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Tonsillar actinomycosis mimicking relapse of diffuse large B-cell non-Hodgkin lymphoma

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Actinomicosis amigdalina imitando una recaída de un linfoma no Hodgkin

We describe a case of tonsillar actinomycosis mimicking relapse of diffuse large B-cell non-Hodgkin lymphoma. Actinomycosis infection is a rare disease, clinical progression it’s usually gradual and diagnoses process it’s challenging. This report outlines the case of a 63-year-old woman, diagnosed with lymphoma in the right tonsil three years ago, actually in complete remission. During follow-up, there was a slight increase in lactate dehydrogenase (LDH) evaluation. Due to the possibility of a relapse of lymphoma, positron emission tomography-computed tomography (PET-CT) was performed, detecting increased activity in the left oropharynx, which appeared to be thicker in the exam. The patient was submitted to surgical excision of the lesion, with a histological diagnosis of left tonsillar actinomycosis. The genus Actinomyces is composed of non-acid-fast, anaerobic or microaerophilic, commensal bacteria of the oropharynx and the respiratory and digestive tracts. The cervicofacial form is the most common. Surgical excision is frequently essential for a definitive diagnosis. Although uncommon, it is important to include this disease in the differential diagnosis when a tumor-like mass is detected in the cervicofacial region.

Key words: Actinomycosis, Lymphoma, Tonsil, PET-CT, Head and neck.

Palabras clave: Actinomicosis, linfoma, amígdalas, PET-CT, cabeza y cuello.

Introduction

Actinomycosis was first described as a clinical entity about 100 years ago. It is a chronic, granulomatous, supplicative, bacterial infection that sporadically occurs due to the widespread use of antibiotics. The genus Actinomyces is composed of gram-positive, non-acid-fast, anaerobic or microaerophilic filamentous branched bacteria. It lives as a commensal organism in the human mouth, respiratory and intestinal tracts, and becomes invasive when it penetrates the subcutaneous tissue through a mucosal lesion. There are three main clinical forms: cervicofacial (50%), thoracic (30%) and abdominopelvic (20%). Diagnosis is based on culture isolation, microscopic visualization of a cytology smear or histopathological examination. Treatment includes surgery and complementary antibiotic therapy; however, there is no consensus on treatment duration. In this study, we report a case of cervicofacial actinomycosis mimicking a relapse of diffuse large B-cell non-Hodgkin lymphoma.

Case report

A 63-year-old woman was diagnosed with DLBC NHL in the right tonsil, three years ago. She received eight chemotherapy cycles consisting of rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine and prednisolone (R-CHOP), every 21 days. Achieving complete remission. In follow-up visits, a slight increase in LDH was observed: 535 IU/L y 567 IU/L, 10 days later and 567 IU/L, 10 days later (reference value: 480 IU/L). Blood count, kidney and liver function showed no changes. Oropharynx, neck, chest, abdomen and pelvis computed tomography didn’t show relevant changes. The patient was asymptomatic and had a completely normal physical examination, i.e. the oropharynx was clear and no peripheral lymphadenopathy or hepatosplenomegaly were observed. She was afebrile, showed no weight loss and reported no night sweats. The patient reported a right tooth extraction two months before. Due to the possibility of a DLBC NHL relapse, PET-CT fusion imaging was performed, using 18F-2-fluoro-2-deoxy-glucose (18F-FDG). This exam revealed high uptake of the radiopharmaceutical, 18F-FDG, in a thickened area of soft tissue in the left lateral wall of the oropharynx (SUVmax=10.23), with poorly defined contours (Figure 1). Therefore the patient was submitted to surgical excision of the lesion. The histopathological examination was negative for malignancy, the palatine tonsil showed nonspecific reactive follicular lymphoid hyperplasia, and Actinomyces spp was detected. Hematoxylin and eosin stain (40x) highlights a bacterial cluster of Actinomyces spp (‘sulphur granule’) on the right of the photomicrograph. The filamentous nature of the bacteria is clearly evident (Figure 2). Treatment with 500/125 mg amoxicillin/clavulanic acid was prescribed.
for two months. Patient follow-up continues with no further changes in the clinical examination and normal LDH values.

Discussion

Cervicofacial presentation is the most common form of actinomycosis. Actinomyces species present low pathogenicity and only cause disease in previously damaged tissue, in most cases by direct invasion. Conditions that favor cervicofacial infection may include caries and tooth procedures, gingivitis and gingival trauma, chronic tonsillitis, otitis, mastoiditis and oral maxillofacial trauma. The predominant clinical compromised site are the submandibular region or mandibular angle, with or without cervical lymphadenopathy. It can also compromised nose, paranasal sinuses, cheeks, parotid glands, gingival sulcus, hypopharynx and tonsils. Reports of its incidence in the tonsils from, goes from 1.3 to 37%, depending mainly on the sectioning and staining method used by different laboratories. The infection most commonly presents as a floating, hardened or suppurative, slow-growing mass that becomes visible over weeks or months. Cervicofacial actinomycosis predominates in males (male:female ratio 4:1), principally aged between 41 and 50 years old. The reasons for this predominance remain unclear. It shows no known racial or geographical predisposition.

