

## Tuberculous Synovitis and TB-Dilated Cardiomyopathy Case Report of a Rare, Fatal and Possibly Reversible Complication of Extra Pulmonary Tuberculosis With Literature Review

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**Background:** Tuberculosis (TB) is a common public health problem in many parts of the world and despite being almost 100% curable, TB is still a leading cause of morbidity and mortality worldwide, representing second most common cause of death from infectious disease globally after HIV. TB is generally believed to spare four organs: heart, skeletal muscle, thyroid and pancreas. Dilated Cardiomyopathy is a multi-factorial disease; early detection and defining the exact etiology/etiologies are still a big challenge in the medical wards all over the world. Involvement of the heart with TB occurs in one to two percent of patients with TB, TB myocarditis may occur by hematogenous, lymphatic spread or directly from the contagious structures like pericardium. Commonest site involved is the pericardium, and tuberculous involvement of the myocardium was thought to be extremely rare. However, here we present a case mortality summary of patient presented with severe dilated Cardiomyopathy and congestive heart failure, work up and emergency investigations specially echocardiography, sequence of events and radiological changes e.g. X-ray images managed to attribute the cause of the rapid and fatal deterioration of the patient condition to delayed unrecognized TB myocarditis and Dilated Cardiomyopathy.

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**Key words:** Tuberculous synovitis, TB myocarditis, dilated Cardiomyopathy.

### Case Report:

A 17 year old female patient known case of childhood bronchial asthma, presented to emergency department of King Abdul-Aziz Hospital "Jeddah" at 15/1/2015 complaining of severe Shortness of breath, diarrhea, and abdominal pain for one week duration.

One week before last presentation, she started to develop vomiting (more than 6 times a day) of food contents without blood, associated with watery diarrhea more than 10 times/day and colicky abdominal pain. On this last admission, the patient presented with left sided chest pain increasing with inspiration, cough and greenish sputum but no hemoptysis. There was also fever, night sweats, weight loss, decreased appetite, palpitations and easily fatigability.

Patient was admitted two months earlier to this presentation under care of orthopedics because of a right elbow abscess and synovitis, incision and drainage were done under anesthesia and histopathological examination of the excisional biopsy report was as follow: fibro fatty tissue with granulomatous changes having central necrosis and exhibiting massive infiltration by mixed inflammatory cells, epithelioid cells and multinucleated giant cells with large area of necrosis (caseation), no evidence of

malignancy, and according to that the diagnosis of TB synovitis was established and accordingly our pulmonologist recommended routine Mantoux interadermal test (PPD), (since pulmonary involvement with TB was not observed in the patient's symptoms, nor imaging, and the sputum was also negative for acid-fast bacilli, the result of PPD test was severe induration response at third day and according to all that the pulmonologist decided to start anti TB medications. During that admission there was chest X-ray (CXR) done and revealed mild cardiomegaly, clear both lung fields, as well as the costophrenic angles, so some investigations including echocardiography to assess the 'mildly cardiomegalic' x-ray accidental finding was recommended (figure 1b).

Upon the patient dramatic improvement after the synovial TB abscess drainage and commencing the anti TB medications the patient's family urged an early discharge at home for social reasons and requested scheduling appointments at cardiology and echocardiography clinic...patient was discharged upon family responsibility and after being well informed about necessity of continuous follow up scheduling program on our outpatients pulmonology, orthopedic, and special concerns to attend the

echocardiography early appointment for further assessment of her x-ray accidental finding of " mild cardiomegaly "...The patient wasn't compliant to her Anti TB medications and the family did not bring the patient for her follow up schedule nor the echocardiography booked date!

On examination patient was conscious, but confused, agitated, looking ill, cachectic and pale, orthopnic, Tachypnoic respiratory rate 33/min, and temperature was 37.2<sup>o</sup>c, her blood pressure was 75/53, pulse was 130/min irregularly irregular and oxygen saturation was 92% on room air. Apex beat was diffuse and displaced to left 6<sup>th</sup> intercostal space, Muffled both first & second but no murmurs or additional sounds. Mild lower limbs edema, there was also diminished air entry bilaterally, some scattered rhonchi, and generalized coarse crepitations. Abdomen was soft and lax, right lobe of liver was tender and pulsatile, palpable 2 cm below right costal margin (mild hepatomegaly), Spleen not palpable.

