

Case Study

**A CASE REPORT ON AYURVEDIC MEDICINE (RED MERCURIC SULPHATE) INDUCED BRONCHIOLITIS OBLITERANS ORGANIZING PNEUMONIA (BOOP) IN SERO POSITIVE RHEUMATOID PATIENT**

ANN MARY PAUL, ANIL ANTONY, SRUTI NU, HYFA HAMEED

National College of Pharmacy India  
Email: annmarypaul091@gmail.com

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**ABSTRACT**

Bronchiolitis obliterans organizing pneumonia (BOOP) is a lung disease that causes inflammation in the small air tubes (bronchioles) and air sacs (alveoli). It can be caused due to wide range of etiologies like viral infections, various drugs, chemicals, and other medical conditions. A 55 y old female patient presented with symptoms of BOOP who had a history for taking ayurvedic medicine (rasasindura-red mercuric sulphate) for rheumatoid arthritis. The patient didn't respond to initial symptomatic therapy and the reports of High-resolution computed tomography (HRCT) and chest X ray revealed the diagnosis as drug induced BOOP. In search of etiologies mercuric sulphate (major ingredient of rasasindura-ayurvedic medicine) was confirmed among all other possible etiologies. Patient was advised to discontinue ayurvedic medicine and completely cured by treatment with steroids for 2 mo. She didn't show any symptoms of relapse in 3 mo observation period.

**Keywords:** Bronchiolitis obliterans and organizing pneumonia (BOOP), Rasasindhoora, Mercuric sulphate, Rheumatoid arthritis.

**INTRODUCTION**

Bronchiolitis obliterans organizing pneumonia (BOOP) is a lung disease that causes inflammation in the small air tubes (bronchioles) and air sacs (alveoli) with a cumulative incidence of six to seven cases per 100,000 hospital admission. The signs and symptoms of BOOP often include shortness of breath, dry cough, and fever. BOOP can be caused by viral infections, various drugs, chemicals, and other medical conditions. It can be diagnosed with Pulmonary Function Test (PFT), imaging techniques like HRCT and lung biopsy. Histology will reveal proliferative bronchiolitis-a nonspecific reaction with an inflammatory intraluminal infiltrate with mucus in the distal alveoli [1].

Rheumatoid arthritis (RA) is a systemic inflammatory disease that has a female predominance. It affects about 1% worldwide, and it is thought that about 40% of all rheumatoid patients have some sort of extra-articular manifestation. Rheumatoid disease with joint and pulmonary manifestations was first described in 1948. Nonspecific symptoms like dyspnoea and chronic cough and with prominent radiological manifestations are commonly seen with RA [2-4]. Treatment of RA includes Non Steroidal Anti-Inflammatory Drugs (NSAIDs), steroids, Disease-modifying antirheumatic drugs (DMARDs) like methotrexate, leflunomide, hydroxychloroquine and sulfasalazine. Long term use of drugs used to treat rheumatoid arthritis can also develop BOOP [5, 6].

Being incurable, most of the people turn to alternative therapies like ayurveda for the treatment for RA. Among wide range of patented ayurvedic products rasasindhura seems to be the commonest one [7]. It is chemically red mercuric sulphate. Besides arthritis rasasindhura have wide range of indications including fever, diabetes, male infertility, hypertension etc [8].

**CASE REPORT**

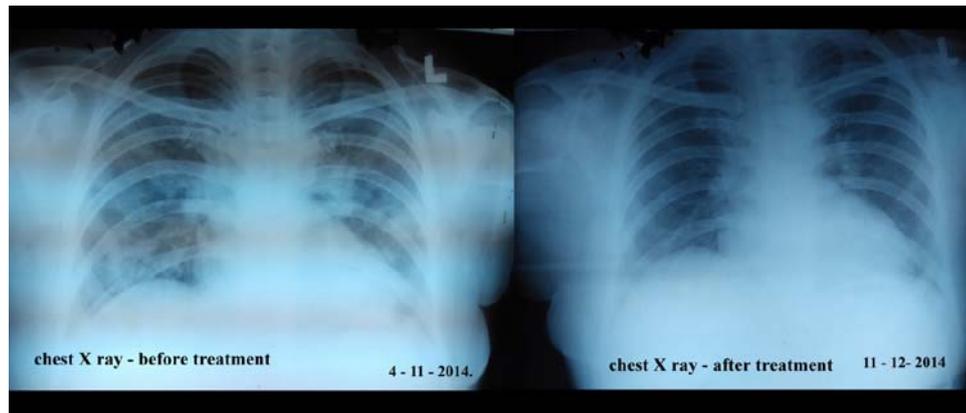
A 55 y old female patient from Calicut, Kerala, India presented with complaints of cough with mucoid sputum and breathlessness that increases on exertion (walking). She is a known case of seropositive rheumatoid arthritis for 6 y and under ayurveda treatment with rasasindhura (red mercuric sulphate), Balarishtam and aswagandharisham for past 6 mo. Before starting ayurvedic treatment patient was undergoing allopathic treatment with Tab. HYDROCHLOROQUINE 200 once daily and Tab. METHYLPREDNISOLONE 4 mg once daily for about 6 y. The above allopathic medications were stopped and she started the alternate medications (ayurveda) for arthritis, 6 mo before the presenting complaints. She also had a history of hypothyroidism and is on Tab.

THYROXINE 50 mcg OD. She had no family history of rheumatoid arthritis and respiratory diseases.

