

## Isolated tonsillar sarcoidosis mimicking malignancy: Diagnostic and therapeutic dilemmas

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**Background:** Sarcoidosis is a multisystemic, granulomatous disease of obscure aetiology. Isolated tonsillar sarcoidosis is very rare and may mimic neoplasia.

**Case report:** We report a case of a 43 year old lady with isolated tonsillar sarcoidosis, whose clinical presentation was initially regarded as malignant tumour of the tonsil. The patient underwent tonsillectomy and received no further treatment. She remains free of symptoms one year following the diagnosis.

**Discussion:** Tonsillar sarcoidosis, in the absence of other systemic manifestations, may not be a straightforward diagnosis. Non caseating granulomas, the histological hallmark of the disease, are non-specific and may be found in granulomatous processes of a known cause (e.g. tuberculosis). The diagnostic approach aims at supporting the clinical findings and revealing the true extent of the disease. Correct and timely diagnosis prevents delays in treatment and institution of contraindicated therapies (e.g. steroids for masqueraded tonsillar Tuberculosis). Sarcoidosis should always be included in the differential diagnosis of asymmetric tonsils therefore histological examination of the tonsils is imperative. Patients suffering from sarcoidosis in the Head and Neck region need long term follow up. The initial diagnosis may change in the light of new symptoms and there may be a risk of developing malignant neoplasms in sarcoidosis. *Hippokratia* 2005; 9 (3): 134-137

**Key words:** *Sarcoidosis, tonsil, diagnosis*

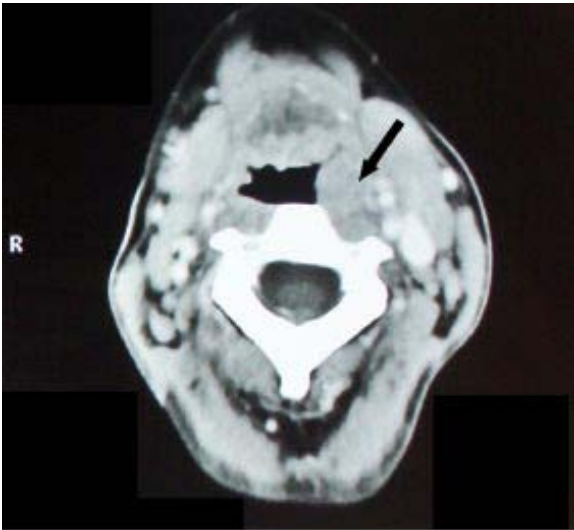
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Sarcoidosis is a multisystemic, granulomatous disease of unknown aetiology. Young and middle aged adults are affected and the prevalence is as high as 50 cases per 100000 per year<sup>1</sup>. The disease presents with pulmonary infiltrations, bilateral hilar lymphadenopathy, ocular and skin lesions. Head and Neck involvement is not infrequent and ranges between 10-15%<sup>2</sup>. Although 2.4% of patients with systemic disease suffer from tonsillar involvement<sup>3</sup>, isolated tonsillar sarcoidosis is very rarely reported in the literature<sup>4-7</sup>. Diagnosis is based on the correlation of clinical, radiological histological findings (noncaseating granulomas) and the exclusion of other granulomatous diseases or sarcoid like reactions. Overall prognosis is good and 60-70% of the patients are cured without treatment. However, 1-5% dies as a result of cardiac, respiratory or neurological complications<sup>1</sup>. In this study we present a case of isolated sarcoidosis of the palatine tonsils which was initially regarded as a malignancy. Furthermore, we discuss the diagnostic difficulties relating to sarcoidosis of the Head and Neck and the factors affecting treatment planning. Finally we propose a stepwise approach for establishing diagnosis in cases of sarcoidosis limited to the Head and Neck region.

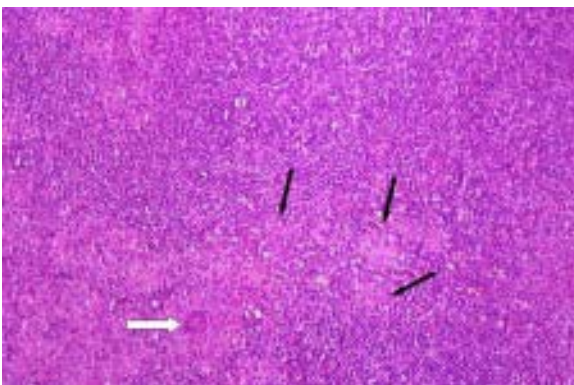
### Case report

A 43-year-old female presented at the Otolaryngology Outpatient Clinic with a 1-month history of dysphagia

