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Case report

Thrombocytopenia as a presenting manifestation of sarcoidosis

Sattavaram Laxma Reddy, Avala Ravicharan, Narahari Narendrakumar, Kakarla Bhaskar, Gongati Krupa Rao Paramjyothi

Department of Pulmonology, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad-500082, Telangana, India.

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Corresponding author

Sattavaram Laxma Reddy
Senior Resident,
Department of Pulmonology,
Nizam's Institute of Medical Sciences,
Punjagutta, Hyderabad-500082,
Telangana, India.
Phone: +91-9966676757
Email: slr.nims@gmail.com

Abstract

Sarcoidosis is a chronic granulomatous disease involving multiple organs. Most commonly affected organs are lungs, followed by skin, lymph nodes. Hematological manifestations of sarcoidosis are uncommon and may include hemolytic anemia, leukopenia, eosinophilia, peripheral lymphopenia but severe thrombocytopenia is very rare. Our patient presented with petechial rash, papular skin lesions and had severe thrombocytopenia. Skin biopsy showed granulomatous inflammation without necrosis with good clinical, radiological and hematological response to oral prednisolone.

Key words: Sarcoidosis, Thrombocytopenia

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Sarcoidosis is a chronic granulomatous disease involving multiple organs. Most commonly affected organs are lungs, followed by skin, lymph nodes. Less commonly affected organs are the eyes, liver, heart, and brain. Any organ, however, can be affected. The cause of sarcoidosis is unknown[1], some believe that it is due to an uncontrolled immune reaction triggered by an infection or chemical exposure in the background of genetic predisposition. Hematological manifestations of sarcoidosis are uncommon and may include hemolytic anemia, leukopenia, eosinophilia, peripheral lymphopenia but severe thrombocytopenia is very rare[2,3]. Hereby we report a case of sarcoidosis presenting with severe thrombocytopenia, petechial rash and papular lesions over skin and successfully treated with steroids.

Case report

A 35 years old male patient with complaints of petechial rash for the past 1 month and gingival bleeding and subconjuctival hemorrhage for the past 3 days went to a local hospital in June 2017. The rash was distributed all over the body and it was non pruritic and painless. There was no history of fever, cough, dyspnea, hemoptysis, hematuria, epistaxis and melena. His appetite was good and there was no weightloss.His platelet count was below 10000 cells per cumm and provisional diagnosis of Idiopathic thrombocytopenic purpura (ITP) was made. He was transfused with 3 units of platelet rich plasma (PRP) and 50 grams of Intravenous immunoglobulins (IVIG) was given. His chest radiograph showed bilateral upper lobe nodular lesions (Fig 1) and he was started on antituberculosis treatment empirically. However his thrombocytopenia did not improve and patient was referred to our hospital for further management after one week.

On the day of admission patient had petechial rash all over the body and subconjuctival hemorrhage and multiple nontender papular lesions were present over the back of the chest, forearm and lower limbs (Fig 2). There was no pallor, clubbing, icter-

us, cyanosis, lymphadenopathy and pedal edema. Temperature was normal; pulse rate was 86/minute, respiratory rate was 20 cycles/minute, blood pressure was 110/60 mm Hg, SpO_2 was 96% at room air. Respiratory, cardiovascular, central nervous system examination was normal. Abdomen was soft and no organomegaly. His complete blood picture was: hemoglobin of 12.5 gm/dl, total leukocyte count of 10,500 with normal differential count and platelets were below 10000 per cu.mm. Renal, liver function tests and coagulation profile was normal. Patient was transfused with 10 units of PRPs and 2 units of Single Donor Platelets (SDP). Viral screening was normal. Ultrasound abdomen showed no organomegaly. CT scan showed multiple mediastinal lymphnodes involving bilateral hilar, right para tracheal, subcarinal region and parenchyma showing multiple nodular lesions along bronchovascular bundles and some giving tree in bud appearance (Fig 3 & 4). Mantoux was <5 mm. Serum calcium and phosphorous were within normal limits. Serum angiotensin converting enzyme (ACE) levels were elevated 74U/L (Range 8-53 U/L). Bone marrow biopsy showed normocellular marrow with megakaryocytosis and no granulomas were detected. Bronchial wash was negative for acid fast bacilli and Gene Xpert® did not detect MTB complex. Biopsy from skin papule showed noncaseating granulomatous lesions without necrosis (Fig 5). A final diagnosis of sarcoidosis was made involving skin, lung parenchyma and mediastinal lymphnodes. ATT was stopped and he was started on steroids (1mg/kg) and gradually tapered over 6 months. His platelet count gradually improved and became symptom free. His chest radiograph after 6 months showed complete resolution of parenchymal lesions (Fig 6) and he is on regular follow up till now.

