Sir,

Sarcoidosis is a granulomatous disorder of unknown etiology with a multisystem involvement, and the most common involved organ is lung. Due to multisystem involvement, atypical presentations are common and varied in sarcoidosis; however, a patient of sarcoidosis presenting with bronchorrhea has not yet been reported in literature. We present a case of a 45-year-old male, a smoker (smoking index 1 pack year) and with no comorbidities, who came with complaints of cough and breathlessness (Modified Medical Research Council Grade II) with bronchorrhea (>100 ml/day) for 1 year and weight loss for the last 4 months. Clinical examination was insignificant. Chest X-ray is shown in Figure 1. Laboratory parameters were within normal limits. He was on empirical antituberculosis treatment (4 drugs-RHZE) for 1 month from outside with no relief. Sputum cytology was negative for any malignancy, acid fast bacilli smear and gene expert were also negative. Keeping in view of malignancy as the most common cause of bronchorrhea, positron emission tomography - computed tomography (PET-CT) imaging was done which showed fludeoxyglucose uptake in lesions in bilateral upper lobe and right middle lobe with mediastinal lymphadenopathy (Figure 2).

Figure 1: X-ray chest showing the bilateral hilar prominence with homogeneous infiltrates in the left side mid and lower zones

Figure 2: Positron emission tomography-computed tomography images showing fludeoxyglucose uptake in lesions in bilateral upper lobe and right middle lobe with mediastinal lymphadenopathy
was done which revealed metabolically active soft-tissue dense fibrous lesion with peribronchovascular thickening in bilateral upper lobes and in the right middle lobe along with metabolically active multiple mediastinal lymph nodes [Figure 2]. Spirometry showed (moderate airway obstruction with no reversibility) forced expiratory volume 1/forced vital capacity (FEV₁/FVC) ratio of 65.8% with FVC pre/post: 3.40 L/3.62 L (77%/82% of predicted normal). FEV₁, pre/post: 2.24 L/2.49 L (62%/69% of predicted normal) with absolute increase of 250 ml and 11%. Videobronchoscopy showed diffuse endobronchial nodules. Bronchoalveolar lavage lymphocytes were 25% and CD4/CD8 = 3.36.

Endobronchial cryobiopsy, transbronchial lung biopsy and endobronchial ultrasound from lymph nodes stations right paratracheal (4R) and subcarinal (7) were done and showed compact, discrete, multiple, noncaseating granulomas [Figure 3] in all tissues sampled (lung, lymph node, and endobronchial mucosa). Further investigations revealed serum angiotensin-converting enzyme of 107 U/L (normal value 8–52 U/L). Mantoux test and interferon-gamma release assays were negative. The case was further discussed in multi disciplinary meeting (MDD) with radiologist and pathologist in view of atypical clinical, typical radiological and pathological findings. Judson et al. have stratified confidence level for the diagnosis of sarcoidosis – highly probable, probable, possible, and unlikely based on clinicoradiological and pathological description. Alternative diagnosis of infections and malignancy were ruled out, and diagnosis of sarcoidosis was made with highly probable level of confidence and the patient was started on steroids (Table deflazacort 6 mg twice daily), on which he showed marked improvement.

We did extensive search on PubMed, Medline, Google Scholar, and EMBASE; however, we could not find any case of sarcoidosis presenting with bronchorrhea which is defined as the production of more than 100 ml of watery sputum per day and is mostly associated with bronchioloalveolar cell carcinoma (mucinous type), rarely reported with nonmalignant processes such as chronic bronchitis, asthma, tuberculosis, and scorpion stings. Although the exact pathophysiology of bronchorrhea is unknown, Takeyama et al. suggested the stimulation of epidermal growth factor receptor causing MUC5AC expression in airway epithelial cells while inflammatory stimuli, increased transepithelial chloride secretion and excessive transudation of plasma proteins are the other possible mechanisms.

