Bronchiolitis Obliterans Organizing Pneumonia Related to Rosai-Dorfman Disease: Case Report

Rosai-Dorfman Hastalığına Bağlı Bronşiolitis Obliterans ve Organize Pnömoni Olgusu

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ABSTRACT Rosai-Dorfman disease is a benign histiocytic proliferative disorder characterized by painless massive lymphadenopathy. It is also known as sinus histiocytosis with massive lymphadenopathy. Although it is a rare disease, it is seen commonly in children and adolescents and diagnosis is made by lymph node biopsy. The etiology of the disease is still unknown. Clinical presentation is usually with painless cervical lymphadenopathy, leukocytosis, fever, high erythrocyte sedimentation rate, weight loss, polyclonal hypergammaglobulinemia and involvement of extranodal organs. Usually Rosai-Dorfman disease has a benign course. Some patients show spontaneous remission, while others have more chronic course defined as stable or progressive disease. We report here a Rosai-Dorfman case with recurrent bronchiolitis obliterans organizing pneumonia.

Key Words: Histiocytosis, sinus; lymphatic diseases; lung

ÖZET Rosai-Dorfman hastalığı ağrısız masif lenfadenopatilerle karakterize iyi seyirli histiositik proliferatif bir hastalıktır. Masif lenfadenopatili sinüs histiyositozu olarak da bilinir. Nadir bir hastalık olmasına rağmen, daha çok çocuk ve adölesanlarda görülür ve lenf nodu biyopsisi ile tanı konur. Hastalığın etyolojisi hala bilinmemektedir. Klinik prezentasyon genellikle ağrısız servikal lenf nodu büyümesi, lökositoz, ateş, yüksek eritrosit sedimentasyon hızı, kilo kaybı, poliklonal hipergamaglobulinemi ve ekstranodal organ tutulumu ile birlikte olmaktadır. Genellikle Rosai-Dorfman hastalığının seyri benigndir. Bazı hastalar spontan remisyon gösterirken, bazıları da stabil veya progresif hastalık olarak tanımlanan daha kronik bir seyir gösterebilirler. Burada tekrarlayan bronşiolitis obliterans organize pnömonisi olan bir Rosai-Dorfman olgusunu bildirmekteyiz.

Anahtar Kelimeler: Histiyositozis, sinüs; lenfatik hastalıklar; akciğer

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Rosai-Dorfman disease (RDD) is a benign histiocytic proliferative disorder characterized by painless and massive lymphadenopathy which is caused by excessive accumulation of lymphocytes and histiocytes distending the lymph node sinuses. It is also known as sinus histiocytosis with massive lymphadenopathy. The etiology of the disease is still unknown. It is usually presented with cervical lymphadenopathy, fever, leukocytosis, elevated erythrocyte sedimentation rate, weight loss, polyclonal hypergammaglobulinemia and involvement of extranodal organs.[1] In 40% of the cases, lymphatics in extranodal sites, like skin, upper respiratory tract, bone and central nervous system are also involved.[2] Pulmonary presentation is rare.[3] Since RDD is characterized by massive lymphadenopathy, it is

important to differentiate it from other diseases characterized by multiple lymphadenopathy such as lymphoma, Kawasaki's disease, Castleman's disease, Kikuchi's disease. Definite diagnosis is made by lymph node biopsy showing marked histiocytic proliferation with lymphocytes and erythrocytes phagocytosed by these histiocytes.[2-4] Usually RDD has a benign course. Some patients show spontaneous remission, while others have more chronic course defined as stable or progressive disease.[3] Almost 50% of cases resolves without sequela, while 33% have residual asymptomatic lymphadenopathy and 17% have persistent symptoms after 5-10 years.[5] We presented here a Rosai-Dorfman case (with her informed consent) with multiple nodular lesions in Thorax CT and having bronchiolitis obliterans organizing pneumonia (BOOP).

CASE REPORT

A 19 year-old female was admitted to our clinic for one month duration of dyspnea and cough that was unresponsive to oral amoxicillin & chlaritromycin combination. Five years ago, she had the diagnosis of seronegative polyarthritis because of migrating arthralgia. She had been using methotrexate (10 mg/week), prednisolone (5 mg/day), diclophenac Na, folic acid, and famotidine for one year. At that moment, biopsy from a submandibular swelling revealed chronic sialadenitis. Three years ago, she had cervical lymphadenopathy and biopsy resulted in the diagnosis of Rosai-Dorfman disease (Figure 1).