There were no signs of meningeal irritations or any focal neurological deficits, Emergency lab work revealed: White blood cells count was  $7.66 \times 10^9$ /L with relative lymphocytosis, hemoglobin was 8.7 gm/dl, platelets was 156000, Reticulocytes of 2.06%. Urea& Electrolytes results: Na= 132mmol/L, K= 4.5mmol/L, urea= 7.5mmol/L, creatinine, Liver function tests were as follows: AST= 83 U/L, ALT= 42 U/L, ALP 176 U/L, albumin = 19 g/L, total bilirubin 25.1 micromole /L, Direct bilirubin 13.22 micromol/L, ESR = 73 mm, LDH 347 mg/dl, Serology for HBV, HCV, HIV was negative (done at the previous admission). Chest X-ray imaging revealed huge cardiomegaly (figure 1c), Electrocardiogram (ECG) showed rapid AF (around 120/min) (figure2). Sputum for acid-fast bacilli again was negative again.

Echocardiography showed Impaired left ventricular (LV) systolic function with ejection fraction 24%, global hypokinesia, Paradoxical septal wall motion, dilated left atrium and right sided chambers, dilated left ventricle with large LV apical thrombus, mild pericardial effusion, Severe tricuspid regurgitation with pulmonary hypertension and moderate to severe mitral regurgitation(figure3).

Our provisional diagnosis was congestive heart failure secondary to Dilated Cardiomyopathy (DCM) ...

Possible etiologies: TB DCM!!! Heridofamilial DCM, Toxic DCM, Autoimmune collagen associated DCM, Drug induced DCM, and idiopathic DCM.

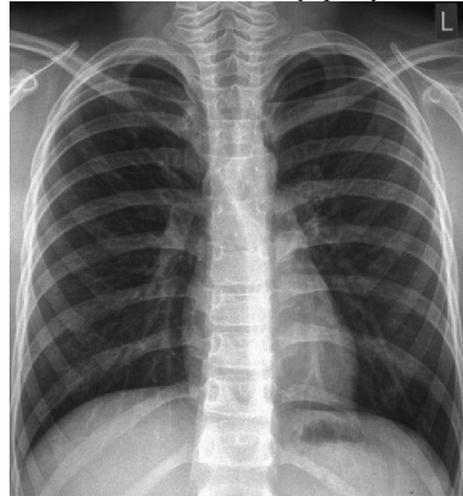
Patient was immediately admitted to CCU and management plan was urgently performed including: Dopamine infusion, CCU admission, Cardiology consultation, ICU consultation, Rheumatology consultation, Anti TB medications, ceftriaxone,

enoxaparin, furosemide, spironolactone, digoxin, Captopril and trying to arrange referral to tertiary care center. MRI delayed enhancement technique was arranged immediately but unfortunately patient condition & urgent ventilation made this helpfully diagnostic technique inconvenient.

Meanwhile, central line inserted, dopamine and dobutamine infusion increased but BP still low (65/45) Patient desaturated (95% to 92% to 88%) 20 hours after admission together with deterioration of her conscious level (Glasgow coma score 11/15 to 9/15). Patient serial ECGs show Rapid AF rate 159 - 165 / min. Patient was intubated with more intense inotropes by ICU for 20 hours. Patient arrested 3 times (within 5 hours) and could not revive the last cardiopulmonary resuscitation (CPR).

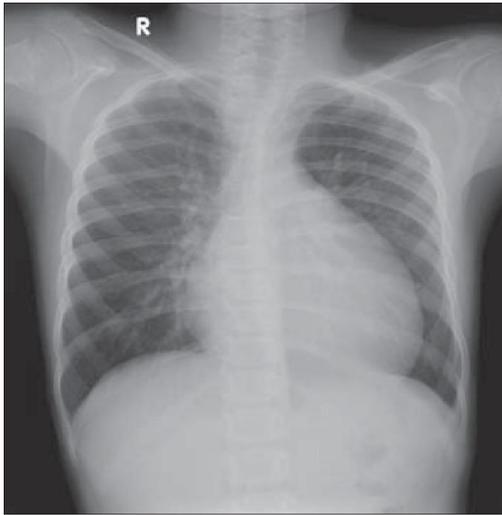
Request for autopsy was refused by the family.

