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Research Article

Exotic associations and presentations of an age old disease: spectrum of tuberculosis in a developing country

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ABSTRACT

Background: To create an awareness of the associations of tuberculosis with various other infections and its atypical clinical manifestations is important especially in regions where tuberculosis continues to be a major public health problem.
Methods: This was an observational study of tubercular cases received in the Department of Pathology during the period January 2014 to January 2015.
Results: A case series of exotic associations of tuberculosis, along with two cases at unusual sites, not suspected clinically, subsequently diagnosed by pathological examination and ancillary techniques.
Conclusions: Tuberculosis continues to be a major cause of morbidity and mortality especially in the developing world. This series of cases goes to demonstrate the seemingly endless forms and presentations of this age-old disease and the importance of timely diagnosis and specific treatment.

Keywords: Tuberculosis, Associations, Presentation, Developing country

INTRODUCTION

Throughout history, tuberculosis (TB) has been recognized as an affliction with an enormous impact in terms of morbidity, mortality and economic cost. John Bunyan, the 17th century English writer and preacher, famously labeled it as Consumption the Captain of all these men of death.[1] In 1882, Robert Koch, German scientist identified the tubercle bacillus, for which he was awarded the Nobel Prize in Medicine in 1905.[2] This landmark discovery was followed by rapid advances in diagnosis, prevention and therapy of tuberculosis.

It was in the early eighties of the last century when the HIV-AIDS pandemic swept the world that tuberculosis came into prominence again, albeit in a different form and tuberculosis and HIV have been closely linked since the emergence of AIDS. HIV has contributed significantly to the increase in the incidence of TB across the world and is recognized as the most common opportunistic infection in HIV positive individuals.[3,4] Concomitant TB and HIV infection leads to a progressive decline in cell-mediated immunity characterized by unusual presentations, frequent extra pulmonary involvement and pauci-bacillary disease which can delay timely diagnosis. Maurice L Sievers also described tuberculosis as the Second Great Imitator and stressed that tuberculosis can imitate various other disease processes.[5] An awareness of the associations of tuberculosis with various other infections and its atypical clinical manifestations is important especially in regions where tuberculosis continues to be a major public health problem, such as India. We hereby present three exotic associations of tuberculosis, along with two cases at unusual sites, which were not suspected clinically and were subsequently diagnosed by pathological examination and ancillary techniques. In all the cases, the involvement was extra pulmonary in nature and all five

patients tested negative for Human Immunodeficiency Virus (HIV) status on serology.

METHODS

The present study is an observational study conducted in the Department of Pathology, at the Hakeem Abdul Hameed Centenary Hospital New Delhi, during the period from January 2014 to January 2015. Our hospital caters to a predominant population belonging to a low socioeconomic status residing in the nearby localities. A total of 68 cases of tuberculosis received in the department, these five cases were of unusual associations and presentations. The data on the age, sex and the presenting clinical features of these cases were retrieved from the accompanying laboratory request forms, or the patients file records wherever they were available. The clinical presentation and the histological features were analyzed and the results were compared with those in the literature.

RESULTS

Table 1: Comparative summary of salient features of case 1 to case 5.

S. No.	Age / Sex	Clinical presentation	Clinical Diagnosis	Diagnosis on Cytology/Histopathology	Special /Ancillary tests
Case 1	32 years male	Left axillary swelling and fever	Tubercular lymphadenitis	Coexistent axillary hydatid disease and tubercular lymphadenitis	Z-N stain for acid fast bacilli was positive. Culture for M.tuberculosis was positive
Case 2	25 years male	Fever with joint pains and skin rashes	Follow up case of tuberculosis on erratic anti-tubercular treatment	Coexistent Erythema Nodosum Leprosum and tubercular lymphadenitis	Slit skin smears positive for acid fast Lepra bacilli. Axillary lymph nodes positive for Z-N stain for acid fast bacilli. GeneXpert MTB/RIF (Xpert) assay system positive for M.tuberculosis
Case 3	40 years male	Hoarseness of voice	Carcinoma larynx	Spindle cell carcinoma of larynx with tubercular lymphadenitis	Immuno histchemistry for spindle cell carcinoma. Z-N stain for acid fast bacilli was positive. MTB PCR positive on lymph node paraffin block
Case 4	34 years female	Painful, tender swelling right breast and fever	Breast abscess	Tuberculosis of breast	Incision and drainage material positive for Z-N stain for acid fast bacilli. Culture for M.tuberculosis was positive
Case 5	24 years female	Irregular vaginal bleeding and low grade fever	Carcinoma cervix	Tuberculosis of cervix	Punch biopsy cervix, Z-N stain for acid fast bacilli was positive. X-ray chest-bilateral non-homogenous opacities. Ultrasound abdomen - enlarged contiguous lymph nodes with necrosis.

