Original Article

Extra Pulmonary Tuberculosis, Clinical and Imaging Overview

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ABSTRACT

Objective: Extrapulmonary tuberculosis is the tuberculosis of the organs other than lungs,caused by mycobacterium tuberculosis. It is endemic in Kingdom of Saudi Arabia (KSA), especially in Makkah as Asian / Southeast people are more here.
Design of Study: Experimental study.
Place and Duration of Study: This study was conducted at King Abdul Aziz Hospital, Makkah during 1st Jan.2007 to 31 Dec. 2008.
Patients and Methods: In our study 13 cases where examined, diagnosed (by both imaging and laboratory work up) and treated for extra pulmonary tuberculosis in King Abdul Aziz Hospital, Makkah. Diagnosis of extra pulmonary tuberculosis is often difficult, especially where lungs are not involved. Radiological findings,especially C.T. were of great help in the diagnosis of extra pulmonary tuberculosis. Final diagnosis was made by histopathological examination and culture for most of the patients. Predominantly (82 %) two systems were involved. 44 % lymphadenopathy, mainly cervical and mediastinal while musculoskeletal system was involved (with involvement of vertebrae and paraspinal muscles) in 38 %. Diagnosis of extra pulmonary tuberculosis requires high clinical suspicion, different imaging work up and special staining / culture media for diagnosis of mycobacterium tuberculosis bacilli (acid-fast bacilli). Patient's delay (average 2 months) and Doctor's delay time (average 7 days) was also observed in individual cases. Various patterns of extra pulmonary tuberculosis (EPT) in Makkah in Saudi and Non-Saudi patients also compared with other parts of KSA by reviewing the literature.
Results: The results showed that disease pattern has changed along with increase incidence rate of EPT in KSA over the last few years. True rates may be higher as there may be incomplete reporting or the patients may be referred to other areas of Kingdom.
Conclusion: The clinical and radiological features of extra-pulmonary tuberculosis may clue to the diagnosis as many other diseases can mimic the imaging. The patterns of extrapulmonary tuberculosis may vary due to extent of disease involvement otherwise inclination of region involvement is same everywhere. Extrapulmonary tuberculosis is relatively less in Saudi patients (from 1:2 to 1:3 depending upon regions) as compared to non Saudi patients.
Key Words: Anti tuberculous treatment, Extra pulmonary Tuberculosis, Human Immune deficiency Virus, Kingdom of Saudi Arabia, Tuberculosis.

INTRODUCTION

There is world wide continuous steady, increase in the incidence of Extrapulmonary tuberculosis (EPT) and decrease in pulmonary tuberculosis from the last one and half decade. In KSA, In 1993, reported EPT has annual incidence rate of 1.7 cases per 100,000 population[1]. In 1997, it was 4.7 cases per 100,000 population. During same period, pulmonary T.B. rates decreased[2]. In U.S.A., EPT percentage of all cases of T.B. was 15% in 1981 which increased to 18% in 1990 without a clear explanation [(3)]. However there was a resurgence of tuberculosis from 1985 to 1992, that considered with epidemic of acquired immune-deficiency syndrome[4]. A recent (2001) study in Riyadh also showed about 66%. cultured confirmed EPT of all tuberculous patients identified at KFSHRC[5]. The possible factors that have contributed to this increase are, the rising number of people with suppression of immune system, the development of drug resistant strains of mycobacterium tuberculosis, aging population demographics and an increase in the number of health care workers exposed to disease[6]. Diagnosis of EPT is often difficult. A negative smear of acid fast bacillus, a lack of granulomas on histopathology and failure to culture mycobacterium tuberculosis do not exclude the diagnosis[7]. Novel diagnostic procedures such as adenosine deaminase levels and polymerase chain reaction can be useful in certain forms of extra pulmonary tuberculosis but these facilities are not available in all centres, so sometimes antituberculous therapy may need to be initiated empirically to reduce

