■ BRIEF REPORTS

Unusual Nasal Clinical Entities

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Three cases of rare entities in nasal pathology are reported. Two of them are high-grade lymphomas (T/NK type), with nasal blockage as the first symptom. Clinical course and treatment response are described. The third case refers to an infrequent benign nasal entity called angiocentric eosinophilic fibrosis. Its aetiology and management remains rather uncertain nowadays.

Key words: Non-Hodgkin lymphomas. Angiocentric eosinophilic fibrosis.

Entidades clínicas nasales inusuales
Se describen 3 casos correspondientes a enfermedades de presentación poco habitual en fosas nasales. Dos de ellos corresponden a linfomas de alto grado, que aparecieron con síntoma principal de obstrucción respiratoria, entidades tipo T/NK. Se describe su evolución, así como respuestas a los tratamientos instaurados. El último caso clínico se refiere a un cuadro benigno poco frecuente, conocido como fibrosis angiocéntrica eosinofílica, de cuyos etiología y manejo terapéutico hay conocimientos escasos en la actualidad.

Palabras clave: Linfomas no hodgkinianos. Fibrosis angiocéntrica eosinofílica.

INTRODUCTION

Primitive lymphomas of the head and neck correspond to non-Hodgkin neoplasias coming from B or T cell strains. Within the T-cell line, T/NK nasal lymphomas are noted for their infrequency and lethality. They were described for the first time by Stewart in 1933[1] and earlier, vaguely, by McBride (1878). For many years the lack of aetiopathogenic knowledge of this disease lead to multiple processes being grouped with it that had the common denominator of mesiofacial destruction. Currently, aetiological diagnosis is reached through a good quality biopsy and a histological, and immunohistochemical study. As T/NK lymphoma is the most frequent of the primitive nasal lymphomas (45%), we cannot overlook T lymphomas, comprising 21% of cases, and B lymphocytes, with 34%. In the development of these types of tumour, with reference to T/NK lymphoma, a probable ethnic factor exists with greater prevalence in Asia and South America, in addition to its association with Epstein-Barr[2,3] viral infections.

Angiocentric eosinophilic fibrosis is a benign and infrequent condition that was described in the 1980's as an intranasal variety of facial granuloma. It produces local obstruction and nasal swelling. Despite its rarity, it has not just been described at the sinonasal level, but also at the laryngeal level that appears with inspiration dyspnoea. It must be diagnosed by pathology analysis and no effective treatment has been described.

The objective of the present paper is to highlight various cases of the above-described entities diagnosed at our department, as well as their evolution, emphasizing the pathology study of fundamental importance for their diagnosis.

MATERIAL AND METHOD

Case 1

Male, 25-year-old, of Colombian origin, without relevant clinical history, came to the emergency department complaining of progressive nasal obstruction in the right nostril on-going for approximately 2 months, associated with foetid ipsilateral purulent rhinorrhea. Upon rhinoscopic examination, a destructured right nostril with intense oedema was noted. Through oropharyngoscopic examination, an ulcerated lesion was noted at the level of the first third of the hard palate, approximately 2×1 cm, ending at the floor of the right nostril. A sinonasal computerized tomograph (CT) scan was performed and provided information on the mucous enlargement in the right nostril and ipsilateral maxillary sinus. Samples were taken for microbiological cultures, with presence of *Candida albicans* and *Klebsiella*

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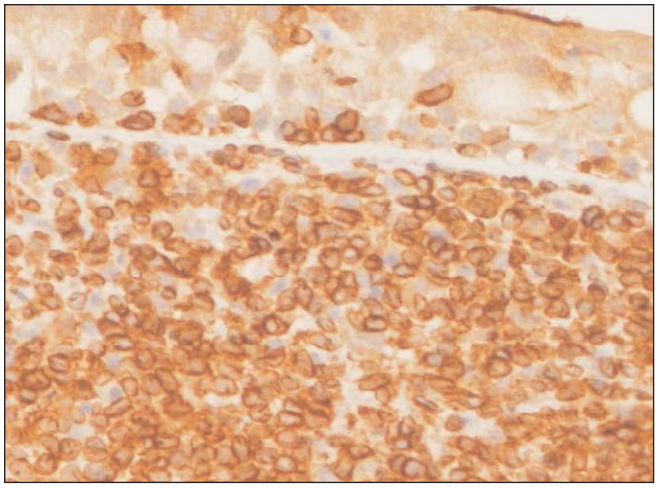

Figure 1. Pathology report was positive for CD3 in the first case.