Case 1

A 32 years old male presented to the surgical outpatient with left axillary swelling and fever. His complaints had persisted for the previous eight months and were preceded by development of furuncles in the axilla. There was no family or past history of tuberculosis or loss of weight or appetite. The patient was referred to the Department of Pathology for FNAC of axillary lymph nodes, with a provisional diagnosis of tuberculosis. Three discreet, firm, mobile lymph nodes were palpated in the left central axilla approximately 0.8 to 2.0 cm. FNAC showed a blood-tinged aspirate and wet fixed and dry smears were prepared. Staining with hematoxylin and eosin, Giemsa, and Ziehl Neelsen (ZN) was done.

Smears were cellular showing intact and degenerated neutrophils, histiocytes, and eosinophils, mononuclear cells along with several epithelioid cell granulomas and giant cells in a necrotic background. During the screening of the ZN stained smears for acid-fast bacilli under oil immersion, classical hooklets of Echinococcus were noticed which were semi-translucent and sickle-shaped. Alerted by this discovery, a further search revealed scolices of Echinococcus, which were large ovoid structures. However, no laminated membrane was identified. In addition, beaded, acid-fast bacilli of Mycobacterium tuberculosis were also seen. The cytological impression was tubercular lymphadenitis with coexistent echinococcal infection. Culture studies of the aspirated purulent material were positive for

Mycobacterium tuberculosis. Retrospectively, a history of canine contact was obtained on direct questioning. The echinococcal indirect hemagglutination test was negative.

Routine hematological tests showed a raised erythrocyte sedimentation rate (ESR) of 28 mm in the first hour by the Wintrobe method. Other hematological parameters, including coagulation profile, were normal. The chest radiograph did not reveal any abnormality. Ultrasound of the abdomen was unremarkable. Ultrasound of the axilla was advised, but was not done due to cost issues. Antihelminthic as well as anti-tubercular therapy was started although subsequently the patient was lost to follow-up. This case has been published as a case report.[6]

Case 2

A 25-year-old man presented with a history of low grade intermittent fever since 10 months. He also complained of joint pains, skin rashes over the face, trunk & upper extremities along with dysuria of recent onset, i.e. since seven days. He gave a past history of having been worked up for tuberculosis, started on 4 drug antitubercular treatment, though he admitted to not being regular with the medication. No other details or documents were available. On examination he was thinly built and weighed 46 kg. Bilateral axillary and left cervical lymphnodes were enlarged and erythematous nodular plaques over nose, bilateral cheek and forehead were present. Pain and touch sensation was intact over these lesions. Few tender nodular eruptions of varying size were also present over trunk and upper extremities. The scalp and oral mucosa were not involved. Bilateral ulnar, radial and common peroneal nerves were enlarged and tender. He also had symptoms suggestive of episcleritis and migratory polyarthritis. His general physical condition was stable and systemic exaimnation was normal. The clinical suspicion was of Hansen's disease and a skin slit smear was taken along with a skin biopsy of an erythematous nodule from the right forearm.