and a left neck swelling. She had suffered a couple of episodes of acute tonsillitis in her childhood and she reported no previous history of malignancy. She was afebrile and had bilateral tonsillar enlargement most prominent on the left side. The neck mass, measuring 1.5X3 cm, was located at the left carotid triangle. On palpation it felt hard and mobile. Basic blood tests revealed mildly elevated erythrocyte sedimentation rate and alanine aminotransferase. The chest x-ray (CXR) was negative and subsequent Computed Tomography scan (CT) of the neck, chest and abdomen showed a few enlarged hilar and axillary lymph nodes and the bilateral enlargement of the tonsils (Figure 1). She was treated with a 5-day course of Piperacillin+Tazobactam without any improvement. A tonsillectomy was performed and histological examination of the specimen revealed non-caseating granulomas (Figure 2). The absence of mycobacteria and fungi was confirmed by negative staining. In order to establish the diagnosis and extent of sarcoidosis the patient underwent further investigation. Toxoplasma serology, serum calcium and angiotensin converting enzyme levels (ACE) were normal. Gallium-67 scintigraphy (Ga-67) failed to reveal areas of granulomatous infiltrates. She was diagnosed with isolated sarcoidosis of the tonsils and received no further treatment. The patient remains free of symptoms a year following initial diagnosis.



**Figure 1.** Computed Tomography of the neck (axial section) demonstrating the left tonsillar enlargement (black arrow).



**Figure 2.** Section of tonsillar tissue characterised by marked lymphocytic proliferation and the presence of multiple non caseating granulomas (black arrows) which are consisted of epithelial-like and a few Langhans-type cells (white arrow) (haematoxylin-eosin, X200)

## Discussion

The aetiology of sarcoidosis is largely unknown. Several environmental factors such as bacteria and chemical substances (beryllium) along with genetic susceptibility are implicated in the initiation of an immunological reaction that accounts for the clinical manifestations of the disease. Dry non-productive cough and progressive dyspnoea are the cardinal symptoms. The clinical picture often includes skin plaques, erythema nodosum, uveitis, iritis, cranial nerve palsies, cystic lesions of the phalanges, metacarpal and metatarsal bones etc.

The diagnosis of sarcoidosis is based on the combination of clinical, radiological and histological findings and the exclusion of other granulomatous diseases because a specific and practical diagnostic test is not available. The Kveim skin test, though highly specific (only 5% false positive results), has been of limited use due to the lack of standardization and the

safety risks arising from the endodermal injection of human tissues<sup>5</sup>.

The basic diagnostic workup comprises of chest X-ray and biopsy. Chest X-ray is positive in 90% of the subjects in the course of disease and findings include hilar lymphadenopathy, pulmonary infiltrates and interstitial fibrosis. Biopsy from accessible sites (skin or mucosal lesions, lymph nodes, lungs) is a sine qua non.

The main histological feature of sarcoidosis is the presence of noncaseating granulomas of epithelial like cells surrounded by lymphocytes. The above picture is non-specific and may be seen in granulomatous diseases of known cause such as tuberculosis (tbc), fungal infection, berylliosis and foreign body reaction. Malignancies such as carcinoma of the lung, non-Hodgkin lymphoma and squamous cell carcinomas may produce a sarcoid like reaction locally or distantly<sup>6</sup>. These conditions should be appropriately investigated before a definitive diagnosis of sarcoidosis is made.

Biopsy is a very important step in investigating suspected sarcoidosis. In cases of pulmonary sarcoidosis with secondary involvement of the Head and Neck region the diagnosis is not difficult. However, if isolated sites such as the palatine tonsils are affected in the absence of pulmonary findings it is imperative that other granulomatous diseases are excluded. A number of relevant tests should be requested: purified protein derivative (PPD) skin test, culture and repeated examinations of the specimen with appropriate stains for acid-fast bacilli and fungi. If the above workup is negative the most likely diagnosis is sarcoidosis. Subsequently, the patient undergoes investigations that will reveal other affected sites. Elevation of ACE is not specific for sarcoidosis. It may be used for monitoring disease progress and response to treatment. Hypercalcaemia and hypercalciuria may occur. The latter is a more frequent finding and may herald nephrolithiasis. A practical guide for diagnosis of isolated sarcoidosis in the Head and Neck is provided in table 1.

## Significance of proper and timely diagnosis

The high index of suspicion, the meticulous and rational investigation of patients with suspected sarcoidosis is important in preventing delays and errors in treatment.

On certain occasions sarcoidosis can mimic malignancy and may confuse clinicians. Vaz and Samuel<sup>8</sup> describe a case of post-cricoid sarcoidosis which was clinically regarded as neoplasia. The first histological examination showed chronic inflammatory changes. Subsequently, the patient underwent a series of microlaryngoscopies-biopsies so that malignancy could be excluded, unsuccessfully. Eventually the patient died of pulmonary sarcoidosis leading to respiratory insufficiency (post-mortem examination). The injudicial use of invasive procedures may not be to the patient's best interests.