the morbidity and mortality. Although the incidence of tuberculosis is decreasing in U.S.A., it remain a major global problem with a prevalence rate of 32%[8]. It is increasing in foreign born persons (53% in 2003)[9]. Extra pulmonary involvement may be seen in more than 50% of patients with concurrent AIDS. The risk of EPT and mycobacteremia increases with advancing immunosupression. The features of AIDS associated tuberculosis may include extra pulmonary disease, disseminated disease, rapid progression,visceral lymphadenopathy, tissue abscess and negative tuberculin skin test. Response to ATT is usually similar to that of patients without HIV infection. Initial therapy (6 to 12 months) is same for all forms of EPT. Extended therapy may be required for bone / joint tuberculosis, delayed response or drug resistance. Adjunctive steroids may be useful in patients who have tuberculous meningitis, tuberculous pericarditis or miliary T.B. with refratory hypoxemia[10]. Directly observed therapy is strongly recommended to encourage medication compliance[11].

PATIENTS AND METHODS

The study consist of 13 patients who presented in different departments (according to region involved) of King Abdul Aziz Hospital, Makkah during 1st January to 31st December 2007. The patients of all ages (average 22 years) and of both sexes (M : F 10 : 3) were included who have the clinical suspicion of extra pulmonary tuberculosis after thorough clinical assessment.

Mixed tuberculosis (EPT + Pulmonary T.B.) and patients who have past H/O pulmonary T.B. were included in study. Isolated pulmonary tuberculosis patients were not included. Along with routine tests as that of CBC, ESR and tuberculin test, special laboratory investigations were also conducted in most of patients. These included the culture, staining and histopathological examination along with PCR (In some patients). In the mean time radiological investigations, x-rays and computed tomography were also done for different regions. C.T. was performed without and with I.V. contrast enhancement on single slice G.E. C.T. scan (CT/e – 2002), having spiral mode. In few cases, especially musculoskeletal and lymph node T.B., U/S or C.T. guided aspiration, both diagnostic and therapeutic, was done.

Most of the cases were followed by both laboratory and imaging work up. Regarding imaging, x-ray, U/S (G.E Logic 500) and C.T. follow up was done depending upon the requirement and region involved. Most of cases (11) responded well to treatment, two patients died due to poor response and other complications especially of brain and spine. 4 patients lost contact though they has responded well to treatment initially. During study it was tried to minimize the Doctors delay time (average 7 days) by starting ATT early even before the final reports came so as to minimize morbidity and mortality.

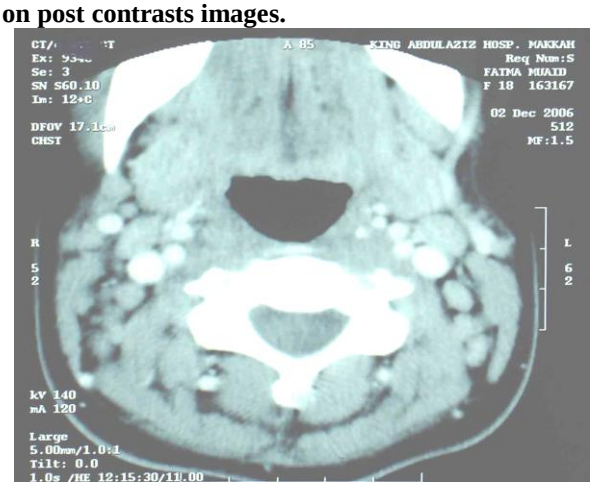
DISCUSSION

Ratio of pulmonary and extrapulmonary tuberculosis varied from region to region and in different times but most of studies (in Riyadh and Jeddah), showed values between 1 : 1 and 1 : 2 respectively. In our study, of 13 total patients. No clinical and radiological evidence of pulmonary tuberculosis seen in 10 (77 %) of cases while only 03 patients had mixed lesions (both pulmonary and extrapulmonary). Five patients (38 %) had isolated lesions either in spine or bones. 62 % had other organs involvement including 6 patients (44%) of cervical or mediastinal lymphadenopathy. We will discuss the patterns of involvement of different organs by tuberculosis in this study.

