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Case Report

Primary Multi Drug Resistant Tuberculosis (MDR TB) Osteomyelitis in Sternum associated with Xeroderma Pigmentosa: A Case Report

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Abstract

Xeroderma Pigmentosa (XP) is an autosomal recessive genetic disorder which causes defective gene repair. This makes XP patients cancer-prone and immunodeficient. A 10-year-old male child with XP was infected with MDR Tubercular Osteomyelitis of sternum. He had constitutional symptoms of TB like weight loss and loss of appetite. He had also developed an abscess in his right pectoral muscles. MRI was done to find out exact location and spread of infection. The abscess was aspirated by Z technique and sent for a Gene Xpert test. Patient was started on second line of anti-tubercular therapy. MDR TB is a growing challenge to treat with anti-tubercular therapy. The link of genetic disorders like XP and infections like TB (which increase in immuno-deficient subjects) needs to be studied further.

Keywords: Immunodeficiency, Multidrug resistant Tuberculosis, Pectoral muscle cold abscess, Xeroderma Pigmentosa

Introduction

A rare autosomal recessive genetic disease, Xeroderma Pigmentosum (XP) starts in the childhood. Clinically, it develops as cutaneous photosensitivity and pigmentary changes in UV exposed areas of the body[1]. DNA damage that is unrepaired and unresolved by the mutated XP genes leads to an increased risk of development of cancer[2]. Continued exposure to UV radiation may lead to development of skin cancer[1]. In 30% of XP patients, there is also development of neurological disorders with more chances for CNS neoplasms[3,4]. Patients with XP have reduced interferon IFN-γ production, lower natural killer (NK) cell activation, and less circulating T cell numbers. These NK cells and T cells are important in preventing infection and neoplasm[5-8]. The ratio of CD3+ to CD4+ circulating lymphocyte is reduced in XP[8]. Studies have shown the role of an inhibitory serum factor to Phytohemagglutinin (PHA) stimulation in XP patients which might cause a serious hampering of the delayed hypersensitivity response[6].

Activated macrophages are the main effector cells involved in the elimination of *M. tuberculosis*. This activation of macrophages is clearly led by lymphocyte products, mainly IFN-γ, and proinflammatory cytokines like TNF-α[10]. Delayed hypersensitivity is a major mechanism of defense against many intracellular pathogenic organisms. These include mycobacteria, fungi, and certain parasites[11]. Immunodeficiency in XP patients is not only associated with increased chances of neoplasms, but also increased susceptibility to infections like tuberculosis.

Case Presentation

A ten-year-old child suffering from XP (Figure 1), started having pain in sternum. Patient had constitutional symptoms of weight loss and loss of appetite. Patient got excoriation on skin near sternal notch. This developed into a non-healing ulcer. Later he started having swelling in right pectoral region

