PERICARDIAL EFFUSION AS A PARADOXICAL RESPONSE TO THERAPY FOR MEDIASTINAL LYMPH NODE TUBERCULOSIS: CASE REPORT

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ABSTRACT
Paradoxical response occurring in a patient of tuberculosis leading to the development of new lesions is a well known phenomenon. However, pericardial effusion occurring due to paradoxical response in an immunocompetent patient is a rare phenomenon. We report a case of paradoxical response in a 19 year old girl who was on anti-tuberculosis treatment for mediastinal lymph node tuberculosis. The patient had resolution of mediastinal lymphadenopathy by anti-tuberculosis treatment, but developed pericardial effusion subsequently. She responded to the addition of oral prednisolone to her regimen.

KEYWORDS: Pericardial effusion, mediastinal lymphadenopathy, tuberculous, paradoxical response.

1. INTRODUCTION
Paradoxical response is development of previously nonexistent lesions or worsening of pre-existing lesions during appropriate anti-tuberculosis treatment (ATT). This phenomenon is reported among patients with tuberculosis of the central nervous system, lymph nodes, lungs and pleura. This immune mediated process needs to be recognised early, to avoid an unnecessary modification of ATT. We searched for a case of pericardial effusion occurring as paradoxical response to ATT for mediastinal lymph node tuberculosis but to the best of our knowledge, only one such case has been reported till now in world literature. We are reporting this case in view of rarity and the need for awareness of this phenomenon.

2. CASE REPORT
A 19 year old female was admitted with chief complaints of progressively increasing breathlessness since the last 1 month followed by orthopnea and low grade fever since the last 15 days. On initial examination, her respiratory rate was 24/minute, pulse rate was 92/minute and BP was 90/60 mm Hg. Her oxygen saturation was 92%. JVP was elevated and a positive hepatojugular reflux was elicited. Auscultation revealed diminished heart sounds and pericardial friction rub.

Laboratory investigations revealed Hb of 11g/dl; RBC count of 4.72 Million/mm³, WBC count of 9600/mm³ with polymorphs 61%, lymphocytes 35%, eosinophils 3% and monocytes 1%, platelet count of 2.15 lac/mm³ and an ESR of 45mm. She was seronegative for HIV and non diabetic. Her immunology profile (ANA, RF factor, ANCA) and s.ACE were within normal limits. Chest x ray PA view revealed cardiomegaly. CECT thorax revealed pericardial effusion and normal cardiac chambers.

Echocardiogram revealed 15 mm thick effusion and no evidence of cardiac tamponade or constrictive pericarditis. An Echo guided pigtail catheter insertion was done and a total of 800 ml of straw-colour pericardial fluid was drained. Pericardial fluid was sent for biochemical and microbiological investigation. Pericardial fluid investigation were reported as: TLC 1100 cells/mm³, DLC-lymphocyte 80% and neutrophil 20% protein 5.4 gm/dl, sugar 80 gm/dl and ADA 72 IU/ml.
Pericardial fluid was negative on ZN and Gram staining and aerobic cultures were sterile. Her sputum was AFB negative on smear. Her past history and treatment history revealed that the patient had developed low grade fever and loss of appetite/weight for 3 months, 4 months back and had undergone a full work-up at previous centre. CECT thorax had revealed mediastinal and hilar lymphadenopathy with 17 mm induration on PPD administration. She was subsequently started on ATT regimen comprising of Rifampicin 450mg, Isoniazid 300 mg, Ethambutol 800mg and Pyrazinamide 1000 mg by physician at the previous centre to which she had responded clinically and radiologically on serial chest x rays.

Pyrazinamide and Ethambutol were stopped after 3 months by the treating physician. After 4 months of treatment, she started developing abovementioned symptoms which increased over 15 days and she was referred to our centre. She no intolerance or interruption during her period of ATT. The patient responded well to pericardial fluid drainage with the subsidence of breathlessness and chest pain. We continued Rifampicin 450mg and Isoniazid 300mg and started her on tablet Prednisolone 40 mg in a dosage of 1mg/kg body weight. Fever subsided over two weeks and she was discharged subsequently, with prednisolone tapered over next two weeks and stopped. The patient responded to the treatment, with no recurrence of symptoms or any signs of deterioration when last followed up, one month after discharge. Her chest x ray PA view one month after discharge showed resolution of pericardial effusion and no new lesions. Subsequently, we stopped her ATT after total duration of therapy of 9 months.

