doi: http://dx.doi.org/10.11606/issn.1679-9836.v102i4e-204043 Rev Med (São Paulo). 2023 July-Aug.;102(4):e-204043.

Case Report

Nasal granulomatosis: case reports and literature review directed to diagnosis

Granulomatoses Nasais: relatos de casos e revisão de literatura direcionada diagnóstico

Mariana Ignacio Gomes[1], Eliane Maria Dias von Söhsten Lins[2], Marcela Giorisatto Dutra[3], Mariana Aguiar Bianco de Abreu[4], Carlos Eduardo Cesário de Abreu[5], Edson Monteiro[6]

Gomes MI, Lins EMDVS, Dutra MG, Abreu MAB, Abreu CEC, Monteiro E. Nasal granulomatosis: case reports and literature review directed to diagnosis / *Granulomatoses Nasais: relatos de casos e revisão de literatura direcionada diagnóstico.* Rev Med (São Paulo). 2023 July-Aug.;102(4):e-204043.

RESUMO: Introdução: As granulomatoses nasais são inflamações crônicas específicas que podem ser divididas conforme etiologia (infecciosa, desconhecida, induzida por trauma e autoimune). Por terem o poder de disseminação sistêmica representam um importante risco para a vida, sendo essencial um diagnóstico rápido e um adequado tratamento. Objetivo: Descrever 4 casos de granulomatoses nasais e realizar uma breve revisão sistemática focada no diagnóstico. Método: Os artigos foram obtidos utilizando-se as plataformas de busca MEDLINE e LILACS, no período dos últimos 5 anos (2017-2022) e nos idiomas português, inglês e espanhol. Os descritores utilizados para busca foram: "Nasal Tuberculosis Diagnosis", "Histoplasmosis Nasal Diagnosis", "Nasal Leishmaniasis Diagnosis" e "Eosinophilic Granulomatosis Polyangiitis Criteria Diagnoses". Dentre os critérios de inclusão, permaneceram na análise apenas os artigos que tratavam da área nasal ou nasossinusal e que focavam no diagnóstico clínico e/ou laboratorial. Relato de casos: Quatro pacientes atendidos no período de fevereiro de 2019 a fevereiro de 2022, com diagnóstico de granulomatose nasal e tratados pelo serviço de Otorrinolaringologia do Hospital Santa Marcelina de Itaquera, São Paulo/SP, sendo um caso de granulomatose eosinofílica com poliangeíte (GEPA), um de tuberculose, um de histoplasmose e um de leishmaniose. Resultados: Dos 208 artigos encontrados, apenas 25 foram selecionados após avaliação. *GEPA:* O diagnóstico atualmente baseia-se nos critérios do Colégio Americano de Reumatologia 2022. *Tuberculose:* O diagnóstico pode ser feito através de achados histopatológicos. *Histoplasmose:* O padrão-ouro é o achado histopatológico do fungo utilizando-se a coloração com ácido periódico de Schiff (PAS). Leishmaniose: O método considerado padrão-ouro é a biópsia com detecção molecular do DNA do parasita pela PCR. Discussão: Houve uma boa correlação entre os métodos empregados pata o diagnostico desses casos e os sugeridos pelos artigos analisados. Conclusão: Embora infrequentes, as granulomatoses nasais geram muita morbidade, são de diagnóstico complexo e devem ser lembradas nos pacientes com inflamações nasais ou sinusais de difícil resolução com os tratamentos convencionais. Utilizando o roteiro diagnóstico descrito nessa breve revisão, acreditamos que seja possível uma melhora substancial na assertividade diagnostica.

PALAVRAS-CHAVE: Diagnóstico; Granulomatose orofacial; Cavidade Nasal; Leishmaniose; Tuberculose; Histoplasmose; Síndrome de Churg-Strauss.