Table 1: Various drugs used for bronchorrhea cases by multiple authors

| Author         | Drug used                        | Diagnosis                      |
|----------------|----------------------------------|--------------------------------|
| Hudson et al.  | Octreotide                       | Bronchioloalveolar carcinoma   |
| Hiratsuka et al.| Clarithromycin with beclomethasone | Bronchioloalveolar carcinoma   |
| Nakajima et al. | Methylprednisolone 1000 mg/day followed by prednisolone 60 mg/day | Bronchioloalveolar carcinoma   |
| Homma et al.   | Indomethacin (inhaled)           | Bronchioloalveolar carcinoma   |
| Takao et al.   | Gefitinib                         | Bronchioloalveolar carcinoma   |
| Popat et al.   | Gefitinib                         | Bronchioloalveolar carcinoma   |

Bronchorrhea leads to significant morbidity by affecting the quality of life as in our patient too. Homma et al. in 1975, reported bronchorrhea in alveolar cell carcinoma with dehydration, electrolyte imbalance, and respiratory failure. Various drugs have been tried to treat bronchorrhea. Table 1 exemplifies unmet need in its treatment as many drugs have been tried. Our patient improved well with low-dose steroids.

A diagnosis of sarcoidosis is as such difficult in India even in typical cases but is arduous in atypical cases. With increasing awareness of the disease, we will see further increase in cases of sarcoidosis with both typical and atypical presentation. Our case highlights an emergent need for algorithmic approach incorporating various clinical, radiological, pathological, and biochemical markers to make a confident diagnosis of sarcoidosis.

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.

Financial support and sponsorship

Nil.
Conflicts of interest
There are no conflicts of interest.

Shweta Mahapatra, Loveleen Mangla, Deepak Talwar
Metro Centre for Respiratory Diseases, Noida,
Uttar Pradesh, India
E-mail: dtlung@gmail.com

REFERENCES
1. Judson MA, Costabel U, Drent M, Wells A, Maier L, Koth L, et al. The WASOG sarcoidosis organ assessment instrument: An update of a previous clinical tool. Sarcoidosis Vasc Diffuse Lung Dis 2014;31:19-27.
2. Takeyama K, Dabbagh K, Lee HM, Agusti C, Lausier JA, Ueki IF, et al. Epidermal growth factor system regulates mucin production in airways. Proc Natl Acad Sci U S A 1999;96:3081‑6.
3. Popat N, Raghavan N, McIvor RA. Severe bronchorrhea in a patient with bronchioloalveolar carcinoma. Chest 2012;141:513‑4.
4. Homma H, Kira S, Takahashi Y, Imai H. A case of alveolar cell carcinoma accompanied by fluid and electrolyte depletion through production of voluminous amounts of lung liquids. Am Rev Respir Dis 1975;111:857‑62.
5. Hudson E, Lester JF, Attanoos RL, Linnane SJ, Byrne A. Successful treatment of bronchorrhea with octreotide in a patient with adenocarcinoma of the lung. J Pain Symptom Manage 2006;32:200‑2.
6. Hiratsuka T, Mukae H, Ihiboshi H, Ashitani J, Katoh S, Mashimoto H, et al. Severe bronchorrhea accompanying alveolar cell carcinoma: Treatment with clarithromycin and inhaled beclomethasone. Nihon Kokyuki Gakkai Zasshi 1998;36:482‑7.
7. Nakajima T, Terashima T, Nishida J, Onoda M, Koide O. Treatment of bronchorrhea by corticosteroids in a case of bronchioloalveolar carcinoma producing CA19‑9. Intern Med 2002;41:225‑8.
8. Homma S, Kawabata M, Kishi K, Tsuboi E, Narui K, Nakatani T, et al. Successful treatment of refractory bronchorrhea by inhaled indomethacin in two patients with bronchioloalveolar carcinoma. Chest 1999;115:1465-8.
9. Takao M, Inoue K, Watanabe F, Onoda K, Shimono T, Shimpo H, et al. Successful treatment of persistent bronchorrhea by gefitinib in a case with recurrent bronchioloalveolar carcinoma: A case report. World J Surg Oncol 2003;1:8.
10. Joshi S, Periwal P, Dogra V, Talwar D. Sarcoidosis as unusual cause of massive pleural effusion. Respir Med Case Rep 2015;16:143-5.