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CASE REPORT Open Access

A case of Rosai-Dorfman's disease as isolated mediastinal lymphadenopathy: a diagnostic challenge

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Abstract

Background: Mediastinal lymphadenopathy is seen in a variety of diseases, like tuberculosis, sarcoidosis, and metastasis. The diagnosis can be confirmed by tissue sampling with endobronchial ultrasound and transbronchial needle aspirate. A middle-aged male presented to us with a history similar to tuberculosis, and was on empirical anti-tuberculosis treatment was evaluated again by EBUS-TBNA and proved to be Rosai-Dorfman's disease. This case report emphasizes on confirming the cases of mediastinal lymphadenopathy with tissue sampling.

Conclusion: All mediastinal lymphadenopathy should be evaluated in detail as the symptoms of the possible diseases, like tuberculosis, sarcoidosis, Kikuchi's disease, Rosai-Dorfman's disease, and malignancy can be similar. Hence, tissue sampling will confirm the diagnosis and help in appropriate management.

Keywords: Mediastinal lymphadenopathy, EBUS, TBNA, Emperipolesis, Sinus histiocytosis, Rare diseases, NORD

Introduction

Mediastinal lymphadenopathy is seen in a wide variety of diseases, like tuberculosis, sarcoidosis, and metastasis. The diagnosis can be confirmed by tissue sampling with endobronchial ultrasound and transbronchial needle aspirate. The need for confirming the diagnosis with tissue sampling is important as many diseases with mediastinal lymphadenopathy have similar presentations.

Case report

The patient was a 45-year-old man, farmer by occupation, non- smoker, presented to us with history of fever for 10 months which was high grade, intermittent nature, and with no diurnal variation. He also lost 4 kg of weight over last 4 months which was associated with malaise.

No past history of tuberculosis, joint pain, connective tissue diseases, and major hospitalization history. No history of contact with tuberculosis patient. He had one CT scan showing enlarged homogenous pre tracheal, bilateral paratracheal, aorto pulmonary lymph node and subcarinal lymph node (Figs. 1 and 2). He underwent CT-guided biopsy in an outside hospital, and histopathological examination showed chronic inflammation. He was started on anti-tuberculosis treatment from peripheral center and referred to us for persistence of symptoms after starting treatment for 3 months.

The physical examination was normal. The patient is moderately built and nourished and no pallor, icterus, clubbing, cyanosis, and peripheral palpable lymphadenopathy. The laboratory investigations were as follows: total WBC 6800 (4000–11000 cells/mm^3), hemoglobin 9 g/dl (12–14 g/dl), PT 27.3 (12–14), INR 2.45 (1–1.5), total protein 7.96 g/dl (6–8 g/dl), albumin 3.34 g/dl (3.5–4.5 g/dl), globulin 4.62 g/dl (2.5–3.5 g/dl), serum calcium 9.27 mg/dl (8.6–10.3 mg/dl). The patient was sero negative for HIV. There is no evidence of autoimmune or immunosuppressive conditions. Serum protein electrophoresis done in view of low hemoglobin

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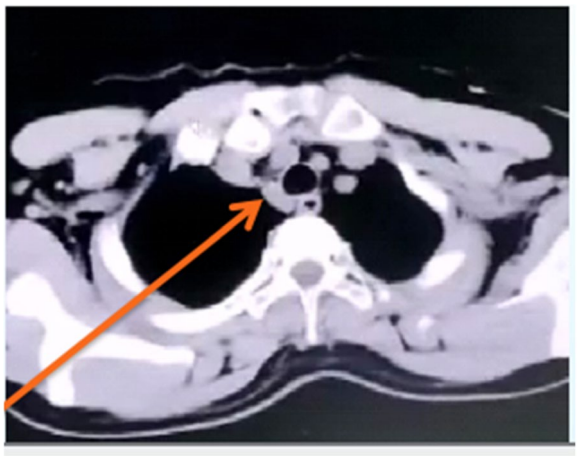