On the day of admission patient's general examination showed pallor, mild edema on limbs and chest crackles. Objective evidences include elevated erythrocyte sedimentation rate (ESR) (54 mm/1st hr) and slightly elevated eosinophils. Peripheral capillary oxygen saturation (SPO2) was dropped to 90% and chest X ray showed bilateral infiltrate and the white patches on both lungs. Pulmonologist treated her symptomatically with bronchodilators, mucolytics and antibiotics, but the symptoms persisted. On third day sputum *acid fast bacilli* (AFB) results obtained and it was negative. On day 4 HRCT scan done which reveals patchy areas of ground glass opacities with smooth intralobular septal thickening and intralobular interstitial thickening (crazy pavement appearance). It also showed areas of central ground glass opacities with denser consolidation in both lungs and confirmed the diagnosis as BOOP. The patient was asked to discontinue all the ayurvedic medicines and steroid therapy with IV PREDNISOLONE 40 mg OD was started on the day 4. After 5 d of therapy, as the symptoms improved IV PREDNISOLONE 40 mg replaced with oral prednisolone 16 mg OD for 2 d. During treatment patient was also administered with conventional antibiotics-AZITHROMYCIN 500 mg OD for 5 d and LEVOFLOXACIN for next 5 d. On day 10, patient symptomatically improved and saturation increased to 97%. Patient got discharged with oral steroid (PREDNISOLONE 8 mg 1-0-0) for 2 w and advised to discontinue ayurvedic treatment for RA.



Fig. 1: HRCT report



**Fig. 2: Chest X ray before and after treatment**

Patient discontinued the ayurvedic medications and restarted allopathic medication for arthritis. Rheumatologist advised her to restart Tab. HYDROCHLOROQUINE 200 mg OD and tab AZATHIOPRIM BD and suggested review in clinic after 1 mo. After 2 w, patient reviewed in pulmonary outpatient department. She appeared to be symptomatically better and respiratory manifestations suppressed. Tab. PREDNISOLONE dose tapered from 8 mg to 4 mg OD and advised to review after 2 w with chest X ray.

On her second review, her chest X ray was clear without infiltrations. Her steroid dose is tapered to Tab. PREDNISOLONE 2 mg OD for 2 w and 2 mg OD on alternate days for next 2 w. She continued her arthritis medications along with prednisolone and reviewed after 4 w.

On next review prednisolone discontinued and patient advised to visit OP after 1 mo. Patient didn't show any symptoms of relapse or recurrence after discontinuation of prednisolone therapy.

#### DISCUSSION

Bronchiolitis obliterans organizing pneumonia (BOOP) was first described in the early 1980s as a clinicopathologic syndrome characterized by sub-acute or chronic respiratory illness. Histopathology studies will show presence of granulation tissue in the bronchiolar lumen, alveolar ducts and some alveoli, associated with a variable degree of interstitial and airspace infiltration by mononuclear cells and foamy macrophages. Cough and shortness of breath for a period of 2 w to 2 mo usually characterizes BOOP [1]. Symptoms persist despite antibiotic therapy. On imaging, air space consolidation can be indistinguishable from chronic eosinophilic pneumonia (CEP), interstitial pneumonitis (acute, nonspecific and usual interstitial pneumonitis) neoplasm, inflammation and infection)

Here the patient presented with all the symptoms of BOOP-cough, breathlessness, saturation drop, elevated ESR and eosinophil counts. HRCT results confirmed the diagnosis as a true case of BOOP.

To find out etiology, patient medical and medication history were critically evaluated. The five possible etiologies in this case are:

1. Rheumatoid arthritis
2. Hypothyroidism
3. Viral infection
4. History of long term use of hydrochloroquine
5. Exposure to mercuric sulphate in Ayurveda medicine for rheumatoid arthritis.

Rheumatoid arthritis is found to be a risk factor in the development BOOP by the mechanism of angiogenesis and infiltration [9] and here the HRCT also shows the similar manner of result. But if disease developed due to arthritis it would relapse after the discontinuation the BOOP medication. Here in this patient the relapse didn't occur after discontinuation of therapy. So we can exclude the probability

of arthritis induced BOOP.

There is no much evidences for hypothyroidism induced BOOP except a case series published by Watanabe K in 2000[10]. The possibility of viral infection induced BOOP can be excluded with HRCT report which reveals noninfectious type infiltrates and patches. If it was a viral infection induced BOOP, long term therapy is required for complete cure otherwise relapse will occur [11]. But in this case, patient completely cured by 2 mo of steroid therapy and no relapses occurred after discontinuation medicines. It strongly indicates that this might be developed due to a drug/chemical exposure. So the possible etiologies are exposure to hydrochloroquine and red mercuric sulphate.

Literature review shows that the hydrochloroquine can cause pulmonary edema and transient infiltrates [9, 12] and there is also evidences for hydrochloroquine induced BOOP [13]. But in this case, patient discontinue HYDROCHLOROQUINE therapy 6 mo the onset of symptoms and also after the episode of BOOP, patient restarted the HYDROCHLOROQUINE therapy for rheumatoid arthritis. The negative report to rechallenging excludes the possibility of hydrochloroquine being an etiology of BOOP in this patient.

Thus we could conclude that the patient developed BOOP because of long term therapy with ayurvedic medicine (red mercuric sulphate). Literature review shows that exposure to mercury can cause pneumonitis, hyaline membrane formation, extensive pulmonary fibrosis and other respiratory complications [14, 15]. In this patient, clinical symptoms of BOOP appeared after the administration of rasisindura (red mercuric sulphate) for 6 mo and it get cured after discontinuing ayurvedic medicines.

In conclusion, mercuric sulphate is yet another addition to the vast etiologies of BOOP.

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#### CONFLICT OF INTRESTS

The authors declare that they have no conflicts of interest that are directly relevant to the content of the case report.

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