The previous history documented in the patient file including normal chest X-ray (figure 1a) and echocardiography (done in her early childhood at age of 10 while in her follow up for childhood asthma), plus the X-ray changes from mild to huge cardiomegaly in two months (from first to the second admission) (figure1b, 1c), were all much supportive to the clinical diagnosis of this rare presentation of TB myocarditis and dilated Cardiomyopathy.

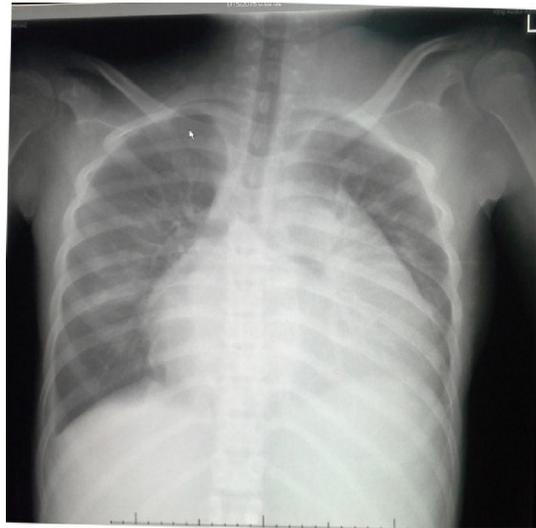


**Figure 1a: CXR of the patient when she was 10 year old showing normal chest X-ray**

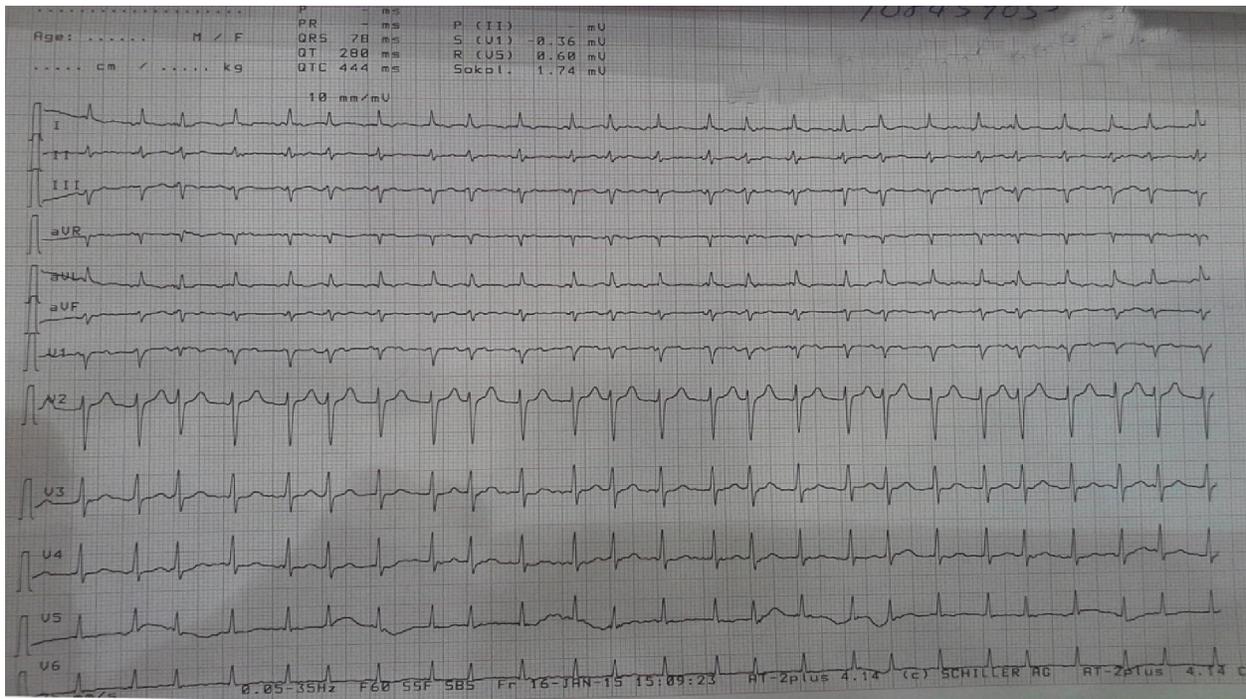
Despite the family reluctance seen in this scenario, when patient condition seems terminal, communication part of medicine & support are the only things can be done, especially when further Advanced management procedures (e.g. Heart Transplantation, or Ventricular Assisting devices VADs) are unavailable. Unavailability of those high technical procedures/devices is still beyond health care service capabilities in most cardiac centers all over the world.