Slit-skin smear from the erythematous nodule showed evidence of multi bacillary leprosy with clumps of Acid Fast Bacilli on Fite stain (Bacillary Index-5) Skin biopsy from right forearm showed collection and sheets of foamy macrophages in dermis. Mixed dermal infiltrate of neutrophils and lymphocytes was seen superimposed on foamy macrophages. Many dispersed epithelioid cells were seen with foci of necrosis and multinucleated giant cells. (Figure 1) Special stain for lepra bacilli ie. Fite-Faraco stain was positive. The final histological diagnosis Hansen's disease, Borderline lepromatous with Type II Lepra reaction (Erythema Nodosum Leprosum).

Fine Needle Aspiration Cytology (FNAC) of axillary lymph node was done. A purulent aspirate was obtained and microscopy showed numerous epithelioid granulomas in a necrotic background. Zeihl Neelsen staining for acid-fast bacilli was done and reported as positive and scanty (1 to 2 bacilli per 100 oil-immersion fields) (Figure 2). Culture studies for Mycobacterium on the aspirated material were reported as negative. At the same sitting, material obtained from a second pass of a 23 gauge needle attached to a 10 ml syringe was processed for Gene Xpert MTB/RIF Assay which was reported as positive. In our hospital we have used the Xpert Assay System for extra pulmonary tuberculosis, especially lymph node aspirates and body fluids i.e. cerebrospinal fluid and ascitic fluid with good results.

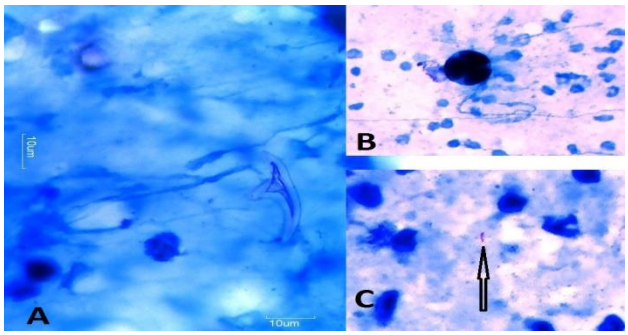

Figure 1:(A) Photomicrograph showing the semi-transluscent, refractile hooklet of Echinococcus (ZN Stain, ×1000). (B) Photomicrograph showing scolex of Echinococcus (ZN Stain ×1000) (C). Photomicrograph showing acid fast bacilli of Mycobacterium tuber).

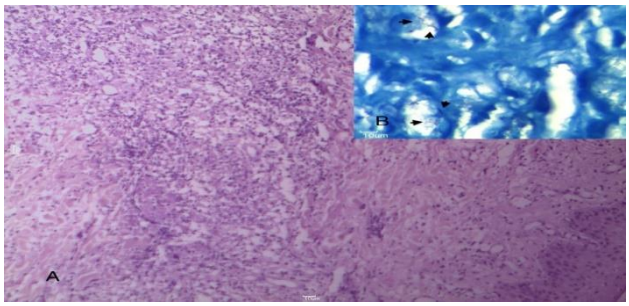

Figure 2: (A) Photomicrograph showing a mixed dermal infiltrate of neutrophils and lymphocytes, superimposed on foamy macrophages and many dispersed epithelioid cells (H and E x 400) Inset: Photomicrograph showing Acid fast Lepra Bacilli on Fite Stain. Bacil).

Other investigations revealed mild anemia and a raised ESR, 26 mm fall in the first hour. Liver and kidney function tests and also X-ray chest were within normal limits. Serological markers for collagen vascular disease, i.e. Anti-Nuclear Antibody (ANA) and Anti dsDNA Antibody were negative.

Hence, with this clinical presentation and investigation profile, a final diagnosis of Borderline Lepromatous leprosy with Type II Lepra reaction, i.e. Erythema Nodosum Leprosum and coexistent tubercular lymphadenitis was made. With the medical management

of Erythema Nodosum Leprosum the general condition of the patient improved. He was discharged on the fifth day after hospitalization on standard anti-tubercular therapy along with anti leprotic drugs, and since then has been on regular follow up.