3. DISCUSSION

"Paradoxical response" in tuberculosis is defined as transient worsening of disease at a pre-existing site, or the development of new lesions in a patient who initially improved during successful anti tuberculosis therapy (ATT). Another term often used is immune reconstitution inflammatory syndrome (IRIS). However, the term IRIS should be reserved for paradoxical responses in HIV seropositive patients due to anti retroviral therapy, while the term paradoxical response is used in both HIV-seropositive and –seronegative patients in whom ATT has been initiated. Although this phenomenon is more common and severe in HIV co-infected individuals, 2% to 15% of HIV-negative patients infected with TB will experience paradoxical worsening during treatment. It is seen more frequently in patients with extra-pulmonary TB, and among those with low baseline lymphocyte counts. Paradoxical responses develop between 4 weeks and 18 months after the initiation of ATT.

The mechanism for this phenomenon remains unclear and it remains a diagnostic dilemma. Rapid killing of bacilli by effective ATT can cause the release of large amounts of tuberculoprotein and other cell wall products. Hypersensitivity to tuberculoproteins released from the dying mycobacteria and enhanced focal immune responses (immunological rebound) will recruit lymphocytes and macrophages at the site of previously inactive tuberculous foci which enlarge and then become evident.

This immunological explanation is supported by a relatively low mycobacterial culture rate from the paradoxically expanded lesions and significant resolution of the paradoxical response after use of steroids. The overall inflammatory response to Mycobacterium tuberculosis would reflect the number and function of immune cells and the amount of antigen that they encounter. The severity and frequency of paradoxical response would therefore be higher if disseminated or extensive single organ disease was present.

Paradoxical response is a diagnosis of exclusion, made after noncompliance, drug resistance, drug fever, alternative diagnoses or progression of original disease have been
FIG:1 CT Thorax before ATT showing mediastinal lymphadenopathy.

FIG:2 CT Thorax showing pericardial effusion and resolution of lymph nodes while on ATT

FIG:3 CXR PA after adding steroid to ATT showing resolution of pericardial effusion
ruled out. The patient experienced an initial clinico-radiological improvement with anti- tuberculous therapy so the phenomenon known as the paradoxical response was suspected. On taking the patient's treatment history meticulously, she revealed that she was regular in her ATT intake and a perusal of prescriptions revealed that ATT was according to weight and of reputed brand. Her mediastinal lymphadenopathy had responded to the ATT without any modification of regimen, ruling out drug resistance, treatment failure or progressive disease. During paradoxical response, she defervesced even while ATT was continued, ruling out drug fever. She was not positive for markers of any other disease and had a successful treatment outcome with ATT; ruling out any alternative diagnosis. We propose that in our patient, successful ATT for mediastinal lymph node tuberculosis, led to enhanced focal immune response causing accumulation of inflammatory exudates at previously invisible microscopic tuberculous foci in her pericardium, appearing as pericardial effusion. The diagnosis of paradoxical response in our patient was based on temporal correlation of occurrence of symptoms with continuation of ATT, absence of any other aetiology on exhaustive investigations and rapid resolution of pericardial effusion on adding steroid to ATT.

She had taken ATT for a longer than recommended duration from previous centre but paradoxical response requires continuation of ATT till the crisis is over. Mild to moderate paradoxical response can be treated symptomatically with continuation of anti-tuberculosis therapy. For severe responses, corticosteroids are added (prednisone 1mg/kg/d for 1–2 weeks followed by a taper). Pericardial effusion is a rare manifestation of paradoxical response in non HIV patients. Extensive search of world literature revealed only one case of pericardial effusion occurring as paradoxical response to ATT in a non HIV person till date. Our case report emphasises the importance of recognising the phenomenon of paradoxical response and diligently differentiating it from treatment failure in order to avoid unnecessary modification of the drug regimen.

4. CONCLUSION

Paradoxical response is a problem for physician and the patient both. It complicates the disease course of tuberculosis during treatment. It has to be diagnosed by exclusion, and therefore poses a challenge to the physician. One should have a high index of suspicion when there is clinical deterioration after an initial improvement with ATT. It might be useful to discuss with patients at time of diagnosis that there will be a possibility of paradoxical reaction.

5. REFERENCES