Fig. 1 HRCT thorax showing right para tracheal lymphadenopathy

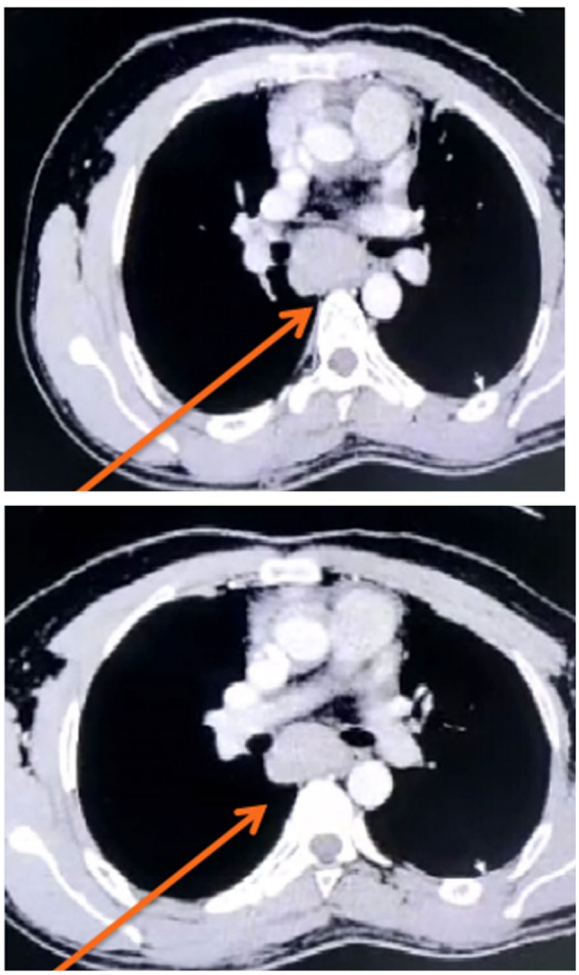

Fig. 2 HRCT thorax showing subcarinal lymphadenopathy

level, deranged INR, and albumin- globulin reversal. Serum protein electrophoresis revealed polyclonal gammopathy. Hemoglobin electrophoresis was suggestive of beta thalassemia heterozygous trait. PET-CT also showed FDG uptake in isolated mediastinal lymph nodes (Fig. 3).

He underwent endobronchial ultrasound under fresh frozen plasma cover, and transbronchial needle aspirations taken from station 7. The aspirated sample was negative for AFB stain and Gene expert. Histology showed foamy histiocytes in emperipolesis form, there was mixed population of small and large lymphocytes with few plasma cells and neutrophils. No granuloma or necrosis or malignant cells seen (Figs. 4 and 5).

Microscopic stains were negative for PAS stain and gram stain. There is no mycobacterium complex grown in the culture. Immunohistochemistry was positive for S100.

Patient initially started on steroids 0.5 mg/kg prednisolone and Thalidomide was also added as per opinion by hematologist. He clinically responded to treatment within 2 weeks. Treatment continued for 3 months with tapering dose of steroids and thalidomide. At the end of 3 months, there is clinical improvement with no fever, and patient had weight gain by 2 kg.

Discussion

Rosai-Dorfman's disease is a rare, benign, non-malignant disease, in which there is overproduction and accumulation of histiocyte in body, characterized by bilateral painless cervical lymphadenopathy. Rosai-Dorfman's disease can also present as axillary, inguinal, or mediastinal lymphadenopathy. There are reported