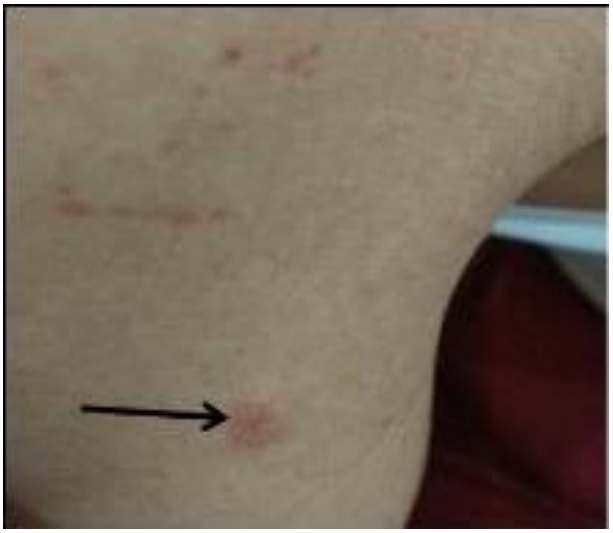

Fig 2. Papular lesion over back of chest

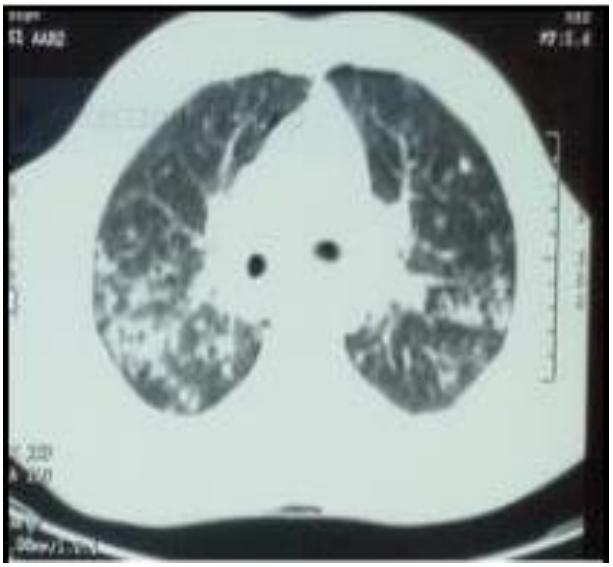

Fig 3. CT scan showing multiple mediastinal lymphnodes

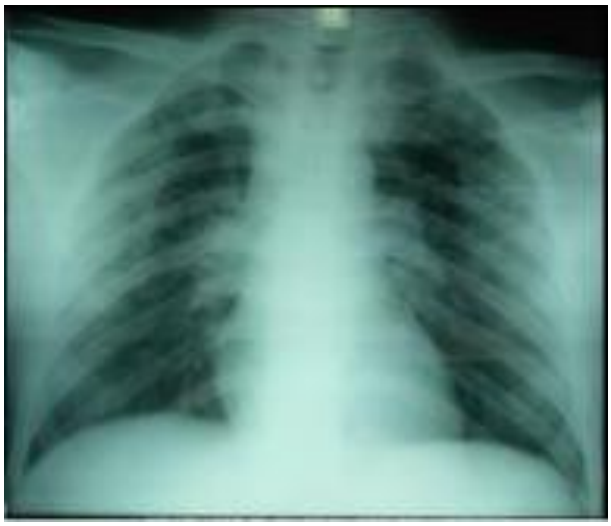

Fig 1. Bilateral nodular lesions in upper lobes

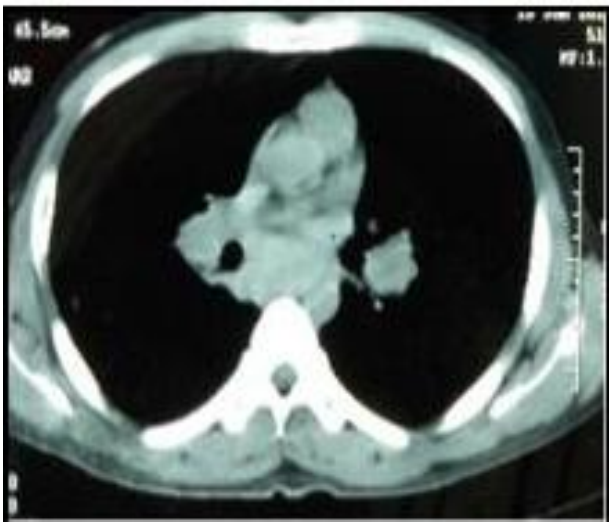

Fig 4. CT scan showing multiple mediastinal lymphnodes

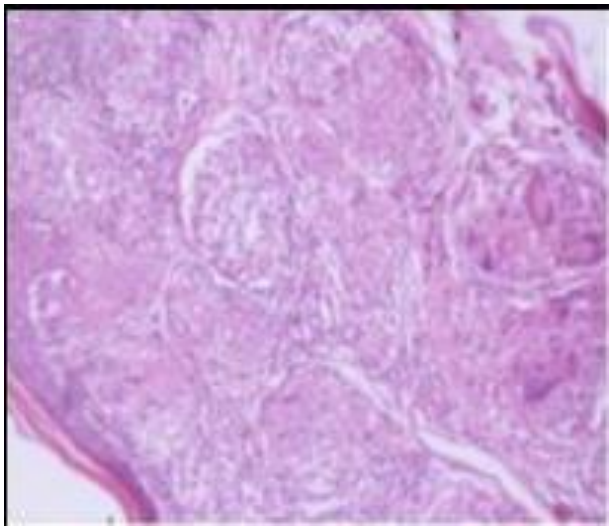

Fig 5. Skin biopsy showing noncaseating granulomatous lesion

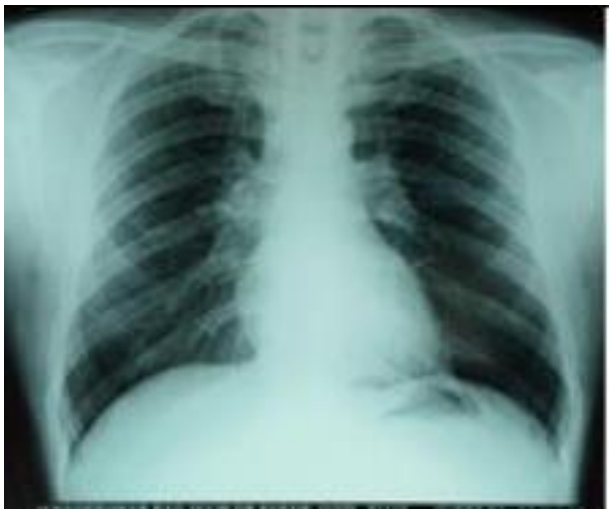

Fig 6. X-ray showing resolution of lesions 6 months after treatment

Discussion

Sarcoidosis is a multisystemic granulomatous disorder of unknown cause.It was first described in 1877 by Jonathan Hutchinson as a non-painful skin disease[4].Sarcoidosis affects people of all ages throughout the world, with the highest incidence in those between the ages of 20 and 40.Incidence is 11 to 36 cases per 100,000 people per year. It affects African Americans 3 times more likely than Caucasian Americans[5]. The exact prevalence of sarcoidosis in India is scarce. It has been estimated that sarcoidosis constituted 10 to 12 cases per 1,000 new registrations in a respiratory unit at Kolkata and 61.2/100,000 new cases at a center in New Delhi in a report published in 2002[6]. Every organ in the body can be affected by sarcoidosis.Hematological abnormalities are present in more than 50% of cases. Lymphopenia is the most common blood abnormality in sarcoidosis and anemia occurs in about 20% of patients. Thrombocytopenia occurs rarely in the course of sarcoidosis[7] and itself as a presenting manifestation has been very rarely reported. In a study by D. Gupta et al[8] from India showed that lymphopenia is the most common hematological abnormality followed by anemia but none of the patients had thrombocytopenia in their study. Our patient presented with severe thrombocytopenia which is manifested by petechial rash all over the body, mucosal bleeding