ABSTRACT: Introduction: Nasal granulomatosis are specific chronic inflammations that can be divided according to etiology (infectious, unknown, trauma-induced and autoimmune). Because they have the power of systemic dissemination, they represent an important risk to life, and a quick diagnosis and adequate treatment are essential. Objective: To describe 4 cases of nasal granulomatosis and perform a brief systematic review focused on diagnosis. Method: The articles were obtained using the MEDLINE and LILACS search platforms, in the last 5 years (2017-2022) and in Portuguese, English and Spanish language. The descriptors used for the search were: "Nasal Tuberculosis Diagnosis", "Histoplasmosis Nasal Diagnosis", "Nasal Leishmaniasis Diagnosis" and "Eosinophilic Granulomatosis Polyangiitis Criteria Diagnoses". Among the inclusion criteria, only articles that addressed the nasal or nasosinusal area and that focused on clinical and/or laboratory diagnosis remained in the analysis. Case reports: Four patients attended from February 2019 to February 2022, diagnosed with nasal granulomatosis and treated by the Otorhinolaryngology service at Hospital Santa Marcelina de Itaquera, São Paulo/SP, one case of eosinophilic granulomatosis with polyangiitis (EGPA), one for tuberculosis, one for histoplasmosis and one for leishmaniasis. Results: Of the 208 articles found, only 25 were selected after evaluation. *EGPA:* Diagnosis currently based on American College of Rheumatology 2022 criteria. *Tuberculosis:* Diagnosis can be made through histopathologic findings. *Histoplasmosis:* The gold standard is the histopathological finding of the fungus using periodic acid-Schiff (PAS) staining. *Leishmaniasis:* The method considered the gold standard is the biopsy with molecular detection of the parasite's DNA by PCR. *Discussion*: There was a good correlation between the methods used for the diagnosis of these cases and those suggested by the analyzed articles. *Conclusion:* Although infrequent, nasal granulomatosis generates a lot of morbidity, are of difficult diagnose and should be considered in patients with nasal or sinus inflammation that are difficult to resolve with conventional treatment. Using the diagnostic script described in this brief review, we believe that a substantial improvement in diagnostic accuracy is possible.

KEYWORDS: Diagnosis. Granulotamosis orofacial; Cavidade nasal; Leishmaniasis; Tuberculosis; Histoplasmosis; Churg-Strauss Syndrome.

1. Faculdade Santa Marcelina Itaquera, Faculdade de Medicina. https://orcid.org/0000-0001-5534-700X. E-mail: mariigomes@icloud.com
2. Faculdade Santa Marcelina Itaquera, Faculdade de Medicina. https://orcid.org/0000-0001-5016-8571. E-mail: elianesohsten@gmail.com
3. Faculdade Santa Marcelina Itaquera, Faculdade de Medicina. https://orcid.org/0000-0001-7075-4017. E-mail: marcelagiorisatto@hotmail.com
4. Faculdade Santa Marcelina Itaquera, Faculdade de Medicina. https://orcid.org/0000-0002-3215-734X. E-mail: mariana.abreu1974@gmail.com=
5. Faculdade Santa Marcelina Itaquera, Faculdade de Medicina. https://orcid.org/0000-0002-1423-6941. E-mail: cecabreu@hotmail.com
6. Faculdade Santa Marcelina Itaquera, Faculdade de Medicina. https://orcid.org/0000-0003-3516-0840. E-mail: edsonmonteiro@pelaordem.blog
Correspondence: Mariana Ignacio Gomes. Rua Marechal Barbacena, 1345, apartamento 74 -Tatuapé. São Paulo- SP, 03333-000. E-mail: mariigomes@icloud.com

INTRODUCTION

Granulomatous inflammations of the nose are distinctive chronic inflammations characterized by the formation of granulomatous tissue observed in histological examinations of the nose and paranasal sinuses. These lesions have a high destructive power[1] and can be divided according to their etiology: infectious (bacterial, fungal, parasitic), idiopathic (sarcoidosis and Crohn's disease), trauma-induced (cholesterol granuloma and cocaine use) and autoimmune (Wegner's granulomatosis, systemic lupus erythematosus, granulomatosis eosinophilic with polyangiitis, recurrent polychondritis)[1,2] .

The most frequently observed clinical manifestations are nasal obstruction, refractory nasal inflammation with crusts, epistaxis and nasal septum necrosis[1,2]. Several conditions can present with granulomas affecting the nose and/or paranasal sinuses, such as tuberculosis, syphilis, rhinoscleroma, leprosy, leishmaniasis, paracoccidioidomycosis, actinomycosis, Wegener's granulomatosis, pyogenic granuloma, eosinophilic granulomatosis with polyangiitis and histoplasmosis[2].