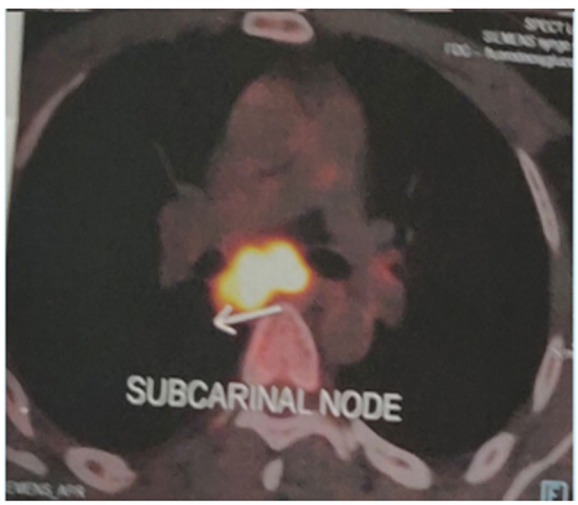

Fig. 3 PET CT showing FDG avid mediastinal nodes—subcarinal 24 × 40 mm

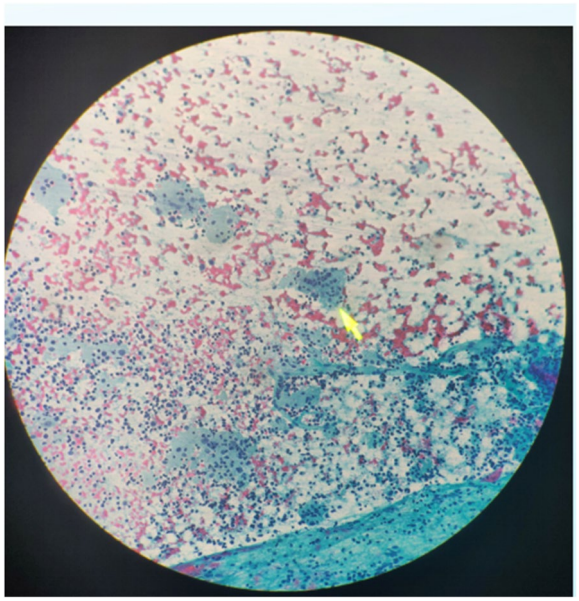

Fig. 4 Histopathology slide showing emperipolesis—foamy histiocytes in emperipolesis form, there was mixed population of small and large lymphocytes with few plasma cells and neutrophils

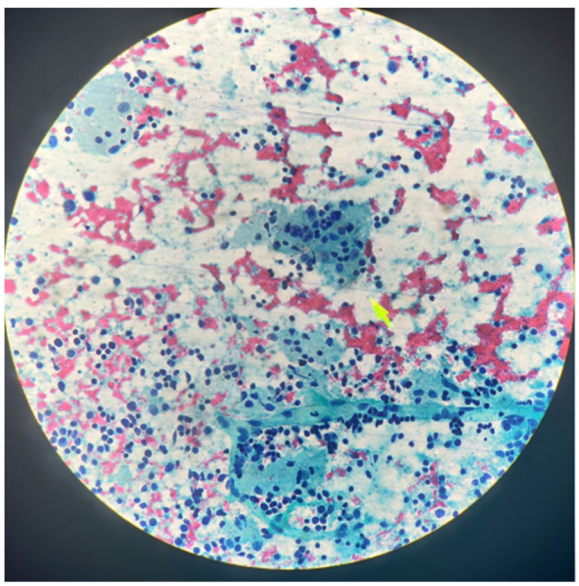

Fig. 5 Arrow mark showing emperipolesis—foamy histiocytes in emperipolesis form, there was mixed population of small and large lymphocytes with few plasma cells and neutrophils

cases of Rosai-Dorfman's disease involving the bones, soft tissue, and liver. Patients usually present with painless lymphadenopathy and associated with constitutional symptoms, like fever, loss of weight, night sweats, and malaise.

Clinical discussion

Mostly, histiocyte accumulates in lymph nodes, especially cervical, axillary, inguinal and mediastinal lymph nodes. They can also involve extra nodally in skin, soft tissue, kidney, digestive tract. The signs and symptoms of disease varies depending on the extent of involvement and the organs affected. The etiology of Rosai-Dorfman's disease is idiopathic. It usually affects individuals less than 20 years [1].

There have been only 9 case reports of intrathoracic diseases reported till now, and isolated mediastinal lymph node involvement is extremely rare.