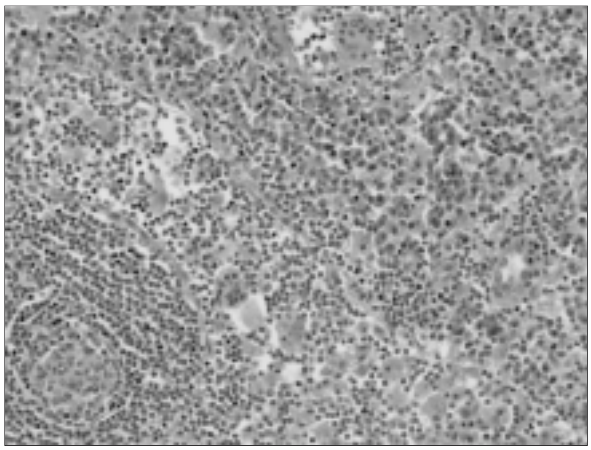

FIGURE 1: Cervical lymphadenopathy biopsy showing sinusal histiocytosis, plasma cells and hemophagocytosis (HE x200).

MRI of the lower extremities showed patchy infiltrations at almost all bones. This finding was thought to be related to Rosai-Dorfman disease. All drugs were stopped and rofecoxib was given for arthralgia.

One and half year ago, she had renal biopsy because of increased serum creatinin level (2.0 mg/dL). Renal biopsy showed "mesangioproliferative glomerulonephritis" and prednisolone 32 mg/day has been started. After six months of prednisolone treatment, creatinin level decreased to 1.0 mg/dL.

On admission to our clinic, physical examination revealed tachycardia (112/minute) and tachypnea (35/minute). She was afebrile. The blood pressure was 100/60 mmHg and the oxygen saturation 94-95% at room air and rest. Cervical, submandibular and supraclavicular multiple lymphadenopathies were remarkable. Auscultation was normal. ECG showed normal sinus rythm. Chest X-ray showed bilateral nodular infiltrations (Figure 2).

Pathologic laboratory findings: WBC:18,800/L Hb: 9.9gr/dL Htc:30% Plt:598,000mm^3 CRP: 149 mg/L ESR: 105 mm/hr, albumin: 3.34 g/dL (4.0-4.7 g/dL), gamma globulin: 1.96 g/dL (0.8-1.35 g/dL). Arterial blood gase showed mild hypoxemia (PaO2: 70mmHg, PaCO2:31mmHg).

Thorax CT showed multiple nodular lesions. Six minutes walking test (6MWT) resulted in desaturation (from 98% to 83% and 200 meters of walking distance). Spirometry showed restrictive ventilatory pattern (FVC 58%; FEV1 57% and FEV1/FVC ratio 87%). DLCO was 55%. Fiber optic bronchoscopic (FOB) biopsy and lavage were not diagnostic. PET-CT scan resulted in heterogenous FDG uptake (SUVmax 9.3) in both lung paranchyme. Cranial MRI which was taken due to severe headache was normal.

For definite diagnosis, thoracoscopic lung biopsy was done. Histopathological examination revealed bronchiolitis obliterans organizing pneumonia (Figure 3). Prednisolone (32 mg/day) was started. With this therapy the patient's clinical condition improved significantly in a short time. After

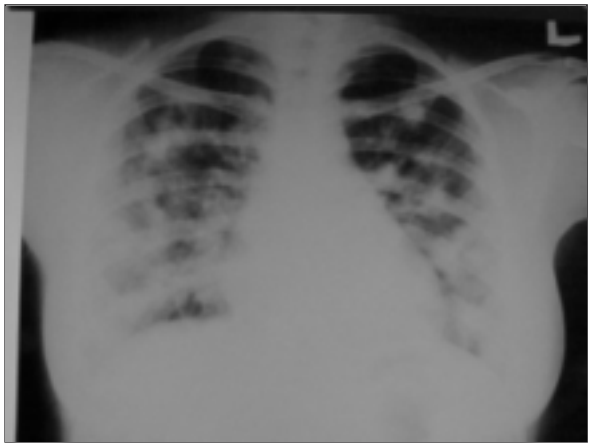

FIGURE 2: Bilateral multiple nodules.