Most of these pathologies are localized; however, there can be cases with systemic dissemination, posing significant risk to life. Therefore, timely diagnosis and adequate treatment are fundamental[1,2]. Comprehensive and thorough anamnesis and physical examination extending beyond the nasal and paranasal regions are essential for an accurate interpretation of signs and symptoms and a correct diagnosis[1,2].

In 2007, the British Society for Allergy and Clinical Immunology (BSACI) released the latest guidelines for the management of patients with rhinosinusitis and nasal polyposis, which included the following recommendations: a) Visual assessment of the patient and biopsy with histological and microbiological examination of the tissue are essential steps that provide crucial information for the differential diagnosis between pathologies; b) Computerized tomography (CT) of the sinuses is reserved for rhinosinusitis patients who do not respond to medical therapy or those with severe illness, with signs such as blood-stained nasal discharge, pain, unilateral symptoms or displacement of the eye; c) Magnetic resonance imaging is not considered useful, unless there are clinical indications of central nervous system (CNS) involvement[3].

Considering the rarity and diagnostic difficulty associated with granulomas of the nose, we decided to present four clinical cases.

From February 2019 to February 2022, the Otorhinolaryngology service of the Hospital Santa Marcelina de Itaquera in São Paulo/SP diagnosed and treated four cases of granulomas of the nose, with one case of eosinophilic granulomatosis with polyangiitis (EGPA), one of tuberculosis, one of histoplasmosis and one of leishmaniasis. Considering the great diversity of the topic "Granulomatous inflammation of the nose", our review will focus on these four etiologies.

Therefore, the objectives of this study are to describe four cases of granulomatous inflammation of the nose, to conduct a concise literature review on clinical and laboratory diagnosis and, ultimately, to serve as a diagnostic reference for future cases with similar etiologies.

METHOD

The MEDLINE and LILACS search platforms were used to search for articles published in the last 5 years (2017-2022) in Portuguese, English, and Spanish. The descriptors used for the search were: "Nasal Tuberculosis Diagnosis", "Histoplasmosis Nasal Diagnosis", "Nasal Leishmaniasis Diagnosis" and "Eosinophilic Granulomatosis Polyangiitis Criteria Diagnoses". The inclusion criteria were articles that addressed the nasal or nasosinusal area, that focused on clinical and/or laboratory diagnosis and that were written in Portuguese, English or Spanish. Articles that did not focus on clinical and/or laboratory diagnosis and that addressed body areas other than the nasal or nasosinusal areas were excluded.

As this research involves case reports, retrospective information was obtained from anamnesis, physical examination and complementary exams found on the electronic medical records of the selected patients at Hospital Santa Marcelina de Itaquera. To access the medical records, the consent from patients or their guardians was obtained, and then a request was sent to the Medical and Statistical Archive Service (SAME), which selected the relevant records.

This research was submitted to and approved by the Research Orientation Committee (COPE) and the Research Ethics Committee (CEP) of Faculdade Santa Marcelina. It was also registered on Plataforma Brasil under the number: 62834022.6.0000.0066.

CASE REPORTS

Case 1

Female patient, 43 years old, white, born in Ipatinga, Minas Gerais, currently residing in a rural area in Suzano, São Paulo, and employed as a housemaid**.** The patient was admitted to the service in May 2018 with complaints of nasal obstruction persisting for 2 years, accompanied by anosmia, rhinorrhea, difficulty eating, and unspecified weight loss. Previous treatment with beclomethasone spray and nasal wash was ineffective. The patient reported intermittent otorrhea in both ears and hearing loss after more severe episodes of nasal obstruction. A fiberoptic nasolaryngoscopy was conducted and revealed grade 3 nasal polyposis, impeding the progression of the fiber scope. Further investigations were requested, including computed tomography (CT) of the paranasal sinuses,

audiometry and radioallergosorbent test (RAST) for fungi (MX1), grass (GX2), dust (HX2), animal dander (EX1); mite (D1, D2, D201) and cockroach allergens (I6). The audiometry was performed in September 2018 and revealed bilateral mixed hearing loss, with a more pronounced effect on the left side. The speech recognition threshold (SRT) was measured at 45 decibels in the right ear and 50 decibels in the left ear. The CT scan of the sinuses (Figure 1) was conducted in April 2019 and revealed pansinusitis, with a soft, tissue-like material extending to the nasal cavities, indicative of diffuse nasal polyposis, as well as a deviated nasal septum to the right. The RAST results were negative for all tested antigens.