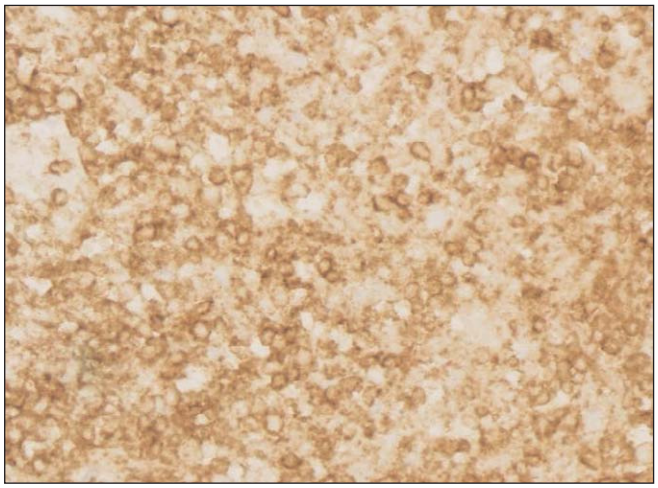

Figure 2. CD56 massively + in the second case using immunohistochemistry.

pneumoniae. At the same time, a biopsy was performed for pathology laboratory study using immunohistochemical techniques, positive for CD3, CD2, and proteins associated with cytotoxic granules such as granzyme B, perforin, and TIA-1 (Figure 1). Detection through in situ hybridization of the EBER-1 sequence of the Epstein-Barr virus resulted positive in numerous neoplastic cells. The molecular study of T-cell receptor rearrangement and of the immunoglobulin genes show germ line configuration. A definitive diagnosis of a high-grade extranodal T/NK cell lymphoma was reached.

After referring the patient to the haematology department, the study of its extension was completed and chemotherapy was initiated with 2 CHOP cycles. After the appearance and persistence of a fever, the therapeutic plan was modified, moving to VACOP-B cycles for 4 weeks, with CFU-6 between cycles and later HyperCVAD-type plans. During this period, renal and pulmonary conditions were detected with imaging technology, with overall worsening of his general state. He passed away after a few days.

Case 2

Male, 73-year-old, without relevant clinical history, arrived at the otorhinolaryngological clinic due to a progressive nasal obstruction in the left nostril, associated with mucosanguineous rhinorrhea. He also had frequent frontal-occipital cephalalgia and mild left facial oedema. Upon rhinoscopic examination, intense oedema of the septum and lateral nasal wall were noted at the level of the left nostril. The rest of the otorhinolaryngological examination revealed no relevant findings. Samples were taken for culture, with identification of *Pseudomonas aeruginosa* grew, prompting the start of oral treatment with ciprofloxacin (antibiogram show it to be sensitive to this). The study was completed with a sinonasal CT scan, which revealed a large mass at the base of the left nostril, without associated osteolysis. Given the inaccessibility of the nasal lesion by ordinary examination, we proceeded to perform, under general anaesthesia, sinonasal endoscopic surgery, with surgical debriding, and the taking of a biopsy. In the latter, *Pseudomonas* was again present, for which reason the ciprofloxacin treatment was continued until the end of the process. The diagnosis was complemented with a sample study using immunohistochemical techniques, finding it positive for CD45 and CD2, in addition to a massive expression of CD56 (Figure 2), TIA-1, CD43, and polyclonal cytoplasmic CD3, with loss of the expression of CD5 and CD7, as well as the absence of CD4 and CD8. On the basis of these data, we reached a diagnosis of an extranodal nasal NK non-Hodgkin lymphoma with high-grade malignancy.

The patient was referred to haematology, and the study of its extension was completed. Chemotherapy with 4 VEACOP-B cycles and a fifth with adriamycin and cyclophosphamide was begun. During this treatment, on 3 occasions hospital admission was required for therapy-related neutropenic fever, which subsided with empirical parenteral treatment with cephepime. During his last admission, he presented dyspnoea on making minimal effort, due to a massive pulmonary thromboembolism, and he passed away after a few hours.

Case 3

Woman, 41-year-old, arriving at the otorhinolaryngological clinic complaining of bilateral nasal obstruction, watery rhinorrhea, and closed rhinolalia, with occasional mild epistaxis, beginning approximately 18 months earlier. Upon examination with anterior rhinoscopy, a large oedema of the entire mucosae in both nostrils (Figure 3) and a subtotal septal perforation were observed. A CT scan was taken and it revealed mucous oedema and destruction of the septum, with striking absence of a paranasal condition and integrity of the medial wall of both maxillary sinuses. Biopsies were taken on 4 occasions, with topical and local anaesthesia, revealing inflammatory infiltration of abundant granulocytes, eosinophils, and lymphocytes, in addition to scant fibrinonecrotic material. The last biopsy was performed under general anaesthesia and with sinonasal endoscopic surgery. Finally, a diagnosis of angiocentric eosinophilic fibrosis was reached through a pathology lab

study. Inflammatory infiltration, predominantly in the eosinophils, abundant fibrosis and "onion skin" arrangement of the perivascular fibrosis of arterioles and venules were noted, as well as the absence of deep necrosis and granulomas of multinucleated giant cells. The presence of tumoral cells was ruled out by using immunohistochemical techniques.

