malhotra et al .7 reported a discrepancy rate

Table 4. Gastrointestinal tract cases.

S. No.	Submitted Diagnosis	Second opinion Diagnosis
1	Esophagus Squamous cell carcinoma	Esophagus: mild non specific inflammation
2	Chronic hepatitis with cholestasis	Liver: Hemosiderosis
3	Pancreas: extra-rena wilm's tumor	Pancreas papillary-solid epithelial tumor (Vimentin, NSE, Chromogranin positive)
4	Liver: liver tumor not further specified	Liver: vascular malformation
5	Liver Teratoma	Liver: hemangiondothelioma, (Vimentin, CD31 positive)
6	Rectum: Ganglion cells not seen	Rectum ganglion cells seen
7	Small intestine: Non Hodkin's lymhoma (Immunoblastic)	Small intestinal inflammatory infectious process (Typhoid, Yersinia etc)
8	Gall bladder: Adencorcinoma	Gall bladder: Xanthogranulomatous cholecystitis.
9	Liver: reactive fibrosis	Liver: Metasatic adencarcinoma lung possible site of primary (CK AE1/AE, CAM 5.2 and CK positive)
10	Gall bladder: Adencorcinoma	Gall bladder: Xanthogranulamatous cholecystits.
11	Colon: ulcerative colitis with dysplasia, grade II (moderate)	Non specific inflammationno dysplasia
12	Stomach: undifferentiated malignant tumor	Stomach: Benign gastric tissue
13	Colon: Adenocarcinoma	Colon: non specific inflammation and granulation tissue formation
14	Partid: Adenoid cystic carcinoma	Parotid mucoepidermoid carcinoma, low grade.
15	Small Intestine: diffuse large cell non Hodgkin's lymphoma	Small intestine: Burkitt's lymphoma, (LCA, B positive)
16	Small intestine ki1 or Hodgkin's lymphoma	Small intestine T cell Non Hodgkin's lymphoma (LCA, Pan T positive, Ki 1 negative)
17	Jejunum: Fibroma	Jejunum: Neurofibroma, (Vimentin, S100 positive)

Table 5. Skin cases.

S. No.	Submitted Diagnosis	Second Opinion Diagnosis
1	Malignant Melanoma	Compound Melanocytic nevus
2	Squamous cell carcinoma	Basal Cell Carcinoma
3	Squamous cell carcinoma	Bowen's Disease
4	Malignant Melanoma	Angiosarcoma (CD 31, Ulex Europeus, vimentin positiv, HMB 45 ngative)
5	Kaposi, Sarcoma	Lobular capillary Hemangioma
6	Rperipheral T cell lymphoma	Anaplastic large cell (kil 1) lymphoma (Ki 1 positive)
7	Non Hodgkin's Lymphoma	T cell pseudolyphoma

of 11.6% among 275 cases. Our overall discrepancy rate was very high 35.71% among 336 cases (results). Various western studies have however, reported high discrepancy rates for specific organ systems. Harris et al. 9 reported a 24% discrepancy rate for bone and soft tissue sarcomas. Our study showed 36.66% discrepancy rate for bone and joint cases (results). However, these include both neoplastic and non neoplastic cases. Jacques et al. 10,11 reported a 23.6% discrepancy rate for endometrial biopsies. Our study showed an 18.51%discrepancy rate for all female genital tract cases (results) and as shown in table 8, 4 out of 5 cases were ovarian in origin Epstein et al.12 reported a 9.1% discrepancy rate for prostatic biopsies. Our study showed a 38.46% discrepancy rate for all male genital tract cases (results) and as shown in Table 9, 4 out of 5 cases were prostatic in origin. Kim et al.13 reported a 16.7% and 27.3% discrepancy rate for Hodgkin's and non-Hodgkin's lymphomas respectively. Our study showed a 30.55% discrepancy rate for lymph node cases, both neoplastic and non neoplastic (results). Bruner et al.14 reported an 8.8% discrepancy rate for

Table 7. Head and neck cases.

