Bilaterally enlarged parotids and sicca symptoms as a presentation of sarcoidosis: Pivotal role of aspiration cytology in diagnosis

ABSTRACT
Sarcoidosis is a chronic multisystem inflammatory disease of unknown etiology characterized by widespread noncaseating granulomas in various organs. The diagnosis of sarcoidosis is based on cytological, clinicoradiological, and radiological findings, and requires careful exclusion of other granulomatous diseases especially tuberculosis. Involvement of parotid glands is uncommon. Presentation of sarcoidosis with sicca symptoms that include dryness of eyes and mouth is an even rarer phenomenon. We present a case of multisystemic sarcoidosis presenting with dryness of eyes and mouth along with bilateral enlargement of parotid glands. Fine-needle aspiration cytology (FNAC) smears showed epithelioid cell granulomas and multinucleate giant cells. Stain for acid-fast bacilli was negative. Careful cytological examination revealed crystalline structures inside the giant cells, which prompted us to evaluate the patient for sarcoidosis. This case report highlights the cytological features that can be useful in clinching the diagnosis of sarcoidosis in conjunction with clinicoradiological and laboratory findings in a clinically unusual case.

Keywords: Cytology; parotid; sarcoidosis; sicca; tuberculosis

Background
Sarcoidosis is a multisystemic granulomatous disease of unknown etiology characterized by presence of noncaseating granulomas in various organs. Lungs are affected in more than 90% of cases. Involvement of parotid glands is seen in less than 6% cases. Sarcoidosis presenting with parotid gland enlargement, dryness of mouth, and eyes, i.e., sicca symptoms is a very rare phenomenon and may occasionally coexist with Sjogren's syndrome. Due to clinicoradiological as well as cytological resemblance of sarcoidosis and tuberculosis, diagnosis of the two conditions may be difficult, especially in the Indian context, where the burden of tuberculosis is high. Moreover, recently, there has been a debate regarding the causal relationship between tuberculosis and sarcoidosis.

We present a case of multisystemic sarcoidosis presenting with sicca symptoms along with bilateral enlargement of parotid glands highlighting the cytological features that can be useful in clinching the diagnosis of sarcoidosis in conjunction with clinicoradiological and laboratory findings.

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How to cite this article: Sharma T, Joshi D, Khurana A, Gupta V, Kapoor N. Bilaterally enlarged parotids and sicca symptoms as a presentation of sarcoidosis: Pivotal role of aspiration cytology in diagnosis. J Cytol 2015;32:281-3.
Case Report

A 54-year-old female presented with complaints of swelling of bilateral parotid glands, dryness of throat and eyes, and dry cough for 6 months. The patient also had a history of enlargement of bilateral submandibular glands that subsided spontaneously. There was no history of prolonged fever, expectoration, or tuberculous contact. However, she complained of decreased appetite and loss of weight. Patient had been seeking treatment elsewhere before coming to us. Her chest radiograph showed bilateral hilar prominences. A fine-needle aspiration cytology (FNAC) done 2 months back from parotid swellings was inconclusive. Polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* done on parotid aspirate was negative.

Physical examination revealed bilateral diffusely enlarged parotid glands with no lymphadenopathy. FNAC was performed on bilateral parotid glands. The smears showed noncaseating epithelioid granulomas and multinucleated giant cells against a background of lymphoid cells, salivary ductal, and acinar cells. Few giant cells showed presence of crystalline structures [Figure 1]. No caseous necrosis or Langhans giant cells were seen. Stain for acid-fast bacilli (AFB) was negative. A diagnosis of granulomatous inflammation with possibility of sarcoidosis was made.

Upon further workup, serum angiotensin-converting enzyme (ACE) level was 156 U/L (reference value 8-53 U/L) and serum calcium level was 9 mg/dL. Patient’s hemoglobin was 9.7 g/dL with neutrophilic leukocytosis. Erythrocyte sedimentation rate (ESR) was 31 mm/first hour and C-reactive protein was 8.3 mg/dL. Anti-Ro and Anti-La antibodies were negative.

