CASE REPORT

Ear, Nose, and Throat sarcoidosis: An etiology that should raise a flag? About two case reports

La sarcoïdose Oto-rhino-laryngologique: Une étiologie qui doit mettre la puce à l'oreille? A propos de deux cas cliniques

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Abstract

Introduction: Sarcoidosis is a chronic inflammatory disease characterized by non-caseous necrotizing epithelial cell granulomas that can affect any organ. Ear, nose, and throat (ENT) involvement is rare. We report two cases of systemic sarcoidosis with ENT onset.

Observation: A 39-year-old woman with no medical history, presented with right submaxillary lymphadenopathy, associated with a nasopharyngeal swelling on the nasopharyngoscopy. Lymph node biopsy revealed numerous granulomas with epithelioid and giant cells. The computed tomography (CT) showed multiple lymph nodes along with interstitial lung disease. The diagnosis of sarcoidosis with pulmonary, mediastinal, lymph node, and nasopharyngeal involvement was retained and the patient was treated with glucocorticoids with disappearance of the submaxillary swelling and of the lymph nodes on the CT. Another 39-year-old woman, with no medical history, presented to the ENT clinic with a three-month history of bilateral nasal obstruction. Nasal endoscopy revealed hyperemia of the nasal mucosa. She was treated with antibiotics without clinical improvement. CT scan of the cranial and facial bones revealed a focal bulge at the nasopharynx's posterior wall, associated with a mucosal thickening of maxillary, frontal, and ethmoid sinuses. A nasal and a lymph node biopsy were then performed, revealing granulomatous inflammation without caseous necrosis. The diagnosis of sarcoidosis with pulmonary, lymph node, and sinonasal involvement was established. The patient was treated with glucocorticoids with clinical improvement.

Conclusion: Nasopharyngeal and sinus involvement may be rare in sarcoidosis but can be part of the initial clinical picture of the disease. Therefore, it should put the flea in the ear in case of ENT granulomatosis.

Key words: case reports, orofacial granulomatosis, sarcoidosis

Résumé

Introduction: La sarcoïdose est une maladie inflammatoire chronique caractérisée par la présence de granulome sans nécrose caséeuse, pouvant toucher plusieurs organes. L'atteinte oto-rhino-laryngologique (ORL) au cours de la sarcoïdose est rare. On rapporte deux observations de sarcoïdose révélée par une atteinte ORL.

Observations: Une femme de 39 ans sans antécédents, a consulté pour une adénopathie sous-maxillaire droite, associée à un gonflement du nasopharynx à la naso-pharyngo-scopie. Une biopsie des ganglions lymphatiques a révélé de nombreux granulomes avec des cellules épithélioïdes et géantes. La tomodensitométrie a montré de multiples ganglions lymphatiques ainsi qu'une atteinte pulmonaire interstitielle. Le diagnostic de sarcoïdose avec atteinte pulmonaire, médiastinale, ganglionnaire et du nasopharynx a été retenue. Une autre femme de 39 ans, sans antécédents médicaux, a consulté en ORL pour une obstruction nasale bilatérale évoluant depuis trois mois. L'endoscopie nasale a révélé une hyperémie de la muqueuse nasale. La femme a été traitée par antibiothérapie sans amélioration clinique. Une tomodensitométrie du massif facial a révélé une protrusion focale de la paroi postérieure du nasopharynx, associée à un épaississement de la muqueuse des sinus maxillaires, frontaux et ethmoïdaux. La biopsie nasale et ganglionnaires a montré une inflammation granulomateuse sans nécrose caséeuse. Le diagnostic de sarcoïdose avec atteinte pulmonaire, ganglionnaire et sinonasale a été retenu. La patiente a reçu alors une corticothérapie avec nette amélioration clinique.

Conclusion: L'atteinte du nasopharynx et des sinus peut être rare dans la sarcoïdose mais peut faire partie du tableau clinique initial de la maladie. Par conséquent, elle doit être envisagée en cas de granulomatose ORL.

