Case Report

Rosai-Dorfman disease presenting as internal jugular vein thrombosis and middle lobe collapse-consolidation

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ABSTRACT

Rosai–Dorfman disease, also known as sinus histiocytosis with massive lymphadenopathy, is a rare and benign disease that usually presents as massive and painless cervical lymphadenopathy. We are reporting this rare disease with systemic manifestations and causing internal jugular vein thrombosis and middle lobe collapse-consolidation.

KEY WORDS: Lymphadenopathy, Rosai–Dorfman, sinus histiocytosis, thrombosis

INTRODUCTION

Rosai-Dorfman Disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a rare disease and around 1000 case reports have been published until today. It is a benign disease that usually presents as massive and painless cervical lymphadenopathy, but extranodal involvement is seen in 40% of patients. It can infiltrate skin, soft tissues, eyes, bones, nasal sinuses, central nervous system, salivary glands, kidneys, respiratory tract, liver, breast, and gastrointestinal tract.[1]

Our patient presented with internal jugular vein (IJV) thrombosis and middle lobe collapse syndrome, which were found to be the complication of compressive massive lymphadenopathy.

CASE REPORT

A 45-year-old married female presented with fever for 1 month. Other symptoms included cough, dyspnea, and painful swelling over the right neck for 7 days. She was a smoker with a history of 10 pack-year. On examination, multiple palpable right cervical lymph nodes were present. She was a farmer by occupation and had no significant past and family history. Her obstetric history was unremarkable. On examination, multiple palpable right cervical lymph nodes were present [Figure 1]. The chest examination was unremarkable except for dilated veins seen on the right anterior chest wall. No other significant systemic findings were present.

Routine laboratory [Table 1] revealed leukocytosis with eosinophilia, hypergammaglobulinemia, raised erythrocyte sedimentation rate, and positive C-reactive protein. The human immunodeficiency virus was nonreactive, and HBsAg was negative. The screening test for connective tissue disease and hypercoagulable parameters was negative [Table 1]. Ultrasonography of the whole abdomen

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was normal. Two-dimensional echocardiography showed mild pericardial effusion. Sputum for acid-fast bacilli smear and Gene Xpert test for *Mycobacterium tuberculosis* (MTB) was negative. Sputum for Gram stain, KOH stain, pyogenic culture, MTB culture, and fungal culture was negative.

Ultrasonography of the neck showed multiple right cervical necrotic lymph nodes and thrombosis of entire length of the right IJV. Chest skiagram showed middle lobe collapse and consolidation. Computed tomography (CT) venogram of neck and chest showed multiple cervical, para-tracheal and mediastinal heterogeneous lymph nodes [Figure 2a and b, stars] and thrombus in right cervical, subclavian, brachiocephalic vein, and superior vena cava [Figure 2a and b, arrow]. One of the enlarged lymph nodes was compressing the IJV in lower cervical region [Figure 2a, five-point star]. There were multiple collateral in the right lower cervical region extending to the right axilla and right upper chest [Figure 2c, arrows]. There was right-sided minimal pleural effusion, mild pericardial effusion, and right middle lobe collapse-consolidation in 2 weeks prior to CT chest [Figure 2d]. Deviated nasal septum on the right side with normal maxillary sinuses was noted in the same CT.

Fine-needle aspiration cytology (FNAC) of cervical lymph node was done as initial workup, which showed few lymphocytes and histiocytes and no granuloma or malignant cells. FNA was negative for ZN stain and Gene Xpert for *Mycobacterium tuberculosis*. The right cervical lymph node excision biopsy was performed, which showed partial effacement of architecture with marked expansion and dilatation of the sinuses with the presence of large number of histiocytes, plasma cells, and few neutrophils. Many histiocytes showed erythrophagocytosis and emperipolesis [Figure 3a, arrows]. Immunohistochemistry was positive for S 100 and CD68 and negative for CD1a [Figure 3b-d] which was suggestive of Rosai–Dorfman disease.

The patient was started on anticoagulation with low molecular weight heparin which was later overlapped and switched over with oral warfarin (target INR: 2–3). She was also started on oral steroids (prednisolone) at 1 mg/kg dose which was later changed to high dose of dexamethasone with methotrexate due to poor response. She also received empirical antibiotics during the hospital stay for 7 days in view of fever, leukocytosis, and collapse-consolidation on chest radiology. The patient improved in her symptoms gradually, and neck pain and fever subsided completely. Her neck lymph nodes started decreasing in size. Pleural and pericardial effusion resolved completely with treatment. Repeat contrast enhanced CT showed re-expansion of the middle lobe.

### Table 1: Laboratory parameters

| Test                              | Results              |
|-----------------------------------|----------------------|
| Hb                                | 10.2 g/dl            |
| Total leucocyte count             | 13,000/cumm          |
| Neutrophils                       | 70%                  |
| Total eosinophil counts           | 510 cu mm            |
| Total IgE                         | 779 IU/ml            |
| ESR                               | 120 mm/h             |
| CRP                               | Positive             |
| Rheumatoid factor                 | Negative             |
| ANA                               | Negative             |
| Anti dsDNA                        | Negative             |
| Anti phospholipid antibodies (IgG and IgM) | Negative |
| Lupus anti coagulant test         | Negative             |
| Anti cardiolipin antibodies (IgG and IgM) | Negative |
| Serum triglycerides               | 82 mg/dl             |
| Serum ferritin                    | 465.8 ng/dl (high)   |
| Serum LDH                         | 471 U/L              |
| Liver and kidney function test    | Within normal limits |
| Serum total protein and albumin   | Within normal limits |
| Protein C and S                   | Within normal limits |
| Prothrombin time, partial thromboplastin time and | Within normal limits |
| INR                               |                      |
| Factor V leiden and anti thrombin III | Within normal limits |
| Serum homocystein level           | Within normal limits |