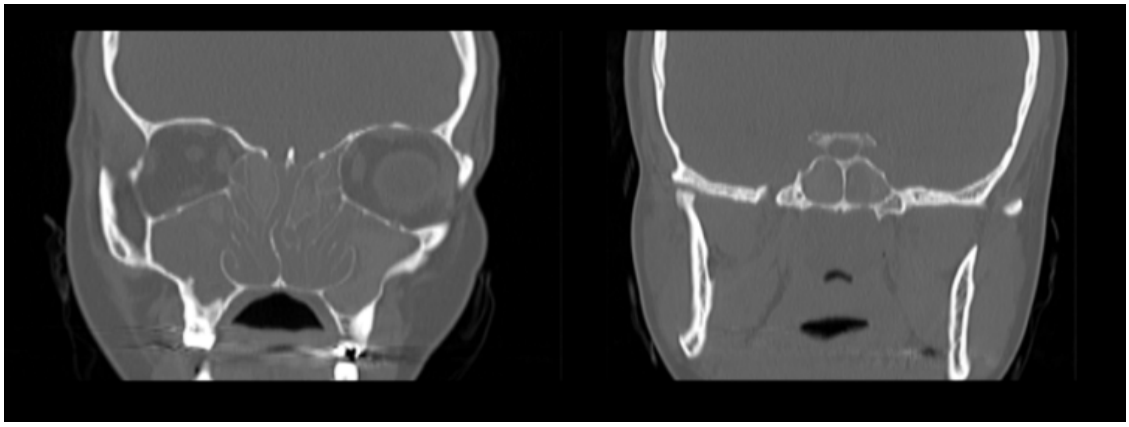

Figure 1 - Coronal CT scan of the paranasal sinuses without contrast enhancement, revealing a soft, tissue-like material indicative of diffuse nasal polyposis.

In June 2021, the patient underwent endonasal polypectomy. Two months later, she developed purulent rhinorrhea and acute otitis media on both sides. Treatment with amoxicillin-clavulanate, cefuroxime, and ceftriaxone was not succesful. The histopathological examination of the polyps removed during the surgery revealed evidence of a chronic inflammatory process and the slide review showed marked inflammatory response with eosinophils, absence of granulomas, vasculitis, and atypia.

The patient returned in September 2021 with complaints of otorrhea and otalgia in the right ear, bilateral hearing loss and abundant purulent rhinorrhea. Physical examination revealed a good general condition, adequate hydration, normal skin color, no jaundice, no fever, and no neurological, pulmonary, or cardiac abnormalities. The patient's abdomen was soft and non-tender, without palpable masses or visceromegaly. Nasopharyngolaryngoscopy showed no septum deviations, purulent secretions and allergic mucin, patent sinuses, recurrent polyps in the anterior and posterior ethmoid and patent middle meatus and auditory tubes. Otoscopy revealed significant bulging and hyperemia of the left tympanic membrane. An outpatient tympanotomy was performed, resulting in the discharge of purulent secretion and a positive culture indicating multisensitive *Pseudomonas aeruginosa*. No abnormalities were observed in the right otoscopy and oroscopy. In October 2021, the patient was admitted to the hospital for further investigation of her clinical condition.

Tomography of the paranasal sinuses (Figure 2) revealed patent frontal sinus ostia, sinus opacification with bubbles, suggestive of acute rhinosinusitis, and bilateral mastoid opacification. Chest tomography (Figure 3) showed bilateral foci of consolidation, and the transthoracic echocardiogram indicated an ejection fraction of 67%.