**Figure1b: Chest X-Ray showing mild cardiomegaly of the patient at orthopedic admission**



**Figure1c: Chest X-Ray (2month later) showing huge cardiomegaly with no lung opacifications and clear costophrenic angle.**



**Figure 2: ECG showing rapid Atrial Fibrillation (rate around 135/min).**



**Figure 3: 2-D echocardiography showing 4 chambers view with LV apical thrombus along with 4 chambers dilatation.**

#### **Discussion:**

Involvement of the heart in TB occurs in one to two percent of patients with TB. TB myocarditis may occur by hematogenous, lymphatic spread or directly from the contagious structures like pericardium<sup>(1,2)</sup>.

Commonest site involved is the pericardium and tuberculous involvement of the myocardium is extremely rare<sup>(1)</sup>, however, case reports are emerging from few medical centers describing the same condition<sup>(2-5)</sup>. The earliest description was in 1664 by Maurocordat and the second was in 1761 by Morgagni<sup>(6)</sup>. The rarity of this condition can be explained by effective anti TB medications in the last century. However, recent emergence of many case reports in the last two decades<sup>(2-5)</sup> can be explained by: the availability endomyocardial biopsies, postmortem autopsies, gene mapping studies either confirming or ruling out diagnosis of myocardial involvement by TB, MRI recently is advancing criteria for diagnosis of TB myocarditis with less invasiveness than the impractical rarely used endomyocardial biopsy approach<sup>(3)</sup>. Myocardial TB was often undiagnosed during life<sup>(2)</sup>, and confirmation of this entity needed evidence based tissue diagnosis by endomyocardial biopsy<sup>(2)</sup>, and the main histopathological pattern described in TB myocarditis: tuberculoma with central caseation, miliary tubercles spreading from miliary TB, or most rarely, diffuse infiltrative type associated with TB myocarditis<sup>(7)</sup> but with emergence of the advancing radiological imaging especially cardiac MRI enhancement technique<sup>(3)</sup> the diagnosis of TB myocarditis has become easier, earlier and more useful for patient's prognosis than before. TB myocarditis can manifest in various forms : the right

atrial and right ventricular involvement are the most affected, most probably due to frequent involvement of the nearby right mediastinal lymph nodes<sup>(8)</sup>, rhythm disturbances like supraventricular tachycardia SVT, Ventricular arrhythmias, attributed to left ventricular involvement had been published in many series<sup>(9,10)</sup>.

In our case study, various arrhythmias had been observed: Atrial fibrillation, Ventricular tachycardia, and ventricular fibrillation during monitoring and intensive care management, the four chamber enlargement associated with severe mitral and tricuspid regurge is the most arrhythmogenic and serious form of DCM carrying the worst prognosis with the poorest chance for reversibility. Other forms of arrhythmias had been rarely reported like complete heart block CHB due to AV nodal involvement<sup>(11)</sup> and other various degrees of Heart block<sup>(12)</sup>. Other patterns of cardiac involvement like right ventricular outflow obstruction<sup>(13)</sup>, ventricular aneurysms<sup>(14)</sup> or ventricular pseudoaneurysms<sup>(15)</sup> has also been reported.