1. Tuberculosis Lymphadenitis:

No doubt, most common (44% in our study) form of extra pulmonary T.B. is tuberculosis lymphadenitis, mainly involving cervical region in almost all studies in / outside KSA. In one study of South west area of KSA, 45% of cervical lymphadenopathy was due to tuberculosis, more involvement of children and females with mean age of 31-32 years.Other regions like inguinal, axillary, mesenteric, mediastinal and intramammary, also have been mentioned in the literature[13,14]. Patients without H.I.V. infection, present with non tendor, chronic lymphadenopathy while patients with H.I.V. infection usually present with night sweats, fever and weight loss[15].Lymph nodes are firm and discrete, with time, may become matted together as

Figure No.1: Tuberculous Lymphadenopathy: Enhanced C.T. of neck showed extensive bilateral, variable sized, relatively solid looking (no necrosis) lymph nodes with mild homogeneous enhancement on post contrasts images.



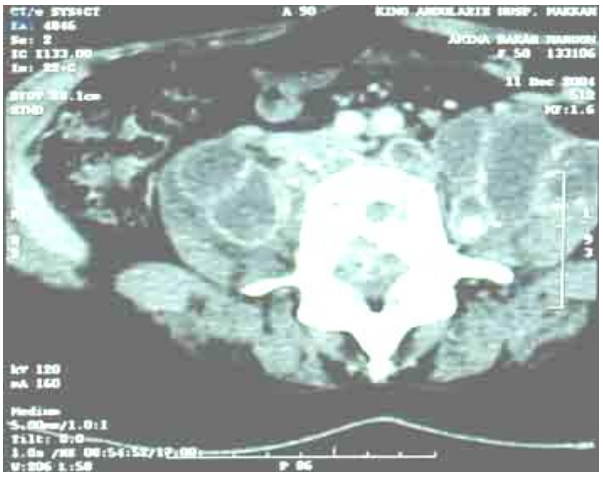
mass. If untreated, the nodes become fluctuant and drain spontaneously with sinus formation. Most patients have positive tuberculin test while chest x-ray is negative. Excisional biopsy of lymph node with histology, AFB stain and mycobacterium culture is diagnostic procedures of choice[16] On C.T. lymph nodes usually demonstrated peripheral enhancement with central low attenuation but not pathognomonic as this pattern can be seen in metastasis, lymphoma and other inflammatory conditions. Few may contain tiny calcification. Some may show homogeneous texture and enhancement (Figure No. 1).

2. Skeletal Tuberculosis:

Bone and joint tuberculosis account for about 35% of extrapulmonary tuberculosis and 3% of tuberculosis as a whole. Skeletal tuberculosis, most often involves spine, mainly dorso lumbar junction.Then comes tuberculous arthritis in weight bearing joints and then extra spinal tuberculous osteomylitis[17]. In middle aged or elderly patients, with active bone / joint T.B., miliary T.B. is sometimes caused by bacillemia originated from infected bone / joint lesions[18].

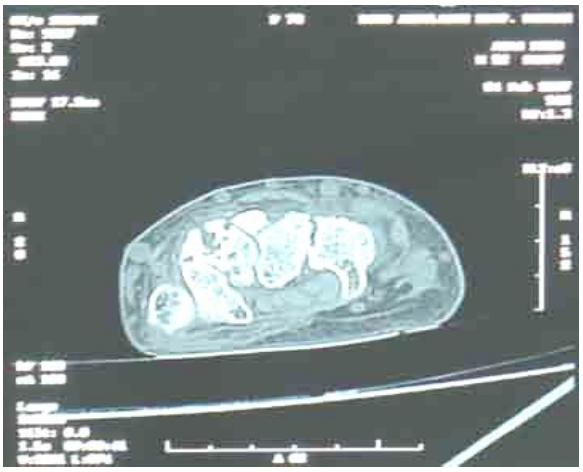
Tuberculous Spondylitis: Most common (50% of skeletal tuberculosis) typically involving more than one vertebra. Usually anterior / inferior part of vertebra is involved with involvement of disc. Later on anterior wedging may lead to classical kyphosis (gibbus), pain and cord compression. Paraspinal and psoas abscesses can develop which can extend upto groin. Calcification in abscess is pathognomonic of T.B. (Figure No. 2).