Kardon and Thompson<sup>6</sup> reported three cases with a

**Table 1.** *Diagnostic approach in isolated sarcoidosis in the Head and Neck region*

Initial workup	<ul style="list-style-type: none"> <li>• Biopsy of easily accessible area (Fine Needle Aspiration Biopsy if possible)</li> <li>• Chest X-Ray</li> </ul>
Tests for exclusion of other granulomatous diseases	<ul style="list-style-type: none"> <li>• Thorough histological examination of the specimen with multiple sections and stains for mycobacteria and fungi</li> <li>• Culture</li> <li>• Purified Protein Derivative skin test</li> <li>• C- and P-Antinuclear cytoplasmic antibodies, Antinuclear antibodies, Rheumatoid factor</li> <li>• Human Immunodeficiency Virus antibodies</li> <li>• Toxoplasma serology</li> </ul>
Tests to reveal the true extent of the disease	<ul style="list-style-type: none"> <li>• Computed Tomography of the chest</li> <li>• Ga-67 scintigraphy (extra-pulmonary lesions)</li> <li>• Trans-bronchial lung biopsy</li> <li>• Bronchoalveolar lavage-cytology</li> <li>• Mediastinoscopy –biopsy (invasive)</li> </ul>
Complementary tests	<ul style="list-style-type: none"> <li>• ACE</li> <li>• Serum and urine calcium</li> </ul>

presumed diagnosis of tonsillar sarcoidosis. In the first case, despite an abnormal CXR, histological staining was omitted and on the basis of a negative PPD skin test, the patient received no anti-tuberculous treatment. A year later he died of fulminating pulmonary tuberculosis. The two other cases are of interest because the initial examination was negative for tbc. The diagnosis of tbc was possible after repeated sections and stains of the specimen. These patients were successfully treated with anti-tuberculous chemotherapy.

Om Sharma<sup>9</sup> describes a case of nasal sarcoidosis misdiagnosed as allergic rhinitis. Functional endoscopic sinus surgery and biopsy revealed chronic inflammation and the patient was discharged. Four weeks later, the patient presented with hearing loss and the possibility of sarcoidosis was raised. Despite negative diagnostic workup, treatment with steroids was instituted. Gradual involvement of the central nervous system (CNS) dictated further testing with MRI which showed lesions in the cerebellum. Subsequent cerebellar biopsy confirmed the presence of non-caseating granulomas and treatment was intensified (high doses of steroids plus hydroxychloroquine) with positive results. Correct and early diagnosis and treatment could have prevented the CNS involvement.

### Treatment

Once disease extent is known several treatment issues need to be tackled in liaison with the Respiratory Physicians. Is medical therapy necessary? What medications and duration of therapy? High rate of spontaneous resolution, any uncertainty with regards to correct diagnosis and a stable clinical condition are all reasons to adopt a “wait and watch” policy. When the

nose is affected, prompt treatment is a wise decision because disease progression is very likely<sup>9</sup>. On the other hand, mild sarcoidosis of the larynx and hilar lymphadenopathy are usually self limiting processes requiring no treatment.

Steroids with or without immunosuppressive agents (methotrexate, azathioprine) are the mainstay of medical therapy. They are administered either locally (e.g. nasal sprays, intralesional injection) or systemically at doses 20-40 mg/day. Antimalarial agents (hydroxychloroquine) are useful in correcting hypercalcaemia and when the nose and skin are affected. Other therapies include anti-leprotic, antifungal agents (ketokonazol) and monoclonal antibodies.

There are no strict rules regarding duration of treatment. Sarcoidosis often relapses with discontinuation of treatment, therefore long therapeutic schemes are proposed<sup>9,10</sup>.

The role of surgery in Sarcoidosis of the Head and Neck region is limited. Upper airway obstruction due to laryngeal sarcoidosis may necessitate a tracheostomy. Similarly, dysphagia due to enlarged tonsils may be managed with tonsillectomy. Nasal polypectomy and submucous resection should be avoided due to the risk of septal perforation<sup>10</sup>.

### Follow up

Patients with sarcoidosis of the Head and Neck region should be seen regularly and for a long period of time. Diagnosis may change with time. There is also a debatable association of sarcoidosis with malignancy. Askling et al<sup>11</sup> found that there is a two-fold increase in the risk of developing lung cancer in the first years following diagnosis of sarcoidosis which subsequently decreases. For lymphomas the risk is doubled, five to nine years after diagnosis. In the Head and Neck region cancer may develop in the paranasal sinuses, oral mucosa, lips and pharynx. However the above epidemiological data have been drawn from patients with sarcoidosis of any extent and no specific information is available for isolated disease in the Head and Neck region.

### Conclusion

Isolated sarcoidosis of the palatine tonsil is very rare. It can mimic malignancy and is difficult to diagnose. Until the histological specimen is thoroughly examined and other granulomatous and neoplastic conditions are excluded, the diagnosis of sarcoidosis cannot be established. Investigation of other systems (mainly the lower respiratory tract) for possible involvement should not be omitted. Usually, treatment with steroids is required, although a “wait and watch” policy may be indicated due to the high rate of spontaneous resolution.

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