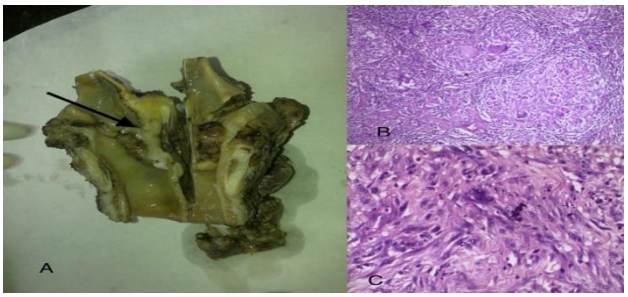

Figure 3: (A) Gross picture of Total Laryngectomy specimen cut open showing a transglottic growth projecting into the laryngeal lumen (B) Coalescing epithelioid cell granulomas with Langhans giant cells in a lymphoid background. (HE x 400) (C) Spindle c).

Case 3

A 40 years old male presented with complaints of hoarseness of voice for the past 2 years. In past history, he was a known case of carcinoma larynx, initially diagnosed as well differentiated squamous cell carcinoma of the larynx (glottic, stage T1N0). The patient underwent a laser excision of the growth, but he developed a recurrence after 5 months. Repeat biopsy of the recurrent growth was done and was now reported as spindle cell carcinoma, glottis region and the patient was given radiotherapy of dose 68 Grey. Patient developed hoarseness yet again 3 months after completion of radiotherapy. There was no associated co-morbidity. An indirect laryngoscopy and subsequent flexible fiber-optic endoscopy examination of the larynx revealed nodular lesion on right vocal cord involving the anterior commissure with restricted movement of right vocal cord. There were no palpable lymph nodes. MRI scan of the larynx revealed an irregular lobulated heterogenous lesion and a lobulated nodular component projecting into laryngeal lumen causing compromise of the airway. There was minimal extension into subglottic region. Multiple mildly enlarged lymph nodes were seen along carotid sheath in level II, III, IV on right side. Direct laryngoscopy and biopsy of the laryngeal growth was done and once again reported as spindle cell carcinoma of the larynx. On immunohistochemistry tumor cells were positive for CK, SMA, CD-34, S-100 and negative for Desmin. The patient was then taken up for a total laryngectomy with selective neck dissection, right side. Postoperative histo pathological examination confirmed a spindle cell carcinoma larynx (pT3N0) with focal myxoid and neural differentiation involving the glottis region extending to subglottic region. Seven lymph nodes were isolated and all showed necrotizing granulomas and stain for acid-fast bacilli was positive. No metastatic deposits were seen in the lymph nodes. Nested PCR assay for Mycobacterium tuberculosis performed on the paraffin embedded lymph node tissue was positive. His post-operative recovery has been uneventful, so far. Patient has been treated with anti-tubercular treatment, in addition.

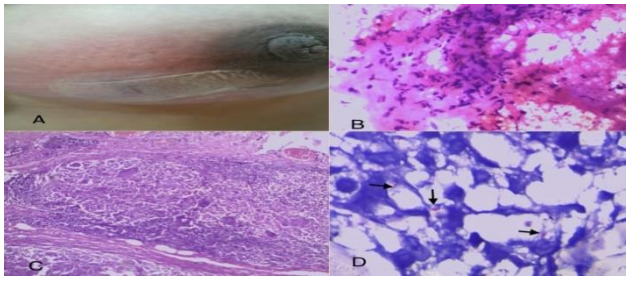

Figure 4: (A) Gross picture of right breast with redness & induration (B) Photomicrograph of FNAC Smear showing epithelioid granuloma in a background of necrosis and fat(HE x 400) (C) Epithelioid cell granulomas with Langhans giant cells and a duct with I).