The laboratory tests showed negative antinuclear antibodies (ANA), negative antineutrophil cytoplasmic antibodies (ANCA), negative rheumatoid factor and negative serology for HIV, syphilis, leishmania, paracoccidioidomycosis and hepatitis B. The CRP level was within the normal range, ESR was 30mm, hemoglobin level was 12.6 g/dl, leukocyte count was 13,000 with 2,500 eosinophils/mm3, and platelet count was 351,000 / mm3. Urine analysis revealed hematuria > 10,000 without erythrocyte dysmorphism. Renal and hepatic function were normal.

The clinical presentation and laboratory tests raised suspicion of eosinophilic granulomatosis with polyangiitis. The patient was initiated on treatment with prednisone at a dose of 1mg/kg/day and methotrexate at a dose of 15 mg once a week, along with 5mg of folic acid on the following day. Additionally, during hospitalization, the patient received antibiotic therapy with sodium piperacillin 4g/tazobactam 0.5g for 14 days, ciprofloxacin eye drops at a dose of 4 drops 3 times a day in the left ear, nasal wash with 60ml of saline solution in high flow 4 times a day bilaterally and intravenous hydrocortisone. The patient was discharged with additional 15 days of antibiotic therapy with levofloxacin, immunosuppression with methotrexate, and instructions for gradual tapering of the corticosteroid.