Mots clés: Granulomatose orofaciale, présentations de cas, sarcoïdose

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Introduction

Sarcoidosis is a chronic inflammatory disease characterized by non-caseous necrotizing epithelial cell granuloma affecting many organs (1). The lung and lymphatic system are most frequently involved (2). However, sarcoidosis might affect any other organ with variable frequency and degree of impairment (2).
Extra thoracic manifestations often occur and are in most cases associated with intrathoracic involvement (2). The most frequent sites of extra thoracic sarcoidosis are the peripheral lymph nodes, skin, eyes and liver, each reported in about 10-25% of cases in most studies (2). Ear, nose, and throat (ENT) involvement is rare (3). It is present in 5-15% of patients with sarcoidosis, often as a presenting feature and require vigilance for swift recognition and coordinated additional treatment specific to the organ (3).
We reported two cases of systemic sarcoidosis with ENT onset.

Observations

Case 1

A 39-year-old woman with no medical history, presented with right submaxillary lymphadenopathy, associated with a nasopharyngeal swelling on the nasopharyngoscopy. Both cervical lymphadenopathy biopsy and nasopharyngeal biopsy showed epithelioid granulomas. Given the epidemiological context, anti-tuberculosis treatment was prescribed. Twelve months later, while on medication, no improvement was observed. Physical examination showed an increase in the size of the submaxillary adenopathy with new cervical lymphadenopathy. Lymph node biopsy showed numerous granulomas with epithelioid and giant cells. A second lymph node biopsy revealed numerous granulomas with epithelioid and giant cells. These granulomas contained eosinophilic fibrinoid necrosis with interspersed lymphocytes. The computed tomography (CT) showed multiple lymph nodes (cervical, axillary, para tracheal, subcarinal, para-oesophageal, hilar, retroperitoneal, para-aortic, aorto-cava, porto hepatic, peri splenic, mesenteric, and inguinal) along with an interstitial lung disease. Blood tests showed lymphopenia (920/mm^3) (1000-4000 lymphocytes/mm^3) and hypercalciuria (6.2 mg/day) (<0.1mg/kg/day) with no hypercalcemia nor other abnormalities. Analysis of bronchoalveolar lavage fluid revealed lymphocytic alveolitis with an increased ratio of T lymphocytes with cluster of differentiation (CD) 4+ to CD8+ T cells at 6.2. Spirometry was normal [forced vital capacity: 87%, forced expiratory volume in one second: 96%]. The diagnosis of sarcoidosis with pulmonary, mediastinal, lymph node, and nasopharyngeal involvement was established. The patient received oral route glucocorticoids (60 mg/day), with clinical and radiologic improvement: In fact, the lymphadenopathy disappeared and the computed tomography showed the disappearance of the lymph nodes and of the parenchymal involvement. One year later, while still on glucocorticoids treatment at a dose of 10 mg/day, the patient presented with a severe nasal obstruction. The CT scan of the cranial and facial bones revealed mucosal thickening of maxillary, frontal, sphenoid and ethmoid sinuses, as well as a nasal septal deviation and a partial lysis of the nasal turbinates. Glucocorticoids treatment dosage was hence increased and oral route methotrexate (15 mg weekly) was added. After one year of follow-up, a favorable evolution of clinical and radiological signs was noted. In fact, the physical examination found no lymphadenopathy and the CT scan showed no evidence of mucosal sinus or nasopharyngeal thickening and the disappearance of the nasal septal deviation.

Case 2

A 39-year-old woman with no medical history, presented to the ENT clinic with a three-month history of bilateral nasal obstruction. Nasal endoscopy revealed hyperemia of the nasal mucosa. She was treated with antibiotics without clinical improvement. A few months later, she was referred to the internal medicine clinic due to worsening nasal obstruction, anosmia, and dyspnea along with cervical and axillary lymphadenopathies. Lung function tests were not conducted because of a lack of adequate equipment. CT scan of the cranial and facial bones revealed a focal bulge located at the posterior wall of the nasopharynx, associated with a mucosal thickening of maxillary, frontal, and ethmoid sinuses. Laboratory test results revealed lymphopenia (860/mm^3) with no other abnormalities. The cervico-thoracic-abdominal scan showed multiple thoracic and abdominal lymphadenopathies and a nonspecific interstitial pneumonia. A nasal and a lymph node biopsy were then performed, revealing granulomatous inflammation without caseous necrosis. The diagnosis of sarcoidosis with pulmonary, lymph node, and sinonasal involvement was retained. The patient was treated with oral route glucocorticoids (60 mg per day) with clinical improvement (i.e.; a decrease in nasal obstruction, and the disappearance of dyspnea).