Case 4

A 34 years old married female presented to the surgical out patient department with a painful right breast swelling and fever for the past two weeks. There was no history of lactation/trauma to the breast or family history of tuberculosis. On physical examination, an erythematous, warm, tender and indurated area was seen on the right breast involving the peri-areolar region and extending into both upper and lower outer quadrants measuring approximately 4X3 cm.There was no regional lymphadenopathy. A provisional clinical diagnosis of breast abscess was made. Investigations showed a raised erythrocyte sedimentation rate (32mm/hr), elevated total leucocyte count with neutrophilia. The patient was referred to Pathology dept for fine needle aspiration, which yielded 1ml pus like material. Cytological examination showed a necrotic background with few epithelioid cell collections and mononuclear cells. As a routine practice all pus aspirated in our laboratory is subjected to Ziehl Neelsen staining, and the smears were negative for acid-fast bacilli. A diagnosis of granulomatous mastitis, tubercular etiology cannot be excluded was given. This prompted a detailed workup of the patient. The tuberculin skin test was strongly positive (22mm) whereas imaging techniques and other ancillary investigations ruled out any other focus of infection. The patient underwent incision and drainage of the breast abscess and irregular shaggy tissue bits received were subjected to histopathological evaluation and culture studies. Epithelioid cell granulomas with caseation necrosis were seen and Ziehl Neelson staining demonstrated acid-fast bacilli. Culture of the irregular debridement tissue bits was also done and was positive for Mycobacterium tuberculosis. A final diagnosis of primary tuberculosis breast was made. The patient was

started on a regimen of four-drug anti-tubercular chemotherapy (2HREZ/4HR3). She has shown significant clinical improvement and is presently on regular follow-up.

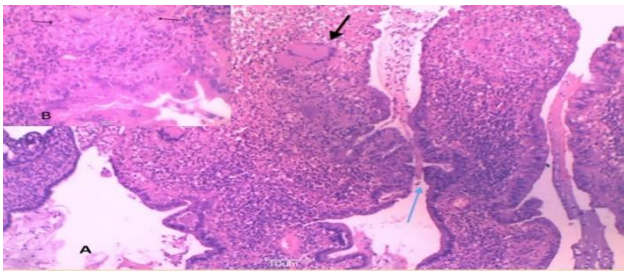

Figure 5: photomicrograph showing endocervix with numerous epithelioid cell granulomas, langhans giant cells and areas of necrosis. (he x 100) inset: epithelioid cells and langhans giant cells (he x 400).

Case 5

A 24 years old, para four female presented with complaints of irregular vaginal bleeding and low grade fever off and on for the last one and a half months. She had a normal vaginal delivery one and a half months back and was not breast-feeding her child. She also gave history of loss of appetite and weight loss. Although there was no history of coitus in last five months, there is was no history of postcoital bleeding before that. There was no history of cough or abdominal pain.

On general examination she was noted to have mild pallor and the systemic examination was unremarkable. Speculum examination showed a growth on the anterior lip of cervix and on the anterior wall of vagina, which bled on touch. The cervical lips could not be delineated clearly. Pelvic examination revealed a normal sized uterus with no tenderness or any adnexal mass. Rectum examination was unremarkable. Colposcopy was done and biopsy of the cervical growth was taken. Colposcopy showed grade 3 aceto-whiteness with irregular vascular pattern in the lesion and the clinical impression after the gynaecologic examination was of carcinoma cervix and a punch biopsy of the cervical growth was taken and sent to Pathology department for histo pathological examination.

Histo pathological examination of the cervical biopsy showed numerous epithelioid cell granulomas, Langhans giant cells and caseation necrosis. There was no evidence of dysplasia or malignancy in the exocervical lining or the endocervical glands. Acid fast bacilli were demonstrated in the necrotic areas. Endometrial biopsy showed glands in proliferative phase. This led to a detailed workup of the patient. Hemoglobin was 9.5 gm % with raised ESR (46 mm). Sputum for acid-fast bacilli was negative. Abdominal ultrasound detected multiple prominent peripheral vessels in myometrium without any obvious mass and multiple enlarged contiguous lymph nodes with areas of necrosis in retro-peritoneum. Her chest X-ray showed non-homogeneous opacities in the right upper zone and the left upper and mid-zones. Based on cervical biopsy report, abdominal ultrasound and chest X -ray findings, a diagnosis of disseminated tuberculosis was made.