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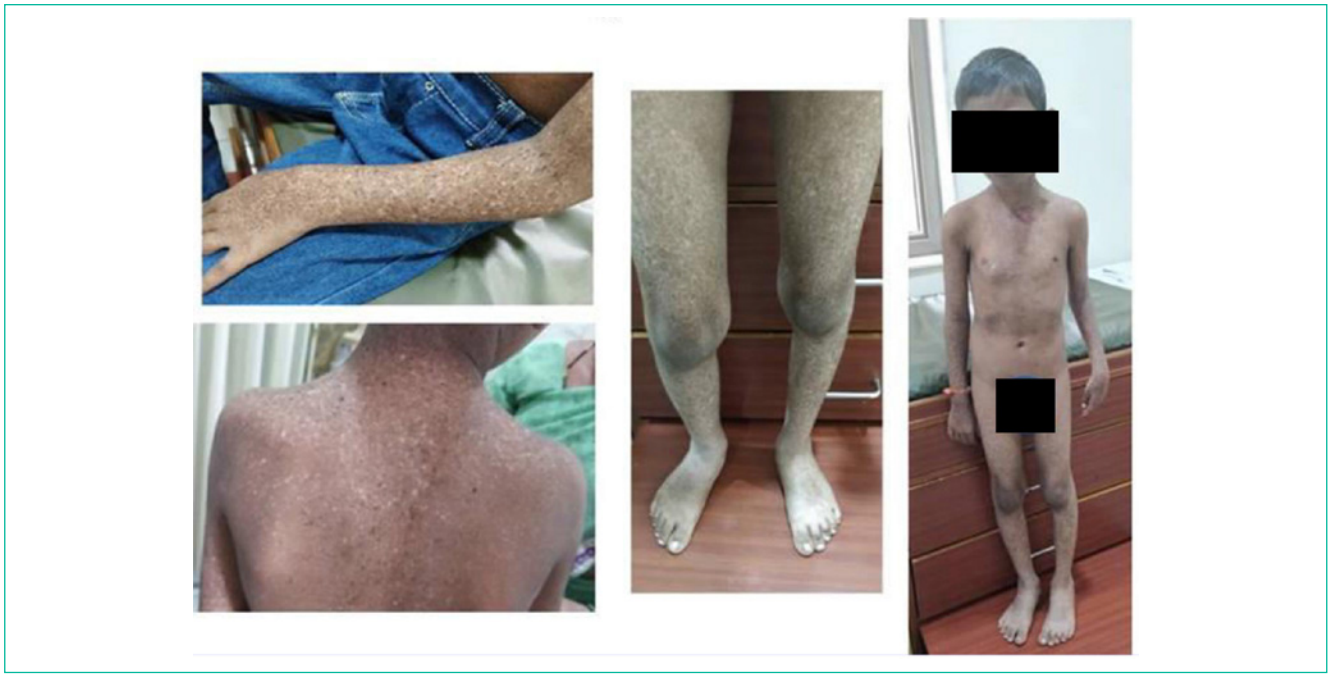

Figure 1. Skin manifestations of Xeroderma Pigmentosa (XP).

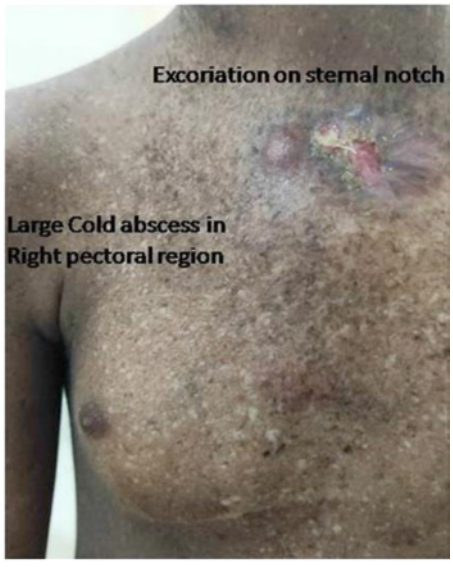

Figure 2. Non-healing ulcer on sternal end and large pectoral cold abscess swelling.

which gradually increased in size in 5 months' time. (Figure 2). He was investigated with blood tests, chest X-ray (Figure 3), CT scan (Figure 4) and Ultrasound scan (Figure 5).

The swelling in pectoral region was fluctuant and no local warmth or gross tenderness on swelling was appreciated. The nodes were non tender, painless, matted and adherent to the underlying structures. No other lymphadenopathy was found on examination.

The patient was found to be anemic with hemoglobin of 8.9 gm/dl and total leucocyte count was 7900/mm^3. His ESR (Erythrocyte sedimentation rate) had raised to 110 mm/hr. HIV ELISA test was negative (Table 1). Ultrasound showed a large abscess of 57 cc which extended from the sinus in suprasternal region to right anterior chest wall. A plain and post contrast CT scan showed 8 cm x 6.2 cm x 2 cm in sternal region. The abscess extended into the right pectoralis muscle. There was destruction of manubrium with sclerosis. Serum Albumin was deficient with level of 2.5 gm%. Rest all liver function tests and renal function tests were normal.