and subconjuctival hemorrhage. A review of 381 cases of thrombocytopenic purpura showed five patients with sarcoidosis (1%) and in a series of 324 patients with sarcoidosis, 2% had thrombocytopenia[9]. Three potential mechanisms of thrombocytopenia in sarcoidosis: 1) autoantibody related platelet destruction, 2) infiltration of bone marrow by granulomas, and 3) hypersplenism are proposed. Skin is affected in 20% to 35% of patients with sarcoidosis. The common cutaneous manifestations of sarcoidosis are papular, maculopapular, and plaque lesions, erythema nodosum and lupus pernio[10]. Our patient presented with papular lesions involving the back of the chest and lower limbs.

The diagnosis of sarcoidosis needs a compatible clinical picture, histological demonstration of noncaseating granulomas, and exclusion of other diseases capable of producing a similar histological or clinical picture[11]. First step is to choose the site for a proper biopsy. In our patient biopsy was done from skin lesion which is an easily accessible site. Transbronchial lung biopsy is the recommended procedure in cases involving only lung. In addition to chest radiography, various imaging studies, such as computed tomography of the chest and 18 F-fluorodeoxyglucose positron emission tomography (18 F-FDG PET) are useful to support the diagnosis[12]. Clinical and/or radiological features alone may be diagnostic for patients with Stage I (reliability of 98%) or Stage II (89%) disease, but are less accurate for patients with Stage III (52%)[13]. Bronchoalveolar lavage with cell count may support a diagnosis of sarcoidosis if there is lymphocytosis of at least 15% and a CD4:CD8 T-lymphocyte ratio greater than 3.5[14]. Reliable biomarkers for diagnosis do not currently exist for routine clinical practice, although the serum angiotensin-converting enzyme (ACE) level may be elevated in up to 75% of untreated patients, it lacks sufficient specificity[15]. Hypercalcemia is also common. Vitamin D is the main cause for hypercalcimia in sarcoidosis and overproduced by