Patient was started on 4 drug (rifampicin, isoniazid, ethambutol, pyrazinamide) anti-tubercular therapy. After two month of starting the anti-tubercular treatment, colposcopic examination of the cervix showed disappearance of growth and the cervical lips were now well delineated. Patient is under follow-up and her general condition has improved. Her husband has also been diagnosed as a case of pulmonary tuberculosis and likewise started on treatment. Her new born baby died at three months of age, at home.

DISCUSSION

India has the world's largest burden of tuberculosis, accounting for one-fourth (24%) of the global TB incidence. The global annual incidence estimate is 8.8 million cases, of which 1.5 million cases are from India. According to Revised National Tuberculosis Control Programme, 0.8 million new cases of extra pulmonary TB (EPTB) were observed in 2010.[7] EPTB constitutes about 15 to 20 per cent of all cases of tuberculosis in immune competent patients and accounts for more than 50 per cent of the cases in HIV-positive individuals. Lymph nodes are the most common site of involvement followed by pleural effusion and virtually every site of the body can be affected.[8]

The association of tuberculosis with cancers and other infectious diseases due to impaired cellular immunity has also been reported and three such exotic associations are presented in this series. The timely diagnosis of EPTB remains a major challenge to physicians due to the frequently atypical clinical presentation that simulates other inflammatory and neoplastic conditions, often resulting in delay or deprivation of treatment. This entails a high degree of suspicion for an early diagnosis and mostly, more than one technique is necessary for the confirmation of the diagnosis. In lower-income countries, lack of diagnostic infrastructure is yet another hurdle.[9] More often than not, available clinical sample volumes are inadequate and paucibacillary in nature.[10] Several potential techniques have been employed for the diagnosis of EPTB specimens i.e. smear microscopic examination, culture test (both manual and automated), serological assays (both antigen and antibody detection), histological /cytological examination, Mantoux test, PCR assays (conventional as well as real-time PCR).[8] Sophisticated imaging techniques such as CT Scan and MRI and procedures such as laparoscopy and endoscopy have tremendously helped in the anatomical localization of EPTB and also to obtain tissue for biopsies for a definitive diagnosis.

Tuberculosis, caused by Mycobacterium tuberculosis and hydatid disease, caused by the larvae of the cestode Echinococcus are public health problems worldwide. The lungs and liver are the primary sites of localization of hydatid cyst, though anecdotal reports of unusual locations such as thyroid gland and submandibular gland have been described.[11] Coexistent hydatid disease and tuberculosis has been mostly reported in the lung, usually detected by imaging techniques. The diagnosis of coexistent tuberculosis and hydatid in this case was achieved using the easy-to-perform, minimally invasive modality of fine needle aspiration and before any imaging techniques, unlike other previously reported cases. FNA has been conventionally contraindicated in a suspected case of hydatid cyst because of risk of anaphylaxis and dissemination. However, this risk has been overemphasized in the past as there are reports on cytological diagnosis of hydatid disease without complications.[12] It has been reported that the hooklets and scolices are better visualized on Ziehl Neelsen stain and this was our observation also.[13] Iynen et al reported an unusual case of a hydatid cyst in the supraclavicular soft tissue.[14] It is also highly possible that in the present case the hydatid cyst was located in the axillary soft tissue closely related to the enlarged axillary lymph nodes which harbored a focus of tuberculosis, and that both the pathologies were picked up during multiple passes of the needle during the fine aspiration of the enlarged axillary lymph nodes.