Figure No. 2: TuberculousSpine: Enhanced C.T. dorsolumbar spine showed extensive vertebral destruction with extension into canal and loculated paraspinal collections, involving both psoas muscles. Calcific foci seen in left psoas abscess.



Tuberculous Arthritis: It is slowly progressive , usually mono arthritis of hip, knee, S.I. joint or elbow. Usual presentation is pain, swelling and reduced movement. Draining sinuses are seen in chronic cases Radiographic changes are non specific however soft tissue swelling and phemister triad (Figure No.3), juxtra articular osteopenia, gradual joint space narrowing and peripheral subchondral erosions, may be characteristic. Fibrous ankylosis is end result. Bony ankylosis frequently seen in pyogenic arthritis.

Figure No. 3: Tuberculous Arthritis: Non enhanced C.T. of right wrist showed soft tissue swelling and lytic, destructive lesions in trapezoid and capitate in right wrist. The radial end was also involved (not shown) in this case.



Tuberculous osteomylitis:

Femur, tibia and small bones of hand and feet are usually involved with local pain and swelling usually metaphysis is involved. Involvement of adjacent structures may result in complications such as carpel tunnel syndrome, tenosynovitis and facial palsy. C.T. / MRI may be helpful to assess degree of bony destruction and to see soft tissue extension and encroachment on adjacent structures (Figure No. 4).

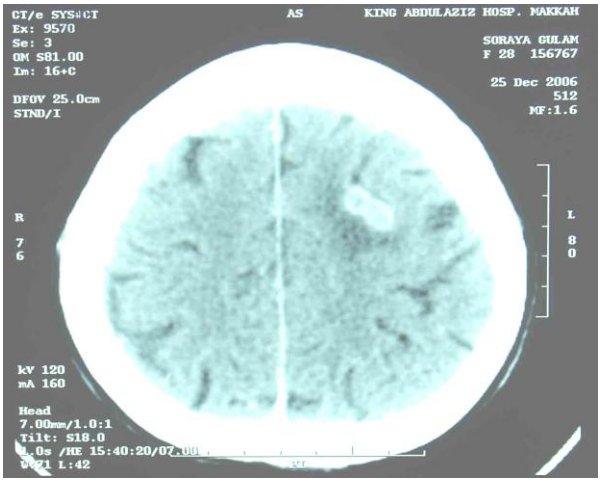
Figure No. 4: Tuberculous Osteomylitis: X-ray of left elbow showed minimally expansile, lytic lesion of upper part of ulna with break of articular surface and cortex as well. Mild soft tissue swelling also seen.

After clinical and radiological evaluation, arthocentesis (culture positive in 80% patients), Synovial and bone biopsy may be required. Small bones may be involved, especially in children,called tuberculous dactylitis. Later on cystic expansile cavity develops giving the appearance of wind filled sail, Spina Ventosa. A well defined cystic tuberculosis also exists with minimal sclerosis. The radiographic features of cystic tuberculosis may resemble with eosinophilic granuloma, sarcoidosis, cystic angiomatosis, plasma cell myeloma, chordoma, fungal infection and metastasis[19].

3. Central nervous system tuberculosis:
May be located in meninges, brain or spinal cord in the form of meningitis (commonest form), tuberculoma, abscess, cerebritis and miliary tuberculosis.

Meningitis:
It results from intense inflammation following rupture of subependymal tubercle (Rich focus) into subarachnoid space leading to arachnoiditis resulting in cranial nerve palsies, vasculitis and communicating hydrocephalus[20]. Tuberculoprotein hypersensitivity may cause meningism and typical CSF picture. Cerebral oedema causes impairment of consciousness, seizures and raised intracranial pressure. C.T. and M.R.I. imaging may show typical enhancement of basal cisterns due to gelatinous exudate.