Its clinical presentation is usually nonspecific, though pain is rare, low fever occurs in about 50% of patients, associated with hardening or erythema around the mass. Clinical evolution tends to become more painful to physical examination and also tends to adhere to the overlying skin, which can show venous congestion resulting in a purplish color. The presence of increased regional lymph nodes it’s rare. Our case was asymptomatic, which may correspond to the onset of infection.

Only 10% of infections by species of the genus Actinomyces are diagnosed following their initial presentation. An accurate diagnosis is achieved by visualization of actinomycotic granules in exudates or in histopathological tissue sections. Regarding the first method, growing Actinomyces spp. is very difficult, even in suitable anaerobic media, and the rate of positive cultu-
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Actinomycosis associated with non-Hodgkin lymphoma is less than 50%. Microscopic examination of biopsy material stained with hematoxylin and eosin typically provides findings of a granuloma zone of granulation and a central zone of necrosis, containing multiple basophilic granules, representative of the lobulated microcolonies of Actinomyces spp. In recent years, less invasive techniques have gained prominence, such as fine-needle aspiration, which allows morphological identification compatible with the material obtained by biopsy, as well as being an efficient means of collecting material for microbiological studies.

Imaging techniques like computed tomography (CT) and magnetic resonance imaging (MRI) do not provide a specific diagnosis, but assist in defining the dimensions and extent of the lesion and the involvement of underlying tissue, which is of great help during surgery. CT findings include an enhancing soft-tissue mass with low attenuation in its center associated with inflammatory changes in adjacent tissues. Abundant granulation and attenuating fibrous tissues in the mass can cause high contrast uptake, while central supplicative necrosis may hinder contrast uptake. MRI T1 and T2-weighted images show intermediate signal intensity associated with moderate contrast uptake. In this case, another factor suggestive of the onset of an infectious process was the absence of changes in the CT.

Regarding its diagnostic difficulties, cervicofacial actinomycosis can mimic other chronic granulomatous lesions, such as tuberculosis or fungal infection, and malignant neoplasms of the head and neck. A malignant neoplasm can result in an enhancing solid mass, but the lesion usually has well-defined margins, with no significant inflammatory changes in adjacent tissues.

The literature has five well described cases of actinomycosis associated with non-Hodgkin lymphoma; however, to our knowledge, this is the first case of tonsil involvement that simulated a DLBC NHL relapse. It was not possible to determine any precise relationship between the two pathologies. Much has been discussed concerning immunosuppression due to cancer and its treatment as a relevant factor in the development of bacterial infection. In our case, the patient presented no clinical or laboratorial compromise when diagnosed with actinomycosis. It is unlikely that the infection was due to a state of immunosuppression caused by the lymphoma, rather it was likely related to the tooth extraction performed two months prior to the infection.

According to our patient’s clinical history, a DLBC NHL relapse was the most reasonable hypothesis, and given the asymptomatic presentation, a primary diagnosis of actinomycosis would have been quite unusual. Thus, a PET-CT was performed to provide a thorough examination and showed high uptake of 18F-FDG in the left tonsil, with no adjacent reactive lymph node. Though this is a highly sensitive marker, it is not a specific radiotracer for infection. Few cases of actinomycosis detected by 18F-FDG PET-CT have been documented in the literature. FDG PET may be useful in distinguishing between benign and malignant lesions, by the evidence of malignancy have generally a higher glycolytic rate and consequently higher FDG uptake. Some doctors use the maximum standardized uptake value (SUV) threshold of 2.5 to distinguish them. However, measurements SUV depends on several parameters: equipment used, the physics (variability scanner, reconstruction parameter changes, calibration error between scanner and dose calibrator, timing mismatch scanner and calibrator dose between, use of contrast material is PET/CT, interobserver variability) and biological factors (weight composition, body size measurement, blood glucose correction, postinjection uptake team, respiratory motion). In addition, infectious and inflammatory processes can lead to increased FDG uptake is much higher than the SUV of 2.5, mostly in acute lesions of infections. Because so many variables, SUV greater than 2.5 should not be decisive to differentiate between benign and malignant lesions. Thus, a biopsy was required to determine the diagnosis.

Treatment is individualized, such that the duration of antibiotic therapy depends on the initial disease burden, the site of infection and the clinical/radiological response. Abscess drainage is indicated. Penicillin remains the treatment of choice, beginning with intravenous administration until clinical improvement and thereafter with oral antibiotics. It can be associated with metronidazole, which makes the medium unfavorable for Actinomyces spp. Amoxicillin/clavulanic acid is another preferred option described in the literature. Penicillin-allergic patients, doxycycline, minocycline, tetracycline, clindamycin, erythromycin, and cephalosporins are valid alternatives. The tetracyclines probably offer the best option. There is no consensus on treatment duration, which can range from 3 to 52 weeks. Generally, the surgical approach combined with antibiotic therapy is effective. It is worth emphasizing that surgery (excisional biopsy) is also used for a definitive diagnosis in the majority of cases, which optimizes treatment, as verified in the case described herein. We opted for surgery complemented by two months of antibiotic therapy (amoxicillin/clavulanic acid), to prevent recurrence of the infection.

The prognosis for cervicofacial actinomycosis is generally good, with complete recovery by over 90% of patients treated with antibiotics. The result tends to be more expressive when combined with the surgical approach.

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