Tuberculosis and leprosy are both endemic in India. It has been proposed that a reduction in the cell-mediated immune response which occurs in multibacillary leprosy leads to the reactivation of an underlying latent tuberculosis infection, or a superinfection with M. tuberculosis.[15] Historically, it was presumed that most cases of tuberculosis were associated with multibacillary leprosy, i.e. lepromatous leprosy and borderline lepromatous leprosy, whereas co-infection of the tuberculoid form of leprosy and tuberculosis was rare.[16] Dual infections of leprosy and tuberculosis have been reported in some specific clinical settings such as presence of HIV (Human Immunodeficiency Virus) infection, diabetes, systemic steroid use and the presence of chronic kidney disease and generally attributed to a mycobacterial genera-specific anergy as a predisposing factor.[17,18, 19] Most reported associations of leprosy are with pulmonary tuberculosis.[15, 20] Arora et al described the association of lymph node tuberculosis in a HIV positive individual.[17] Lymph node tuberculosis in association with lepra reaction, as in the present case has, to the best of our knowledge not been reported previously.

Reactions in leprosy are periodic acute inflammatory episodes occurring in an otherwise chronic course of the infection. They are usually caused by immune responses to *Mycobacterium leprae* or its antigens and two main types are described, Type I or reversal reaction & Type II, which is an immune complex manifestation. Type II reaction is also called as erythema nodosum leprosum and is reflected by deeper infiltration of foamy histiocytes into the subcutaneous fat and presence of neutrophils, superimposed on multibacillary leprosy, as was seen in the present case. It is an inflammatory systemic reaction with varied presentations when immune complexes are deposited in organs and tissues. Neuritis, orchitis, uveitis, periostitis, lymphadenitis, arthritis and glomerulonephritis can occur rarely. Our patient developed painful erythematous nodules with episcleritis and arthritis. It is reported that one-third of all leprosy patients may present with Type II lepra reaction (erythema nodosum leprosum) at the time of diagnosis, as occurred in our case also. Gene Xpert MTB/RIF (Xpert) assay for Mycobacterium tuberculosis has been shown to be very useful for non-respiratory samples, and this assay helped clinch the diagnosis of tubercular lymphadenitis in this case. Ligthelm et al demonstrated the excellent diagnostic accuracy of the Xpert test in patients with tubercular lymphadenitis with sensitivity of 96.7% and specificity of 90%.[21]

The association of tuberculosis with malignancy has been recognized since many years. Histological evidence of coexistent pulmonary tuberculosis and bronchogenic carcinoma was first reported in the 19th century by Penard as brought out by Meyer in his treatise on the relationship between bronchogenic carcinoma and tuberculosis.[22] Subsequently coexisting necrotizing granulomas in the tumor and regional lymph nodes have been reported by many workers in association with adenocarcinoma colon, Hodgkin's lymphoma, bronchial carcinoid, infiltrating carcinoma breast, mucinous cystadenoma ovary, follicular adenoma, metastatic deposits of medullary carcinoma thyroid and ampullary carcinoma.[23] Chaturvedi et al reported a case of extensive tubercular neck lymphadenopathy in a man with early-stage tongue cancer.[24] Other case reports of coexistent tuberculosis and malignancy in the head and neck region are a case of tuberculosis of the buccal mucosa with concomitant adenoid cystic carcinoma and two cases of a tubercular osteomyelitis co-existing with a central mucoepidermoid carcinoma of the jaw.[25,26,27] Spindle cell carcinoma is a highly malignant, uncommon variant of squamous cell carcinoma of the larynx, comprising 2 to 3% of all laryngeal cancers.[28] To the best of our knowledge and based on our literature review we have not come across any report of an association between spindle cell carcinoma larynx and tuberculosis. The diagnosis of spindle cell carcinoma requires histological demonstration of both the squamous cell component and the spindle shaped cells with sarcomatous appearances with immune histochemical confirmation of the epithelial and mesenchymal markers.[29] Immuno histochemical studies showed tumor cells were positive for CK, SMA, CD34, S-100 and negative for Desmin. Coexistent tuberculosis in the regional lymph nodes was diagnosed on the basis of the characteristic histology, AFB staining and positive PCR for Tuberculosis. PCR has successfully been used to detect M. tuberculosis from paraffin-

embedded tissues and is specially useful in clinical settings in which the diagnosis is uncertain.[30] The patient is on anti-tubercular treatment and on regular follow up in the otolaryngology outpatient department.