ESR: Erythrocyte sedimentation rate, CRP: C reactive protein, ANA: Antinuclear antibody, dsDNA: Double stranded DNA, LDH: Lactate dehydrogenase, INR: International normalised ratio, Hb: Haemoglobin, IgE: Immunoglobulin E, IgG: Immunoglobulin G, IgM: Immunoglobulin M

#### DISCUSSION

Rosai-Dorfman Disease is a rare non-Langerhans cell histiocytosis (LCH) first described in 1965 by a French pathologist, Pierre-Paul Louis Lucien Destombes[^2^] and later in 1969 by Juan Rosai and Ronald Dorfman.[^3^] It is commonly seen in children and young adults with male preponderance. The etiology of RDD is not very clear, and studies have found its association with virus infections, neoplasia, inheritance, immunological mediated, or Ig G4 related. The diagnostic pathologic features of nodal RDD include the sinus expansion of large histiocytes, emperipolesis (intracytoplasmic phagocytosis of inflammatory cells) and positive S100 and CD68 markers and negative CD1a markers on immunohistochemistry.[^1^]

The disease characteristically presents as massive, painless, bilateral cervical lymphadenopathy with other nodal sites including axillary, inguinal, para-aortic, and mediastinal lymph nodes.[^4^] Our case too had multiple,
massively enlarged cervical (unilateral), pre-paratracheal, and mediastinal lymph nodes. We kept our first differential diagnosis as tuberculosis as India has a high prevalence of tuberculosis and lymph node is the most common extrapulmonary site for tuberculosis. This was supported by CT neck and chest which showed heterogeneously enhancing (probably necrotic) lymph nodes. However, FNAC and biopsy of lymph node did not reveal any granuloma and ZN stain, gene Xpert and culture for MTB was negative. Malignancy was our second differential as it can many times present with multiple necrotic lymph node. Lymphoma and sarcoidosis can have similar presentations but rarely have necrosis. Histopathological examination (HPE) of excisional biopsy is gold standard for diagnosing malignancy, lymphoma, and sarcoidosis, and the same was excluded as HPE was not suggestive of any of these in this case.

RDD needs to be differentiated histopathologically from nonspecific sinus hyperplasia which does not show lymphophagocytosis and emperipolesis and the histiocytes are S100 protein negative. Other differentials include LCH which shows Langerhans cell proliferation which has a small, irregular elongated nucleus with prominent grooves and many eosinophils, and are reactive for langerin and CD1a in addition to s100 protein. Leprosy and rhinoscleroma can mimic RDD, but in leprosy, the histiocytes show numerous AFB, whereas rhinoscleroma shows many plasma cells with Russell bodies. Leprosy and rhinoscleroma both do not show emperipolesis. Malignant melanoma also resembles RDD, but it shows prominent eosinophilic nucleolus with pseudoinclusions and shows Melan-A positivity in addition to S100 protein on immunohistochemistry.

One of the enlarged lymph nodes in the lower cervical region was seen compressing IJV on CT scan. This most probably led to venous stasis and caused thrombosis as other parameters responsible for the hypercoagulable state were found negative on blood investigations. The extension of thrombus in the right cervical, brachiocephalic vein, and superior vena cava was causing signs and symptoms of superior vena cava syndrome. On literature search, we have found one case of caval compression in RDD-correlated massive mediastinal and abdominal lymphadenopathy, one case of pulmonary artery compression, and one case of peripheral vascular arterial insufficiency with lower-limb deep venous thrombosis caused by extra-lymph node RDD.

Our patient also had middle lobe collapse-consolidation at presentation, which again was the result of compression of middle lobe bronchus by enlarged mediastinal lymph nodes. Around 19% of patients have multisystem involvement, and prognosis is found to be related to the number of nodal and extranodal systems involved. Our case had pleural and pericardial effusion along with nodal involvement. Pleural and pericardial effusion resolved with steroid therapy.

The consensus recommendations on RDD suggest tailoring management as per individual case scenario. Observation can be done for patients with uncomplicated lymphadenopathy or asymptomatic disease. Debulking surgery is advised mainly for spinal cord or airway obstruction. Observation can be done for patients with uncomplicated lymphadenopathy or asymptomatic disease. Debulking surgery is advised mainly for spinal cord or airway obstruction.
compression, or large lesions causing end-organ damage. Steroids are effective in reducing nodal size and symptoms. Prednisone is indicated for symptomatic nodal or cutaneous disease whereas dexamethasone is recommended for a nonresectable or multifocal extranodal disease. Chemotherapeutic agents are used preferably in resistant or relapsed cases but have also been used in disseminated and life-threatening RDD.[1] Our patient was initially started on prednisolone 1 mg/kg dose but did not respond and was later switched to dexamethasone and methotrexate. Prognosis is favorable for nodal and cutaneous RDD but disseminated systemic disease can result in poor outcome.[1] Our patient improved clinically, and medications were gradually tapered. Pericardial and pleural effusion resolved completely and middle lobe re-expanded.

**CONCLUSION**

This report presents a rare case of systemic RDD with multiple cervical and mediastinal lymphadenopathy, mild pleural and pericardial effusion, right middle lobe collapse, and upper extremity deep vein thrombosis.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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