Figure No. 5: Tuberculoma: Enhanced C.T. brain, axial images showed left subcortical lobulated tuberculoma with moderate surrounding oedema in precentral area causing occasional fits.

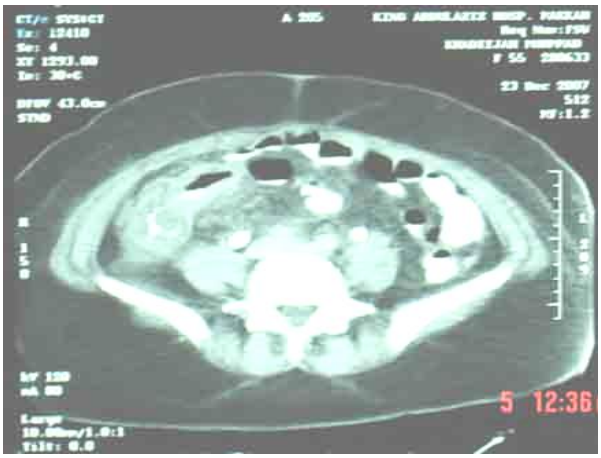


Most commonly communicating hydrocephalus is seen however obstructive hydrocephalus can be seen. Ischemic infarcts may be seen in basal ganglia and internal capsule. Tuberculomas may be seen on C.T. as variable sized, homogeneous or ring enhancing lesions with surrounding oedema (Figure No.5). M.R.I. appearance will depend whether tuberculoma is caseating or non caseating. Non caseating tuberculomas are often hyperintense on T_2 weighted images with homogeneous enhancement while caseating tuberculomas isointense to markedly hypointense on T_2 W images and exhibit ring enhancement[21].
This patient also had vertebral T.B.

Miliary tuberculosis:
It may appear as numerous rounded, homogeneously enhancing lesions less than 2 mm in diameter. Rare forms of parenchymal T.B. are cerebritis and abscess (sequelae of cerebritis). Contrast enhanced spinal meningitis may reveal nodular, thick, linear intradural enhancement. Syringomyelia can occur as complication of arachnoiditis and is seen as cord cavitation that typically demonstrates CSF fluid signal intensity on both T_1 and T_2 weighted images and does not enhance. CSF chemistry, AFB smears and culture are certainly helpful in diagnosis. CSF, PCR examination should not be done to exclude tuberculous meningitis as it has sensitivity of only about 56%[22].

4. Abdominal Tuberculosis:
Abdominal tuberculosis may involve gastrointestinal tract, peritoneum, mesenteric lymph nodes. Other organs like liver, spleen and adrenals usually are effected by miliary T.B.

Figure No. 6: Ileocecal Tuberculosis: C.T. abdomen with oral and I.V. contrast showed significant thickening of ileocecal region with relatively patulus ileocecal valve and peri ileocecal strandings. Few lymph nodes, not seen in this image, were also present.



Gastrointestinal Tuberculosis:
Tuberculous enteritis may result from swallowing of infected sputum or food. Hematogenous spread and extension from adjacent organs also seen. G.I. lesions are mainly ulcerative, however hypertrophic and ulcerohypertrophic types also seen. Pain, diarrhea, weight loss and malena is seen. Right lower quadrant mass with tenderness seen in 25-50% of patients.

Ileocecal and jejunoileal regions (90%) usually involved. Ultrasound, Barium studies and C.T. scan can delineate the lesions well. Thickening of the valve lips or wide gaping of the valve with narrowing of terminal ilium (The Fleischner sign) characteristically seen in tuberculosis. Greater thickening of wall and relatively larger ulcers are seen in T.B. rather than Crohn's disease. In advanced disease, characteristic deformities include symmetric annular "napkin ring" stenosis, obstruction, shortening, retraction and pouch formation. The caecum classically amputated. C.T. show thickening (circumferential or medial wall) of caecum and terminal ileum, enlargement of ileocecal value and mesenteric lymphadenopathy. Differential diagnosis of tuberculous enteritis includes Crohn's disease, Amoebiasis, Neoplasm, Yersinia infection and adinomycosis. Surgery is reserved for patients with complications.