The coincidental paradoxical anti TB medications response phenomenon<sup>(16)</sup>, where pulmonary or extra pulmonary TB lesions (like TB synovitis) improve while paradoxical deterioration of cardiac muscle contractility and development of Dilated Cardiomyopathy had been observed in the chronological sequence of events in our case study as well as in similar many case reports<sup>(2)</sup>, all research work up failed to explain the exact etiology of this phenomenon, however Immunorestitution phenomenon has been suggested as a possible explanation<sup>(16)</sup>. In patients with active *Mycobacterium*

*tuberculosis* infections, there is a biased T-helper2 immune response as evident by an increase in the percentage of interleukin-4 and interleukin-10 positive lymphocytes together with a low percentage of interleukin-12 positive lymphocytes in the peripheral blood, especially in those patients with tuberculin anergy<sup>(17)</sup>. Furthermore, purified protein derivative stimulated production of interferon-gamma by peripheral blood mononuclear cells was depressed, whereas levels of transforming growth factor-beta and interleukin-10 were increased<sup>(18)</sup>. However, when the mycobacterial load was significantly reduced after the initiation of anti-tuberculosis therapy, the cellular and cytokine patterns reverse which may result in an inflammatory response leading to a paradoxical phenomenon<sup>(16)</sup>. Immunorestitution changes of subclasses of T lymphocytes is not much reflected on total lymphocytic count in peripheral blood and this may explain the difficulty in predictability of Immunorestitution occurrence. However, The clinical severity of paradoxical deterioration is dependent on the exactness and appropriateness of immune recovery<sup>(16)</sup>. An overwhelming Immunorestitution may produce excessive immunopathological damage at the tissue level<sup>(19)</sup>. Paradoxical deterioration more frequently occurs in patients with extra pulmonary involvement but (contrary to our case presentation) is usually associated with a lower lymphocytes counts at the baseline<sup>(20)</sup>. Again, this proves that total lymphocytic count is not reliable for prediction of this phenomenon... Suggestive initial glucocorticoids administration together with the anti TB medications especially in extensively affected TB patients like miliary TB is an "non- evidence based" yet commonly used protocol in many centers and its role in prevention of paradoxical cardiac involvement needs further research work up to confirm its value in TB management.

### Conclusion:

Tuberculosis (TB) is a common public health problem in many parts of the world and despite being almost 100% curable, TB is still a leading cause of morbidity and mortality worldwide, representing second most common cause of death from infectious disease globally after HIV.

Involvement of the heart with TB occurs in one to two percent of patients with TB, TB myocarditis may occur by hematogenous, lymphatic spread or directly from the contagious structures like pericardium. Commonest site involved is the pericardium, and tuberculous involvement of the myocardium was thought to be extremely rare. However, the rarity of myocardial TB and TB DCM needs to be reconsidered in the literature and research work, since the reported cases of myocardial TB in

many different parts of the world was found in the last decades with different modalities of diagnosis (including endomyocardial biopsies, the delayed enhancement MRI technique of imaging of the myocardium or by clinical suspicion and diagnosis), or at autopsies. Different forms and presentations of TB (either pulmonary or extra pulmonary TB like TB synovitis) may end up with further extra pulmonary fatal complication as TB-DCM during the course of illness and during recovery. This makes TB-DCM an under- diagnosed entity that should be focused on for prevention and/or early diagnosis, and management.

In addition, the actual prevalence of TB myocarditis and TB-DCM may explain a modest percentage of mortalities in TB patients, together with the paradoxical anti TB medications response phenomenon (Immunorestitution), where pulmonary or extra pulmonary TB lesions improve while paradoxical deterioration of cardiac muscle contractility and development of dilated Cardiomyopathy occurs, as been observed in the chronological sequence of events in our case study as well as in many similar case reports, **proving again that "many diseases are there, while the physicians are not yet"**.