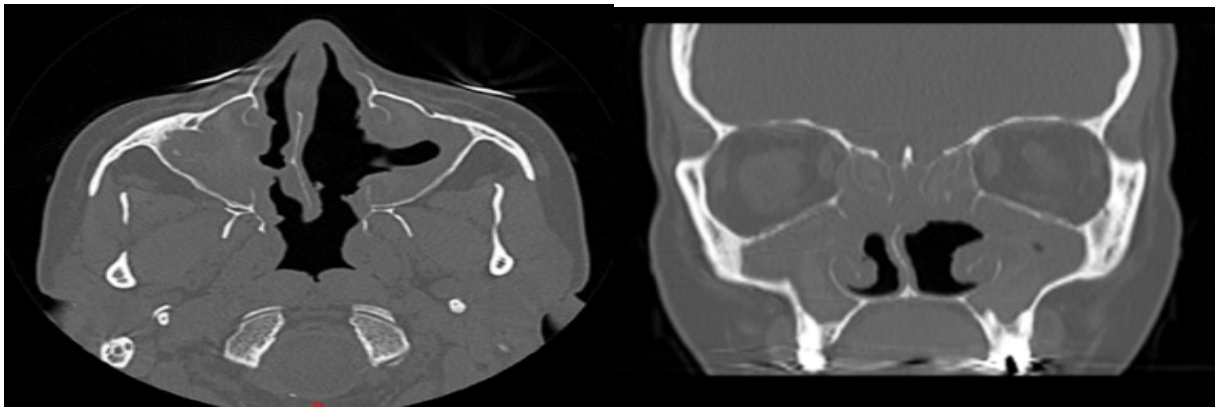

Figure 2A Figure 2B

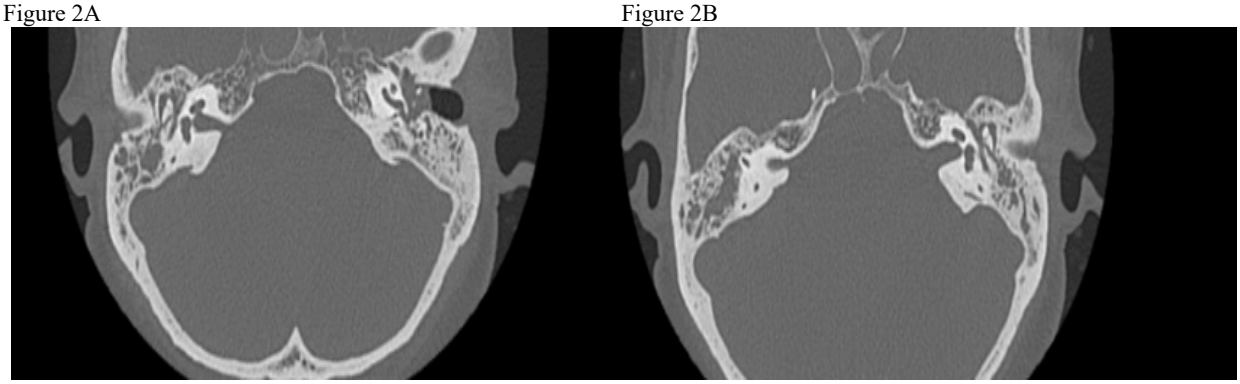

Figure 2C Figure 2D

Figure 2 - Non-contrast CT of the facial sinuses. Figure A shows an axial section and Figure B shows a coronal section, revealing sinus opacification with bubbles, suggestive of acute rhinosinusitis. Figures C and D show axial sections demonstrating bilateral mastoid opacification.

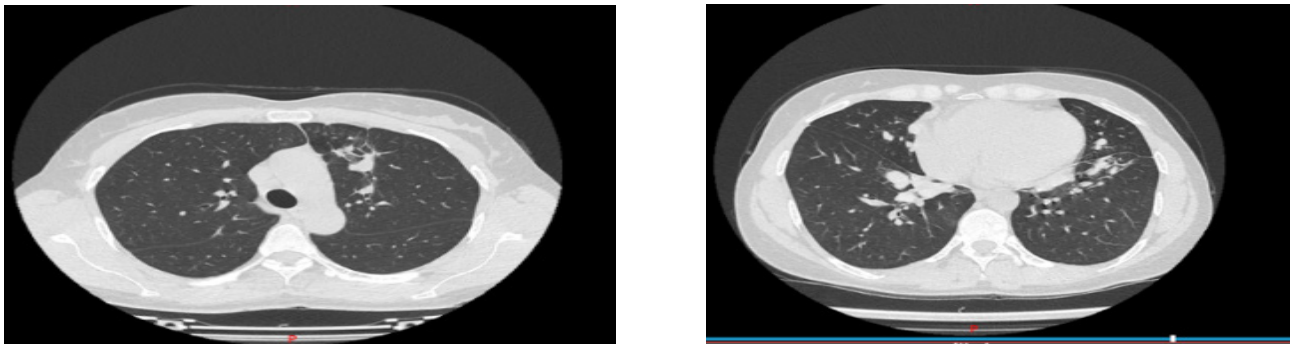

Figure 3A Figure 3B

Figure 3 - Chest CT in lung window showing bilateral foci of consolidation.

Case 2

A 34-year-old male patient was admitted to the medical service with a complaint of purulent rhinorrhea accompanied by frontal headache persisting for 20 days. He also reported edema, erythema and blurred vision in the right eye for 15 days, and denied any other symptoms or similar previous history. He reported a history of asthma, use of cocaine and marijuana, and allergy to penicillin. Physical examination revealed edema and erythema in the right eye, with reduced eye opening and no changes in eye movement (Figure 4). Rhinoscopy showed anterior septal perforation and significant bilateral nasal crusting. There were no signs of pulmonary involvement. A non-contrast CT scan of the sinuses revealed hypodense material filling the right maxillary sinus, mild thickening of the skin and periorbital adipose tissues, blocked tear ducts on the right eye, and approximately 1 cm of bone erosion in the anterior part of the nasal septum (Figure 5). A

sinusotomy was performed, resulting in copious amounts of purulent drainage. The nasal cavities, which had damaged mucosa and abundant blood crusts, were cleaned, and the necrotic area of the septal perforation was debrided, resulting in enlargement of the perforation. Further screening was requested to evaluate various granulomatous diseases, including secretion culture and histopathological examination. Immunohistochemistry revealed evidence of necrotizing granulomatous inflammation in the nasal mucosa, and the GeneXpert MTB/RIF rapid test detected genetic material of Mycobacterium tuberculosis in the secretions. The patient was started on a treatment regimen consisting of rifampicin, isoniazid, pyrazinamide, and ethambutol, which yielded a positive response (Figure 6).

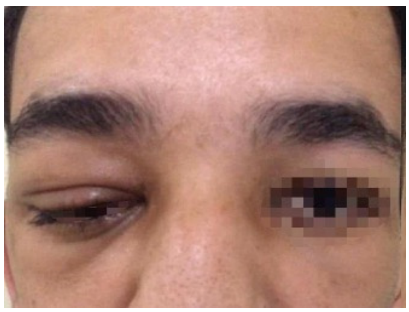

Figure 4 - Physical examination of the right eye showing edema, erythema, and reduced eye opening.