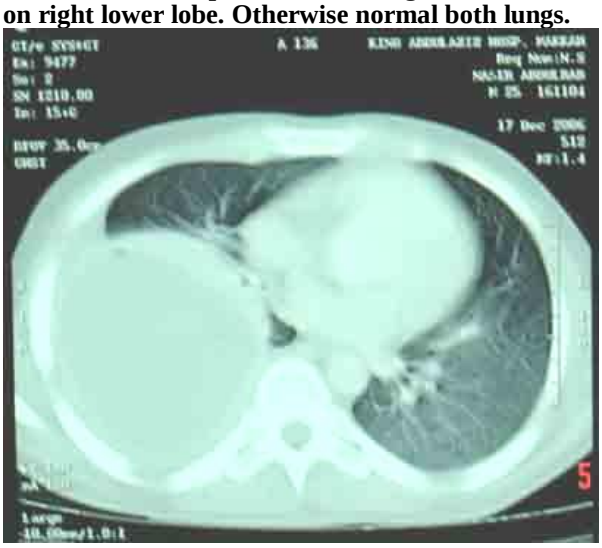
5. Genito-Urinary Tuberculosis:

Virtually all genitourinary organs can be involved by hematogeneous spread of tuberculous bacilli except testes which may be involved by direct spread from epididymis. Renal tuberculosis usually present with dysurea, hematuria or flank pain. More than 90% asymptomatic patients have sterile pyuria with or without microscopic hematuria. Intravenous urography may show moth eaten calyx due to erosion, followed by papilliary necrosis. Poor renal function, dilatation of pelvicalyceal system due to ureteropelvic junction stricture or focal dilatation due to infundibular stenosis can be seen. Cavitation / Cicatization may lead to calyceal or renal pelvic traction. C.T. may reveal renal calcification, calculi, scarring, hydronephrosis or evidence of extra renal disease. Culture of three morning specimens is about 90% diagnostic. Renal function is usually preserved except in tuberculous interstitial nephritis. End result may be autonephrectomy. Surgery may be reserved for persistant flank pain or hypertension[10]. Similar lesions can be found in acute focal bacterial nephritis, xanthogranulomatous pyelonephritis or with small benign and malignant lesions. Renal assessment is best achieved with I.V.U, U/S, C.T. or MR imaging[25]. Urethral or urinary bladder tuberculosis also seen with reduced bladder capacity. Calcified tuberculous cystitis may be differentiated from schistosomiasis, cyclophosphamide therapy, radiation induced changes and calcified urinary bladder carcinoma.

Male Genital Tuberculosis: May involved prostate, seminal vesicles, epididymis and testes. No specific radiological feature however MR may show diffuse, radiating, streaky areas of low signal intensity in prostatic T.B. (Water melon skin sign) on T_2 W images So diagnosis is usually made by biopsy / surgery.

Female genital tuberculosis: may involve fallopian tubes (94%), spreading to peritoneum, endometrium, ovaries, cervix and vagina. Response to chemotherapy is excellent for all form of genital tuberculosis. Surgery is necessary for large tubo ovarian abscesses.

Figure No. 7: Pleural Tuberculosis: C.T. chest, lung window revealed large loculated collection in right hemi thorax with pleural thickening and mass effect on right lower lobe. Otherwise normal both lungs.



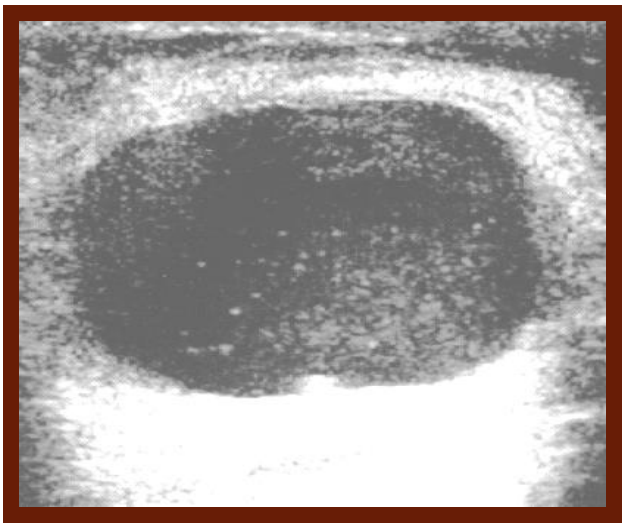
6. Pleural Tuberculosis:

More common in Eastern provinces and in non Saudi patients (only 34% Saudi patients). Usually presented with pleural effusion and diagnosed by pleural biopsy and pleural fluid analysis. On C.T. pleural effusion with non specific pleural enhancement and mild thickening is seen.

7. Breast Tuberculosis:

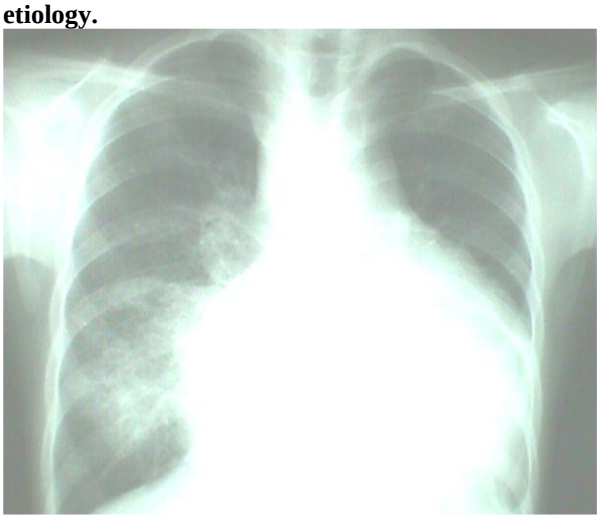
Is extremely rare, young, multiparous, lactating women are commonly affected. U/S reveals complex cyst / mass with sinus and abscess formation. Minimal debris and tiny calcification are pathognomonic (Figure No.8). Mammography is non specific.On MRI, parenchymal asymmetry with enhancement, microabscesses and peripherally enhanced mass can be seen.

Figure No. 8: Breast tuberculosis: 35 years female, a well defined, thick walled hypoechoic lesion with debris, peripheral tiny calcification and posterior acoustic enhancement.



8. Pericardial Tuberculosis:
Most common cause (80-85%) of constrictive pericarditis, though rare may be found in adolescent to young patients (Figure No. 9). In studies from Riyadh and Jeddah, it was found to be 3% and 1% of pericardial diseases respectively.
Other regions like parotids, pancreas and sternum have also been reported for tuberculous involvement.

Figure No. 9: Tuberculous Pericarditis: 13 years old male with right mediastinal distortion, lower lobe consolidation (non tuberculosis) and cardiomegaly. Aspiration cytology proved to be of tuberculosis etiology.



CONCLUSION

The clinical and radiological features of extra-pulmonary tuberculosis may clue to the diagnosis as many other diseases can mimic the imaging. So a high index of suspicion is required, especially in high risk population and some times in patients who are not responding to conventional antibiotic therapy. Routine laboratory investigations like ESR and tuberculin test may support the diagnosis. A positive culture, PCR, Deaminase test and histopathological analysis of biopsy specimen may still be required in many patients to yield the definitive diagnosis. Recognition and under standing of spectrum of imaging features of extrapulmonary tuberculosis can aid in diagnosis, especially with experience as some regional involvement may have classical imaging findings. Radiological imaging not only helps in diagnosis of the extrapulmonary disease, it can be used as follow up analysis with full confidence to see the progress of disease after proper chemotherapy. The patterns of extrapulmonary tuberculosis may vary due to extent of disease involvement otherwise inclination of region involvement is same everywhere. Extrapulmonary tuberculosis is relatively less in Saudi patients (from 1:2 to 1:3 depending upon regions) as compared to non Saudi patients.

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