High resolution computed tomography (HRCT) and contrast enhanced computed tomography (CECT) chest showed widespread nodular opacities having peribronchovascular distribution in bilateral lungs. Multiple enlarged lymph nodes were seen in the pretracheal space, left para-aortic, and right hilar region. No definite caseation was seen [Figure 2a]. Multiple small nonenhancing hypodense lesions widely distributed in liver and spleen were also seen. The patient was advised fiberoptic bronchoscopy and transbronchial needle aspiration from the hilar lymph nodes. However, the patient refused to undergo this procedure.

Hence, a final diagnosis of sarcoidosis was made on the basis of clinicoradiological, cytological, and laboratory findings. The patient had multisystem involvement of bilateral parotid glands, lacrimal glands, lungs, mediastinal lymph nodes, liver, and spleen. The patient responded well to steroids, with complete regression of bilateral parotid swellings, relief from cough and increase in appetite. The repeat HRCT and CECT after a period of 6 months showed near complete resolution of lung, mediastinal, and hepatosplenic lesions [Figure 2b].

Discussion

Sarcoidosis is a granulomatous disease of unknown etiology. It commonly affects young and middle-aged females. It most commonly presents with involvement of lungs and bilateral hilar lymphadenopathy; however, various other organs may be involved and patients may present with diverse complaints. The diagnosis requires the demonstration of typical lesions in the involved organ and exclusion of other disorders known to cause granulomatous disease.\[1\]

Sarcoidosis may uncommonly present with bilateral parotid gland enlargement. Since, Sjogren's syndrome may commonly present with enlarged parotid glands, dryness of mouth and eyes; the first clinical differential diagnosis was with Sjogren's syndrome, which was excluded on the basis of cytology findings and serology. While aspirate of salivary gland in sarcoidosis shows presence of granulomatous inflammation. Sjogren's syndrome shows predominantly lymphocytic infiltrate with positive anti-Ro and anti-La antibodies.\[3\]
Parotid gland involvement by tuberculosis is extremely rare, bilateral involvement being even rarer. However, since the prevalence of tuberculosis is high in India, exclusion of tuberculosis may be challenging and critical in such a case due to clinicoradiological resemblance of sarcoidosis and tuberculosis, and their different treatment modalities. Furthermore, there are reports on the occurrence of sarcoidosis and tuberculosis in the same patient either concomitantly or sequentially, indicating not only a possible link in their etiopathogenesis, but also a need to be highly cautious in the diagnosis and management.

In the present case, aspirate from parotid gland was negative for AFB and no caseous necrosis was seen. The aspirate showed presence of crystalline structures in few giant cells. Though no definite Schaumann or asteroid bodies were seen, presence of these crystalline deposits prompted us to evaluate the patient for sarcoidosis. Although these inclusions are nonpathognomonic for sarcoidosis, these may help in clinching the diagnosis. Crystalline inclusions composed predominantly of calcium oxalate may serve as the nidus for deposition of calcium leading to formation of Schaumann bodies. In previous case reports of parotid sarcoidosis diagnosed on FNAC, such as crystals, have only been occasionally reported. Most have reported the presence of noncaseating epithelioid granulomas and multinucleated giant cells in their aspirates without any evidence of caseation. Possibility of foreign body granulomas, tuberculoid leprosy, Crohn’s disease, toxoplasmosis, cat scratch disease, and fungal infections should also be kept in mind.

Apart from the presence of noncaseating granulomas, elevated ACE levels and a negative Montoux test favor a diagnosis of sarcoidosis over other granulomatous lesions. Although, elevated serum ACE levels may be seen rarely in tuberculosis, they are usually not raised to such high levels as in the present case. The level of serum ACE levels reflects the granulomatous load in sarcoidosis.

Multisystemic sarcoidosis can rarely present with bilaterally enlarged parotid glands and sicca symptoms. The clinicians and the pathologists should be aware of the rare manifestations of disease as the diagnosis of sarcoidosis is based on a constellation of clinical, radiological, and morphological findings. The cytological diagnosis of granulomatous inflammation should also be interpreted in the appropriate clinical context. A careful cytological examination for unique features of sarcoid granulomas, such as crystalline structures within the giant cells, may help us clinch the diagnosis of sarcoidosis even at uncommon sites. Our case report highlights the importance of salivary gland cytology in reaching at a diagnosis of multisystemic sarcoidosis in a clinically unusual case.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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