### References:

1. Wallis PJW, Branfoot AC, Emerson PA: Sudden death due to myocardial tuberculosis. *Thorax* 1984, 39:155.
2. Agarwal, R., Malhotra, P., Awasthi, A., Kakkar, N., & Gupta, D. (2005). Tuberculous dilated cardiomyopathy: an under-recognized entity? *BMC Infectious Diseases*, 5, 29.
3. Dixit, R., Chowdhury, V., & Singh, S. (2009). Case report: Myocardial tuberculosis-MRI. *The Indian Journal of Radiology & Imaging*, 19(1), 57-59.
4. Barman, B., Mishra, A., Ete, T., Jha, P. K., Warjri, S. B., Lynrah, K. G., & Beyong, T. (2015). Tuberculosis and Dilated Cardiomyopathy-Case Report of a Rare Entity with Literature Review. *American Journal of Medical Case Reports*, 3(2), 49-52.
5. Njovane X. Intramyocardial tuberculosis-a rare underdignosed entity. *South African Medical Journal* 2009; 99 (3): 152-153.
6. Rose AG: Cardiac tuberculosis: a study of 19 patients. *Arch Pathol Lab Med* 1987, 111:422-426.
7. Horn H, Saphir O: The involvement of the myocardium intuberculosis: a review of the literature and report of threecases. *Am Rev Tuberc* 1935, 32:492-506.
8. Maeder M, Ammann M, Rickli H, Schoch OD: Fever and night sweats in a 22-year-old man with

- a mediastinal mass involving the heart. *Chest* 2003, 124:2006-2009.
9. Bali HK, Wahi S, Sharma BK, Anand IS, Datta BN, Wahi PL. Myocardial tuberculosis presenting as restrictive cardiomyopathy. *Am Heart J* 1990; 120: 703-6.
  10. Kapoor OP, Marcarenhas E, Rananaware MM, Gadgil RK: Tuberculoma of the heart. Report of 9 cases. *Am Heart J* 1973,86:334-340.
  11. Kinare SG, Deshmukh MM: Complete atrioventricular block due to myocardial tuberculosis. Report of a case. *Arch Pathol* 1969, 88:684-687.
  12. Kinare SG: Interesting facets of cardiovascular tuberculosis. *Indian J Surg* 1975, 37:144-151.
  13. Rawls WJ, Shuford WH, Logan WD, Hurst JW, Schlant RC. Right ventricular outflow tract obstruction produced by a myocardial abscess in a patient with tuberculosis. *Am J Cardiol* 1968, 21: 738-745.
  14. Kinare SG, Bhatia BI: Tuberculous coronary arteritis with aneurysm of the ventricular septum. *Chest* 1971, 60:613-616.
  15. Halim MA, Mercer EN, Guinn GA: Myocardial tuberculoma with rupture and pseudoaneurysm formation: successful treatment. *Br Heart J* 1985, 54:603-604.
  16. Cheng, V. C. (2006, January). Paradoxical Response during Anti-tuberculosis Therapy. *The Hong Kong Medical Diary*, 11, 20-21.
  17. Baliko Z, Szereday L, Szekeres-Bartho J. Th2 biased immuneresponse in cases with active Mycobacterium tuberculosis infection and tuberculin anergy. *FEMS Immunol Med Microbiol*. 1998 Nov;22(3):199-204.
  18. Hirsch CS, Toossi Z, Othieno C, Johnson JL, Schwander SK, Robertson S, Wallis RS, Edmonds K, Okwera A, Mugerwa R, Peters P, Ellner JJ. Depressed T-cell interferon-gamma responses in pulmonary tuberculosis: analysis of underlying mechanisms and modulation with therapy. *J Infect Dis*. 1999 Dec;180(6):2069-73.
  19. Cheng VC, Yuen KY, Chan WM, Wong SS, Ma ES, Chan RM. Immunorestitution disease involving the innate and adaptive response. *Clin Infect Dis*. 2000 Jun;30(6):882-92.
  20. Cheng VC, Yam WC, Woo PC, Lau SK, Hung IF, Wong SP, Cheung WC, Yuen KY. Risk factors for development of paradoxical response during antituberculosis therapy in HIV-negative patients. *Eur J Clin Microbiol Infect Dis*. 2003 Oct;22(10):597-602.

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