The patient was aspirated by a 16-gauge needle by Z-track technique (to prevent sinus tract formation). 6 ml of thick pus was aspirated. The pus was sent for MGIT (Mycobacteria growth indicator tube) test and Gene Xpert test along with culture and sensitivity. All methods detected Multi drug resistant TB with low grade rifampicin resistance. No surgery was performed on the patient. Patient was started on second line of anti-tubercular therapy based on protocols set by RNTCP in India (Table 2). The drug regimen for the patient was as follows:

Intensive Phase: Km Eto Cs Z Lfx E (6 months)

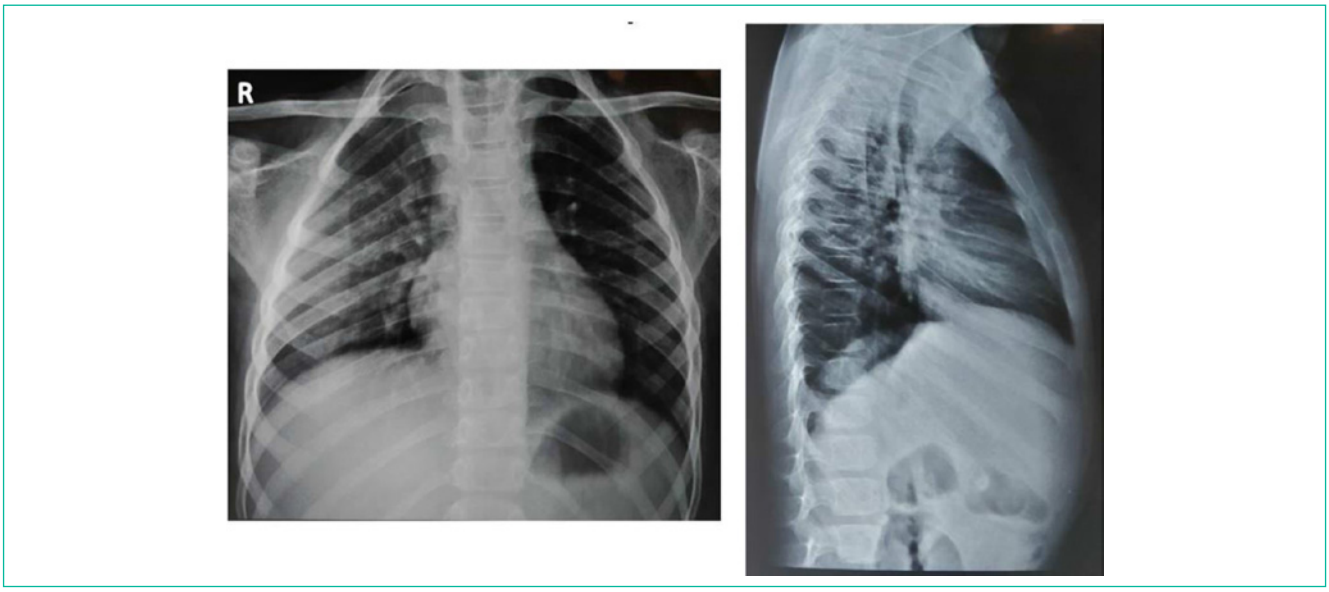

Figure 3. X-Ray AP and Lateral view of Chest.