Rosai-Dorfman's disease was first reported in 1969 by pathologists. This is considered as idiopathic histiocyte proliferative disorder predominantly involving lymph nodes. The etiology of Rosai-Dorfman's disease is considered as unknown, but there can be autoimmune and infectious causes associated with this disease. This disease can be associated with infection with Epstein-Barr virus, human herpes virus, klebsiella, and cytomegalo virus [2]. This disease is coming under a group of sinus histiocytosis diseases, like Langerhans cell histiocytosis (LCH), Erdein-Chester disease. In a review by Gaitonde et al., Rosai-Dorfman's disease is seen with extra nodal site involvement also including skin and soft tissues (16%), nose and paranasal sinuses (16%), eyes, orbit, ocular adnexa (11%), bone (11%), salivary gland (7%), and central nervous system (7%) [3].

Our patient had isolated mediastinal lymphadenopathy with clinical features similar to tuberculosis and no lung parenchymal involvement. Rosai-Dorfman's disease presenting with only mediastinal lymphadenopathy is rare.

The differential diagnosis of extranodal Rosai-Dorfman's disease include sarcoma, lymphoma, metastasis, IgG-4 diseases, tuberculosis, and fungal infections [4].

Imaging discussion

Based on studies, around 33% cases of Rosai-Dorman's disease have lymph node involvement and isolated lymph node involvement was 3 cases. The size of lymph nodes were 1–2 cm commonly [5–7]. The PET CT showed high SUV uptake in our case which can be confusing as it point towards malignancy also. The generalized lymph node involvement was the most common type which occurred in 7 (11%) cases, followed by isolated cervical and axillary lymphadenopathy was seen in 5 (8%) cases each. These cases had multiple lymph node involvement whereas isolated thoracic lymphadenopathy was seen in 4 (6%) patients which include para-tracheal lymphadenopathy [5].

Pathological discussion

The differential diagnosis of extranodal Rosai-Dorfman's disease include sarcoma, lymphoma, metastasis, IgG-4 diseases, tuberculosis, and fungal infections [4].

The diagnosis of Rosai-Dorfman's disease can be confirmed by histopathology showing evidence of emperipolesis in which lymphocytes and erythrocytes engulfed by histiocyte-like cells and immunohistochemistry showing S 100 positivity. The tissue can be positive for CD163, CD68, α1-antichymotrypsin, α1-antitrypsin, and HAM-56 while CD1a is typically negative [8].

Review of literature

This is a self-limiting disease, with spontaneous remission in some cases. Additional treatment options include steroids, alfa interferon, and some chemotherapeutic agents [1]. Steroids were used as the first-line therapy with 56% response in the cases, and a relapse rate of 53%. Prednisolone 1 mg/kg is usually used and taper over 6–12 weeks. Clinical and radiological response can be seen [5]. Our patient was started on 0.5 mg/kg body weight prednisolone, but he had persistent symptoms. Then, we added thalidomide 100 mg twice a day after discussing with hematologist and he had shown considerable improvement with treatment.

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Relevance of this case report
1) All mediastinal lymphadenopathy needs to be evaluated and take tissue biopsy as it confirms the diagnosis.
2) High SUV uptake in PET CT always does not indicate malignancy.
3) Even if clinical differential diagnosis puts tuberculosis as first possibility, we need to consider other rare diseases, like Kikuchi diseases, Castleman's disease, Rosai-Dorfman's disease also as possible diagnosis.
4) Radiologically, there is not much points to differentiate the above-mentioned diseases; hence tissue examination before confirming the diagnosis is always performed.

Authors' contributions
MM and KD worked in this case together and did work up and management of the patient together. This manuscript has been read and approved by all authors, and this is an honest work done in a real case scenario.

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Availability of data and materials
The data and material for the case report has been obtained from the patient with his consent.

Declarations

Ethics approval and consent to participate
Case report has been written after taking an informed consent from patient. The case report was an observational study and hence ethics committee approval has been waived off.

Consent for publication
The authors are giving complete authorization for the journal to publish the article under the names Dr. Mahavir Modi and Dr. Kaumudi Devi in the journal.

Competing interests
Both authors declare that they have no competing interests.

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