Breast tuberculosis is a rare condition and was first described by Sir Astley Cooper in 1929.[31] Its importance is due to the infrequent occurrence and the chances of mistaken identity with breast cancer and pyogenic breast abscess, which entails a high index of suspicion. It has been suggested that, like the skeletal muscles and spleen, breast tissue too is remarkably resistant to tuberculosis as it provides an infertile environment for the survival and multiplication of the TB bacillus.[32] Hence tubercular involvement of these organs is rare. In endemic countries like India, incidence of breast tuberculosis ranges from 3 to 4.5% , whereas it is a miniscule 0.1% in Western countries.[33,34] Tewari and Shukla categorized breast tuberculosis as nodulocaseous tubercular mastitis, disseminated/confluent tubercular mastitis, and tubercular breast abscess. Our case was breast tuberculosis masquerading as a breast abscess and belonged to the last category. It has been reported that breast tuberculosis occurs more frequently in pregnant and lactating women and it is the increased vascularity & the dilated ducts which predispose to trauma making it more susceptible to tuberculosis.[35] In the present case breast tuberculosis was diagnosed in a non-lactating breast which is unusual. Fine needle aspiration cytology (FNAC) of the breast lesion is recognized as an important diagnostic tool for breast tuberculosis. Approximately 73 per cent cases of breast tuberculosis can be diagnosed on FNAC when both epitheloid cell granulomas and necrosis are present.[36] In addition; biopsy and culture studies of the excised material also confirmed tubercular etiology in this case.

Cervical tuberculosis represents 0.1 to 0.65% of all cases of tuberculosis.[37] Tuberculosis of the female genital tract involves the fallopian tubes (95-100%), endometrium (50-60%) and ovaries (20-30%) in a decreasing order of frequency and TB of the uterine cervix is the rarest, accounting for approximately 5% of all genital tuberculosis.[38] The cervix is relatively resistant to tuberculosis infection because the stratified squamous epithelium of the ecto cervix prevents bacterial penetration. In addition, cervical mucus is known to have antibacterial action. With the re-emergence of tuberculosis globally, it is important to have a high index of suspicion in case of an abnormal cervical appearance. Tuberculosis thus remains an important differential diagnosis of a malignant appearing lesion of the cervix and its presentation can be variable. Singh et al reported two cases of cervical tuberculosis, one was a young woman presented with primary infertility and secondary amenorrhoea and the other a peri menopausal woman with irregular vaginal bleeding and postcoital blood-stained discharge.[39] The gross appearance of cervical TB on per speculum examination can also be variable. There may be a hypertrophy of the cervix or a friable papillary or vegetative growth mimicking invasive cervical cancer.[40] The diagnosis of cervical TB rests upon the histological examination of a cervical punch biopsy specimen. Microscopically, caseating or non-caseating granulomas are seen in most of the cases. Staining for acid fast bacilli was positive in the cervical biopsy. Isolation of tubercular bacilli on culture studies is the gold standard but one-third of cases have been reported to be culture negative, as was also this case.[37] The clinical impression was that of disseminated tuberculosis based on the clinical, radiological and histo pathological findings of the cervical biopsy. She responded well to standard anti-tubercular treatment with disappearance of the cervical growth. The infant death in the present case may possibly be due to undiagnosed perinatal tuberculosis, which is a fatal condition if untreated.

CONCLUSION

Tuberculosis continues to be a major cause of morbidity and mortality especially in the developing world. Extra pulmonary involvement can occur in isolation or along with a pulmonary focus as is seen in patients with disseminated tuberculosis (TB). Its incidence is rising worldwide as a result of occurrence of multi-drug resistant strains and the increasing incidence of HIV-AIDS. This series of cases goes to demonstrate the seemingly endless forms and presentations of this age-old disease and the importance of timely diagnosis and specific treatment.

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