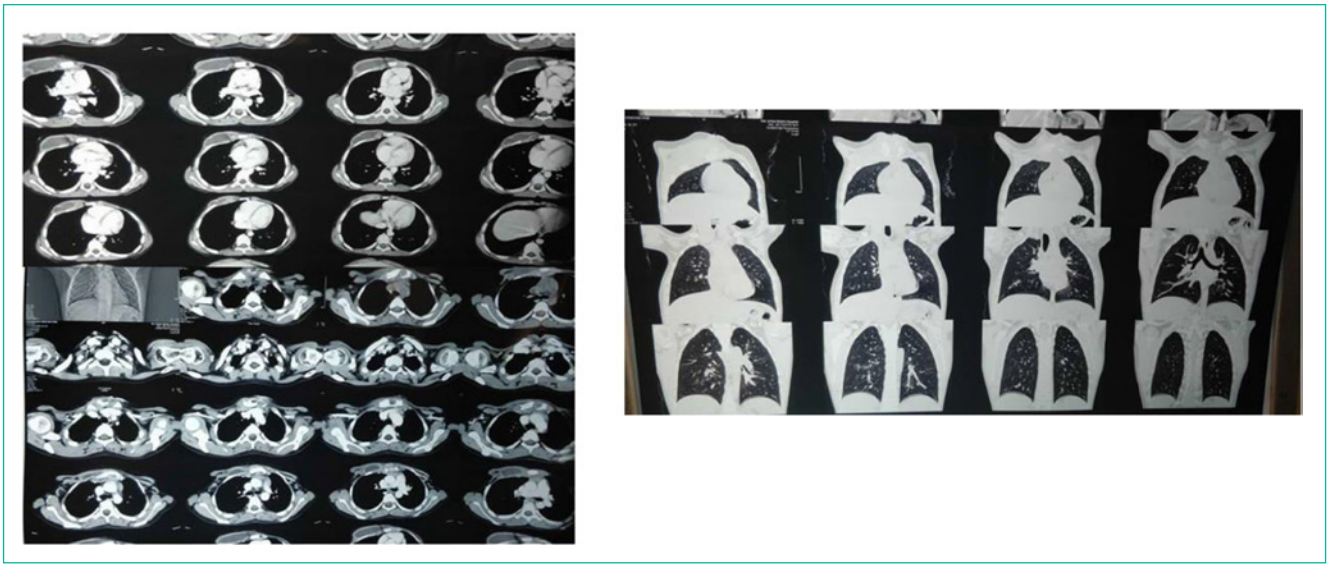

Figure 4. CT scan images showing a collection in sternal region extending up to right pectoral region.

Continuous Phase: Lfx Eto Cs E (18 months)
The patient healed in 11 months with no side effects of the medications.

Discussion

Our case is the first case of Primary extrapulmonary multi-drug resistant tuberculosis in a patient suffering from XP. Xeroderma pigmentosum (XP) has some typical clinical features. Those include sensitivity to the sun (extreme sunburn with blistering, constant erythema on mild sun exposure) with marked freckle-like pigmentation of the face before two years of age in most affected individuals. These patients suffer from sunlight-induced ocular problems including photophobia, keratitis, and atrophy of the skin of

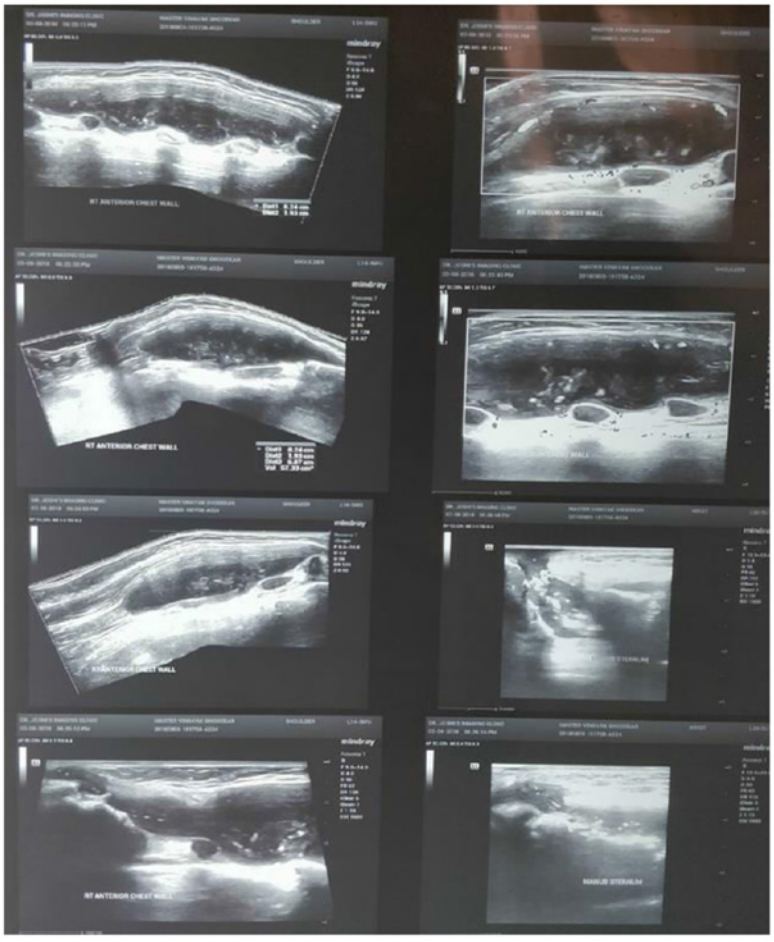

Figure 5. USG of the chest wall showing collection on 57 cc pus collection in right anterior chest wall.