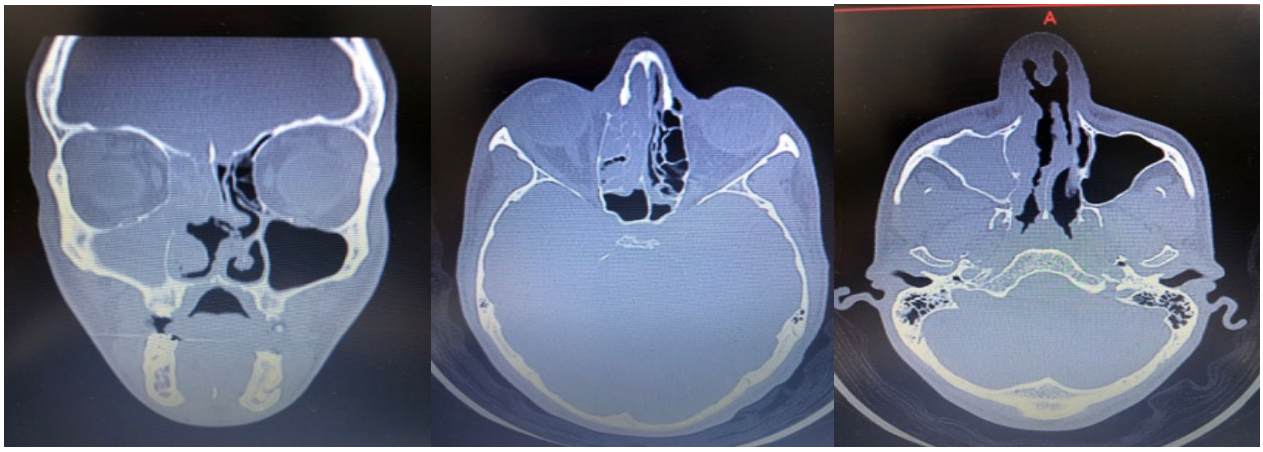

Figure 5A Figure 5B Figure 5C

Figure 5 - Non-contrast CT of the facial sinuses. The axial section in Figures A and B and the coronal section in Figure C show opacification of the ethmoid sinus, particularly on the right side (A), erosion of the nasal septum, and opacification of the right maxillary sinus (B). The findings support the previously mentioned observations, showing a predominantly unilateral aspect.

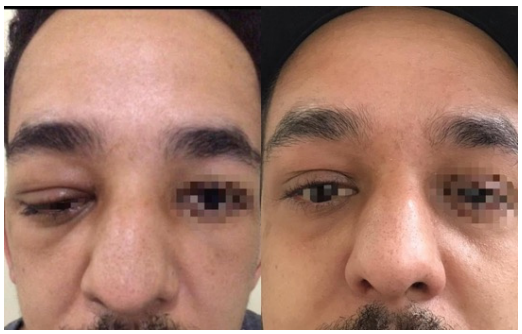

Figure 6 - Physical examination of the right eye after treatment, showing improvement in edema, erythema and eye opening.

Case 3

A 41-year-old female patient, born in São Caetano, São Paulo, currently residing in the city of São Paulo but having resided in a rural area until she was 8 years old was admitted to the service with a long-standing history, worsening over the last 4 years, of moderate-intensity frontal headaches accompanied by episodes of epistaxis, nasal dryness, night fever, unquantified weight loss, and ocular changes (burning sensation). She reports that in 2018, due to a deterioration in her general condition, she was hospitalized and underwent magnetic resonance imaging (MRI) of the face, which revealed heterogeneous material measuring 1.6x0.5cm in the lower right nasal fossa, and a biopsy of the right nasal cavity, which revealed fibrinopurulent material with negative acid-alcohol-fast-bacilli (AAFB) and fungal findings on anatomopathological examination. The physical examination showed no abnormalities on facial inspection. However, previous rhinoscopy and rigid nasal endoscopy revealed a septal perforation in areas 2-4, with friable, hyperemic, and tender edges, as well as hematic crusts in the inferior and middle meatus. Laboratory tests showed a leukocyte count of