S. No.	Submitted diagnosis	Second opinion diagnosis
1	Nose Liposarcoma	Malignant Melanoma (Vimentin, S100Protein HMB 45positive)
2	Nasopharynx: Nasopharyngeal carcinoma	Large cell NHL of B phenotype (LCA, B positive)
3	Hard Palate sarcoma	Diffuse large cell NHL of B phenotype (LCA, B positive)
4	Cheek: Non Hodgkin's lymphoma	Neuroblastoma (NSE, S100 protein positive, LCA negative)
5	Ehomoid Sinus Chronic granulomatous inflammation T.B No fungus seen.	Chronic granulomatous inflammation fungus positive no T.B
6	Nose: Plasmacytoma	Peripheral T cell Non Hodgkin's lymphuma (PTCL)(LCA, T positive)
7	Nose malignant neoplasm D/D carcinoma/ NHL	Malignant Melanoma, (Vimentin, S100 protein, HMB 45 positive)
8	Parapharyngeal area: Heman giopericytoma	Solitary fibrous tumor (Vimentin, CD 34 positive)
9	Ethmoid Sinus: Malignant neoplasm D/D rhabdomyosarcoma	poorly differentiated Carcinoma, (CK MNF, CK CAM 5.2 positive)
10	Vocal cord: Carcinoma	Inflammatory pseudotumor (Vimentin, ASMA positive cytokeratins negative)
11	Cheek Carcinoma	Diffuse large cell non Hodgkin's lymphoma of B phenotype, LCA B positive)
12	Oral cavity: poorly differentiated carcinoma	Diffuse large cell Non Hodgkin's lymphoma of B phenotype (LCA, B positive)

Table 8. Female genital tract cases.

S.No.	Submitted diagnosis	Second opinion diagnosis
1	Cervix Dysplasia	Sqyamous metaplasia and non-specific inflammation No dysplasia

2	Overy: Bordeline serous tumor	Endometriotic Cyst
3	Overy: Sertoli leydig cell tumor	Gramulosa cell tumor, (Vimentin, ASMA, S100 protein, MIC 2 positive)
4	Overy: Malignant tumor	Benign ovarian tissue
5	Ovary: poorly differentiated carvinoma	Dysgerminoma

Table 9 Male genital tract cases.

S.No.	Submitted diagnosis	Second opinion diagnosis
1	Prostate: Adenocarvinoma	Atypical adenomatous hyperplasia
2	Prostate: Adenocarvinoma	Rhabdomysosarcoma. (Vementin, Desmin pisitive Keratins negative)
3	Prostate: Adenocarvinoma	Transitional cell carcinoma (PSA negative)
4	Testis: Seminoma	Benign testicular tissue
5	Prostate: sqyamous cell carcinoma	Infarction with squamous metaplasia

Table 10. Miscellaneous cases with difference in diagnosis.

S.No.	Submitted diagnosis	Second opinion diagnosis
1	Lung: Pulmonary blastoma	Orfanizing pneumoia
2	Glomus Jugulare: Glomus Jugulare tumor	Choroid plexus papilloma (Kerains, EMA pisitive)
3	Breast: Mammary dysplasia	Severe chronic non-specific inflammation and fat necrosis
4	Breast: Mammary dysplasia	ProstateAdenocarcinoma (PSA positive)
5	Urinary bladder: Transitional cell carcinoma, grade III	prostate Adenocarcinoma (PSA positive)
6	Pleura: malignant mesothelioma	Reactive mesothelial cells
7	Thyroid: Follicular carcinoma	Papillary carcinoma
8	Thyroid: Papillary carcinoma	Medullary carcinoma (CK MNF, CK, CAM 5.2,S100 protein NSE, chromofranin pisitice Thyroglobin negative)
9	Kidney: soindle cell carcinoma	Leiomyosarcoma, (Vimentin, ASMA positive: cytokeratins negative)
10	Breast infiltrating ductal carcinoma	Fibrocystic disease
11	Kidney: Renal cell carcinoma	Xanthogranulomatous pyelonephritis
12	Brain:Desmoplastic Medulloblastoma	Neuroblastoma, (GFAP, NSE, Chromgranin positive)

neuropathology cases. In our study, neuropathology cases for second opinion were very few except for one case (Table 10). Our study also showed high discrepancy rates of 53.84%, 44.44% and 32.69% for skin, head and neck (excluding neuropathology) and gastrointestinal tract cases (results). Malhotra et al.7 reported a 7% discrepancy rate in skin cases. As shown in Table 10, significant diagnostic differences were also seen in breast and thyroid cases. It was concluded from the study that a second opinion for determining a diagnosis of difficult cases by histopathology examination, is highly recommended. This practice is implemented worldwide

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