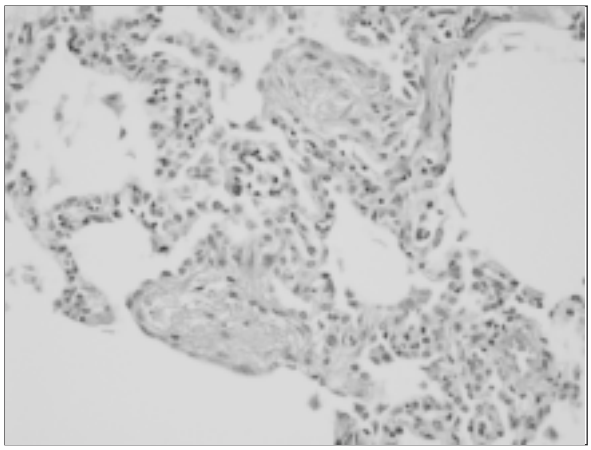

FIGURE 3: Open lung biopsy specimen showing bronchiolitis obliterans and organising pneumonia

ten days, 6MWT showed no desaturation and the lung function test improved (FVC 70%, FEV1 73%, FEV1/FVC ratio 89%). With the prednisolone therapy, CRP (0.3 mg/L) and ESR (6mm/hr) decreased. Chest-X-ray showed complete resolution (Figure 4). Prednisolone therapy was stopped in 6 months by slow tapering. She was free of symptom for a long time. Two years later, she was again admitted with exertional dyspnea. Chest X-ray and Thorax CT showed bilateral multiple nodular images that was accepted as relaps (Figure 5). FVC was 68%, FEV1 69% and DLCO 46%. She had Prednisolone (32 mg/day) was started for the relaps and rapid clinical and radiological improvement was seen again in a short time (Figure 6). Lung function tests improved (FVC 80%, FEV1 78%, and DLCO 87%). Prednisolone therapy lasted for 9 months. One month later, another relaps was detected and a new prednisolene therapy (32 mg/day) was started again. The response to the therapy was again quick and well.

DISCUSSION

Rosai-Dorfman disease (RDD) is a rare disease of the mononuclear phagocytic system with a benign nature and a good prognosis. Extranodal involvement is very common.[2,3] Every organ system can be affected by RDD, the most common ones being bone, skin, soft tissue, upper respiratory tract, eyes, digestive system and breast.[6] Our case presented with cervical and submandibular lymphadenopathy and bilateral pulmonary nodules. Her past history also revealed bone involvement. Although

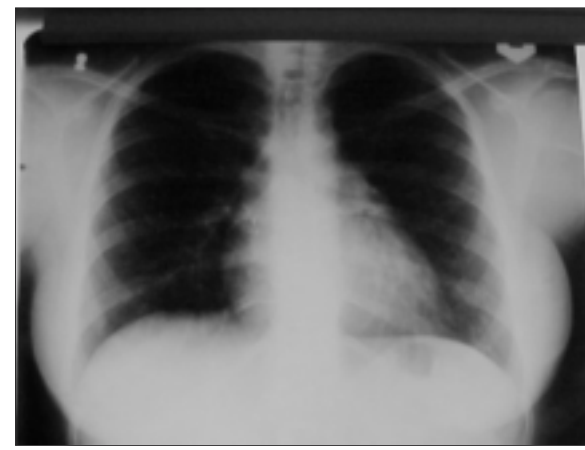

FIGURE 4: Radiological improvement (after treatment).

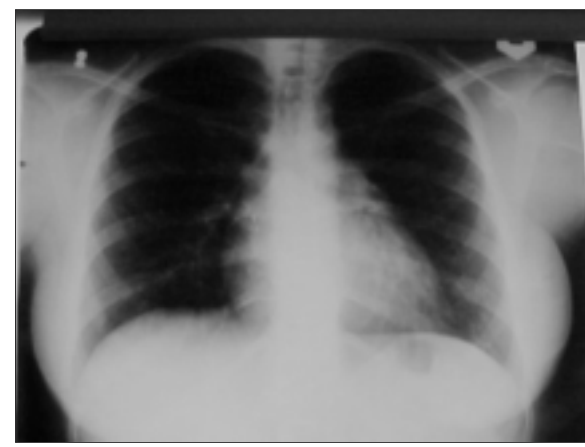

FIGURE 5: After two years bilateral multiple nodules as relaps.