the lids (Figure 1). Due to defective DNA repair mechanisms, there is enhanced risk of sunlight-caused cutaneous neoplasms (squamous cell carcinoma, basal cell carcinoma, and melanoma) in XP patients. Eight different gene mutations are involved in XP. The clinical symptoms usually vary depending on the specific gene involved[3,4]. Defect in Nucleotide Excision Repair (NER) is a result of mutation of seven genes (XPA-XPG). The eighth gene mutation (XPV) results in defective DNA polymerase n. This failure to repair DNA damage caused by UV radiations causes a higher risk for developing cancer[4]. The diagnosis of XP should be suspected in patients who have immune abnormalities and history of persistent sunburn to mild exposure of sunlight or UV radiation. Patients of XP who suffer from repeated viral or bacterial infections should be evaluated for cellular and humoral immune deficiencies[5].

Xeroderma Pigmentosa is a rare condition. Its prevalence is of 1 in million in USA and 2.3 in million in Western Europe. In Japan, the prevalence is as high as up to 45 per million[13]. A high incidence of XP has been seen in the Middle East and North Africa. The plausible cause is wide-spread consanguinity in certain communities and the recessive

Serological markers investigated	Patient's Values
HIV	Negative
HCV	Negative
HBsAg	Negative
ESR	110 MM/hrs
CRP	22 mg/L

HIV: Human Immunodeficiency virus; HCV: Hepatitis C virus; HBsAg: Hepatitis B surface Antigen; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.

Table 1. Patient serological markers at the time of presentation.

Antibiotics	Dosage
Kanamycin; Km	250 µg OD ATD
Ethionamide; Eto	250 µg OD
Cycloserine; Cs	250 µg OD
Levofloxacin; Lfx	250 µg OD
Ethambutol; E	400 µg OD
Pyrazinamide; Z	500 µg OD

Table 2. Antibiotics and their dosage as administered to the patient.

inheritance of the disease[12,13].

Differential diagnosis of Xeroderma Pigmentosa includes various autosomal dominant diseases like Leopard syndrome, Peutz-Jeghers syndrome, Cockayne syndrome, and Carney complex[14]. Wysenbeek et al. found that there was significant decrease in the T4 positive lymphocyte subpopulation. This kind of decrease is seen often in acute viral infections in agammaglobulinemic patients[15], AIDS (acquired immunodeficiency syndrome)[16], after irradiation[17] and after immunosuppressive therapy[18].

The estimated incidence of Tuberculosis in India was 2.1 million cases in 2013 out of which 16 percent were new extra-pulmonary TB cases, that is, 336,000 people with extra-pulmonary TB[19]. A meta-analysis of the prevalence of MDR-TB in India found it to be 35 percent[20] in comparison to 11.6 percent found in the National level Survey[21]. Extra-Pulmonary TB accounts for 10-20% of global TB cases. The incidence of Extra-Pulmonary TB and disseminated forms of TB increases with worsening immunosuppression[22,23]. TB is more prevalent in populations with immunodeficiency especially antigen-specific T-cell immunity. Also, Major Histocompatibility Complex (MHC) 1 and 2 play role in protection against TB[19].

Our case is the first reported case of Primary Extra-pulmonary multi-Drug resistant Tuberculosis in a patient suffering from Xeroderma Pigmentosa.

Conclusion

The prognosis of MDR TB in XP patients is not known in detail. In many parts of the world, MDR TB is posing a serious threat to success of antibiotic therapy. More research to explain the intricate correlation between immunity and infections can help us formulate better adjuvant therapies like vaccines and gene therapy. These could be new ways to tackle the emerging MDR TB wave.

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