sarcoid granuloma[16]. In our patient ACE levels are elevated and serum calcium was normal.

Oral corticosteroids are the first line of therapy in patient with progressive pulmonary or extrapulmonary sarcoidosis requiring treatment. Treatment with prednisolone (or equivalent) 0.5 mg/kg/day for 4 weeks, with tapering to achieve a maintenance dose which will control symptoms and disease progression, should be used for a period of 6–24 months. Other immunosuppressive or anti-inflammatory treatments only have a limited role in sarcoidosis, but should be considered in patients when corticosteroids are not controlling the disease or side effects are intolerable. At present, methotrexate is the treatment of choice. Lung transplantation should be considered in end stage pulmonary sarcoidosis[17]. Infliximab appears to be an effective, safe treatment and steroid sparer for patients with refractory sarcoidosis, including manifestations as lupus pernio, uveitis, hepatic sarcoidosis, and neurosarcoidosis[18]. Our patient was started on oral prednisolone (1 mg/kg) and tolerated well, did not develop any side effects of steroids. Dose was gradually tapered and he was on maintenance steroid dose(5mg/day). He is under regular follow up.

Conclusion

Sarcoidosis is an important interstitial lung disease with increased recognition recently. Lung is the most common organ to be involved. Thrombocytopenia is a rare manifestation. Clinical examination may offer the diagnostic clue as in our patient with sarcoid papules which are easy to biopsy. High index of suspicion and prompt recognition of clinical features may lead to early diagnosis with good clinical outcomes as it can respond to steroids and other immunosuppression.

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Conflict of interest: None

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