Given that this disease has no described treatment, periodic reviews continue and a stable evolution is present.

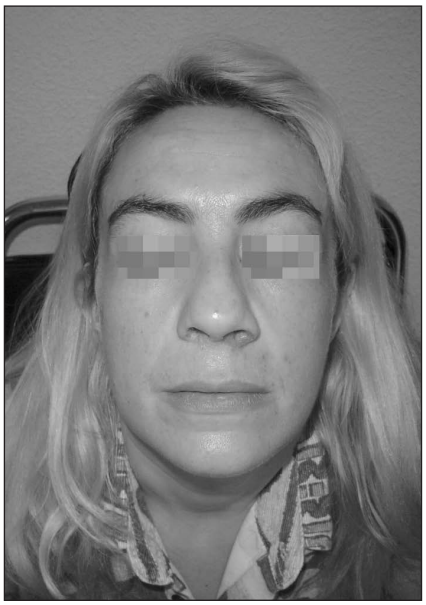

Figure 3. Image of patient with eosinophilic angiocentric fibrosis and intense nasal congestion.

DISCUSSION

With respect to the first 2 cases, most of the findings concur with the material published to date on nasal lymphomas. They appear more prevalent in males and in ages varying between youth (in our case, the youngest was 25) and in the elderly.[1,2] Clinically, the dominant symptom was nasal obstruction, without forgetting the appearance of mucosanguineous rhinorrhea. There is no disagreement with previous publications in terms of the findings at the nasal level, and the intense oedema with ulcerated, infiltrating lesions affecting the integrity of the first third of the hard palate in the first case is particularly noteworthy.

From a histological point of view, both cases turned out to be high-grade, with elevated proliferative indices (T/NK type). Despite the importance of the cytological study, where the polymorphic nature is shown with regard to the cellularity of these tumours, a definitive diagnosis currently requires immunohistochemical study. When performed, the characteristic data obtained in the NK cases included positivity for CD45, CD2, and CD56,[3] but negativity for the monoclonal CD3 T marker (it tested positive for the polyclonal variant). The utilization of antibodies associated with cytotoxic granules, such as TIA-1, granzyme, and perforin, is also important.

It is noted in the first case that the study was completed though in situ hybridization techniques for the detection of parts of the Epstein-Barr virus genome. It thus detected that the malignant cells contain EBER-1 messenger RNA in the Epstein-Barr virus, which correlates with a high degree of malignancy.[1,2]

In terms of molecular biology, in the first case a re-arrangement of the T-cell receptors is shown with germ-line configuration. This does not concur with previous case reports, in which NK and some T lymphomas tend to lose their T arrangement.[4] This finding may be due to the fact that, in using nasal biopsies with abundant necrotic material, there is scant material left for study.

In summary, we must point out the rarity of the appearance of these tumours in clinical practice; given their aggressiveness and lethality, an early diagnosis is mandatory. The prognosis is basically constrained by the extension,[5] although the T/NK nature may itself also be influential.

The last case refers to nasal angiocentric eosinophilic fibrosis. This is generally defined as an increase in the thickness of the intranasal structures. The possibility of nasal destruction in indicated, without further detail, in only 1 of the publications consulted.[6] In our case the wide septal perforation and inflammatory aspect of the entire nasal mucosa are notable. If the paranasal sinuses are involved, the sinus affected is the maxillary sinus, while the ethmoidal, frontal, and sphenoid sinuses remain unharmed.[7] There is no systemic condition and the patient only has localized discomfort. Half the patients described to date have been associated with asthma, allergies to antibiotics, or skin rash, which suggests a greater predisposition to the disease among allergic patients. Our patient presented peripheral eosinophilia, found in only 1 case of those reported to date.[8] The course of the symptoms' development is long (approximately 18 months or more).

The diagnosis is by pathological analysis through multiple biopsies, as the first histological reports tend to be non-conclusive, and their extraction also requires general anaesthetic. Normally inflammatory infiltration appears with predominance in the eosinophils and perivascular fibrosis in "onion skin" around the arterioles and venules.

There tends to be no necrotizing vasculitis, fibrinoid necrosis, intravascular thrombosis, or granulomas. Two phases are described: an early one with eosinophilic vasculitis and a later one with perivascular fibrosis.[6,8]

In some publications, there are some data allowing the establishment of a tenuous relationship between Wegener and AEF,[6] though currently there is no scientific basis worth mentioning. However, the clinical entity closest to AEF is in the facial granuloma, that presents a centrofacial subdermal disposition when the AEF is submucous.[7]

Two cases of subglottic conditions have been described to date,[6,9] in which the process was able to be eliminated through laryngotracheoplasty.

In summary, we can state as a conclusion that it involves a benign, idiopathic, slowly progressive, and destructive process, that almost exclusively affects the upper respiratory tract and has no treatment, except symptomatic treatment to relieve local discomfort.

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