Discussion

Sarcoidosis is a multisystemic granulomatous disorder that can involve the ENT area. Lymph node enlargement may be the first sign of the disease and may mislead the diagnosis. ENT involvement may also start with nasal obstruction. In both cases, the histopathology was important to help set the diagnosis, along with other arguments for the absence of differential diagnosis (such as the absence of fever, extreme sweating, weight loss, and lethargy). Our findings are in line with Milton's report (4), which states that patients presenting to the ENT clinic may complain of nasal obstruction, often associated with epistaxis and crusting, or may have symptoms referrable to the larynx, including hoarseness, dyspnea and perhaps stridor. Other patients may be referred with soft tissue swellings in the region of the head and neck. These

swellings may be due to enlargement of local lymph nodes (4).

Sarcoidosis is characterized by a T-helper response, in which CD4+ lymphocytes and activated macrophages accumulate in affected organs, resulting in the formation of granulomas (5). The clinical expression, natural history, and prognosis of sarcoidosis are unpredictable, and no reliable indicators of clinical outcome are available (6). Sarcoidosis can involve any organ (5). The lung, skin and ocular signs are the mostly affected (5). The diagnosis of sarcoidosis is based on clinical, radiologic findings and histological evidence of non-caseous epithelioid-cell granulomas (5). Biopsies are usually taken from the most accessible affected organ (5). Approximately 10–15% of patients have symptomatic specific otolaryngological involvement including, the larynx (0.5–1.4%), the major salivary glands, such as Heerfordt's and Mikulicz's syndromes (5–10%), and the nose and paranasal sinuses (1–4%) (7). A large epidemiological study reported that 36 patients (0,04%) had nasal mucosal involvement out of 818 patients with sarcoidosis (8). The clinical manifestations of ENT involvement depend on the anatomic location of the granulomatous inflammation and/or scarring, that often occurs in chronic forms (9). On examination, the nasal mucosa is generally hypertrophic, erythematous and granular (9). Polyps, masses and/or asymmetric crust-like patches can be also observed (9). Septal perforation is rare (9). Patients with sarcoidosis of the sinuses can experience recurrent infections, epistaxis, periorbital tenderness, post-nasal drip and headache (9). The appearance of sarcoid lesions in the sinus mucosa is common (9). Examination shows erythematous, friable, hypertrophied mucosa. Crusting, studding, plaque-like changes or polyps may also be visualized (9). Rarely, granulomatous lesions extend out of the sinuses and inside the orbit, resulting in proptosis and/or decreased unilateral visual acuity (9). Nasal and sinus granulomatous disease includes infectious diseases (e.g.; tuberculosis, syphilis, actinomycosis, aspergillosis, blastomycosis, histoplasmosis, leprosy…), neoplastic, and inflammatory diseases (e.g.; granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis) (9). Many treatments have been proposed in the literature for the management of nasopharyngeal and sinonasal sarcoidosis: local corticosteroids (local nasal corticosteroids, intralesional injections of corticosteroids), systemic oral corticosteroids, hydroxychloroquine, methotrexate, azathioprine, cyclophosphamide, thalidomide, pentoxifylline, rituximab or infliximab (9). Sinus surgery has been suggested (endoscopic sinus surgery or laser surgery) in some cases (10).

Our paper has some limitations. First, the study is based on only two cases, which limits the generalizability of the findings. Larger studies are needed to confirm these observations and provide more robust data. Second, while the paper mentions short-term outcomes, it lacks information on the long-term prognosis of the patients. Long-term follow-up would provide insights into the chronic management and recurrence of the disease. Third, the paper does not discuss how the cases were selected, which may introduce selection bias. It is unclear if these cases are representative of the broader population with ENT sarcoidosis.

To conclude, nasopharyngeal and sinus involvement may be rare in sarcoidosis, but they can be part of the initial clinical picture of the disease. Therefore, it should put the flea in the ear in case of ENT granulomatosis.

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