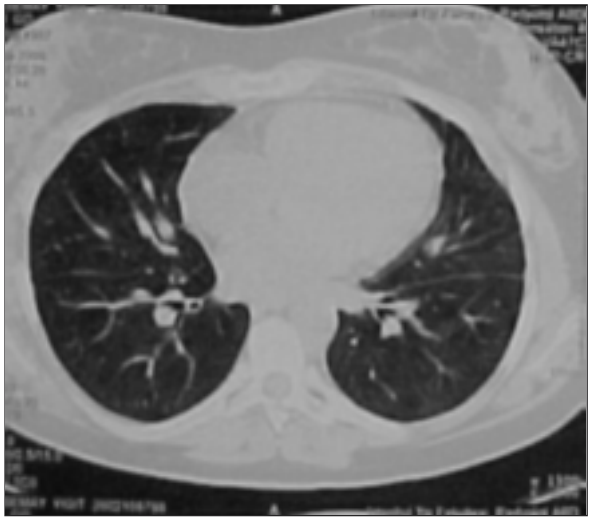

FIGURE 6: After treatment radiological improvement.

renal presentation is very rare in RDD, our patient had mesangioproliferative glomerulonephritis with elevated serum creatinin level in the past history.

Definite diagnosis of RDD requires lymph node biopsy showing marked histiocytic proliferation with lymphocytes and erythrocytes phagocytosed by histiocytes.[2,7] In our patient, the diagnosis came from cervical lymph node biopsy.

Thorax involvement of RDD is very rare and usually seen as pulmonary disease.[3] Most commonly, tracheabronchial tree is affected. Intraluminal polypoid growth related to RDD may cause airway obstruction.[3,8] Diffuse interstitial involvement is uncommon. Pleura can also be affected.[8,9] The characteristic of pulmonary involvement is the presence of other extranodal sites and lymphnode involvements. Our case presented with bilateral paranchymal pulmonary nodules without mediastinal lympadenopathies. Biopsy showed bronchiolitis obliterans organising pneumonia (BOOP) and it was related to RDD.

PET-CT can be used in RDD to evaluate the extend of the disease and metabolic characteristic of the lesions. Accumulated macrophages in the sinusoids may cause an increased FDG uptake in the involved tissue. It has been demonstrated that macrophages uptake FDG even more than viable tumor cells.[10] Also PET-CT can be used to evaluate the treatment response.[11] PET-CT of our case showed high SUVmax in both pulmonary paranchyma. High uptake in the patient was thougt to be related to the inflammatory process of RDD.

RDD is a benign disease with relapses and remissions. The prognosis is usually good and most patients undergo spontaneous remission. Treatment is neccessary in patients with vital organ dysfunction like upper airway obstruction or motor deficit caused by spinal lesion or severe renal impairment.[3,12,13] There are several treatment options in RDD. Most commonly ones are corticosteroid, chemotherapeutic agents and methotrexate. Local radiotherapy and surgical resection may be neccessary in some cases for the compression of massive lymphadenopathy.[12-15] Antibiotics and acyclovir can be used because of hypothesis of infectious etiology.[16] The problem with corticosteroid therapy is steroid dependance and recurrence when the dose is tapered.[15,17] Our case had BOOP related to RDD. Corticosteroid is effective for both BOOP and RDD. Good and rapid clinical and radiological remission was seen in our patient with prednisolone, but relapses occurred when the therapy stopped. In the literature, other alternative agents are usually recommended for the cases with relapses. Methotrexate and 6-mercaptopurin combination, alone or combined with steroids and vinblastin, are among treatment protocols for relapses and resistant cases.[14] Recently, some new treatment modalities were reported such as vitamin A derivatives, thalidomide, 2-Cd2A, imatinib and rituximab.[11,18]

In conclusion, pulmonary involvement of RDD is extremely rare. We report here a case with pulmonary involvement of RDD who had relapses after prednisolone therapy.

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