16,300/mm3 (86% segmented), platelet count of 224,000/mm3, hemoglobin level of 12.6 g/dl, hematocrit of 37.3%, urea level of 21 mg/dl, creatinine level of 1 mg/dl, and ESR of 40 mm/h. Serological tests for syphilis, HIV, hepatitis B, leishmaniasis, aspergillosis, paracoccidioidomycosis, galactomannan, and human T-lymphotropic virus (HTLV) were non-reactive. Sputum AAFB smear was negative, and serology for histoplasmosis was positive. A biopsy of the nasal septum was performed, and the anatomopathological examination revealed a nonspecific chronic inflammatory process with suppuration and necrosis. AAFB, Periodic Acid-Schiff stain (PAS) and leishmaniasis tests were negative. CT of the facial sinuses showed thickening of the mucosal lining of some ethmoid cells, loss of continuity in the cartilaginous septum (Figure 7A) and complete loss of definition of the inferior nasal concha on the right side (Figure 7B). Treatment was initiated with Itraconazole 200mg every 12 hours for 12 weeks.

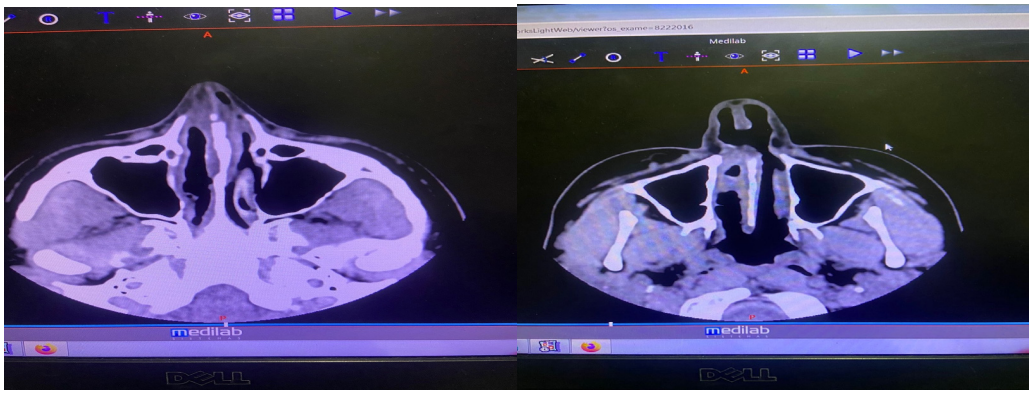

Figure 7A Figure 7B

Figure 7 - Non-contrast CT of the sinuses. Figures A and B show axial sections revealing loss of continuity in the cartilaginous septum (A) and loss of definition of the inferior nasal concha on the right side (B).

Case 4

A 70-year-old male patient, born in Ibirataia, Bahia and currently residing in São Paulo, employed as a farmer, was admitted to the hospital service in August 2021 for clinical stabilization and treatment of cutaneous-mucosal leishmaniasis, diagnosed through a biopsy performed in June 2021. At that time, he presented with complaints of epistaxis and a lesion in the left nasal cavity (Figure 8), which had been observed two years prior. Laboratory tests revealed negative serology for hepatitis B, hepatitis C, HTLV, syphilis, HIV, paracoccidioidomycosis, galactomannan, and leishmaniasis (IgG and IgM). PPD, ANA and ANCA tests were also negative. The anatomopathological examination of the columella, vestibulonasal region, and left nasal fossa was negative for AAFB and leishmania, but revealed a granulomatous inflammatory process in the nasal vestibule and ulceration in the nasal mucosa. Molecular biology testing for American tegumentary leishmaniasis yielded positive results, and the microscopy and immunohistochemical examination for Leishmania sp. were positive, confirming the diagnosis of leishmaniasis. Liposomal amphotericin B was initiated at a dosage of 5mg/kg/day (weight of 70 kg) for a total duration of 5 days, resulting in lesion improvement and subsequent discharge for outpatient follow-up.

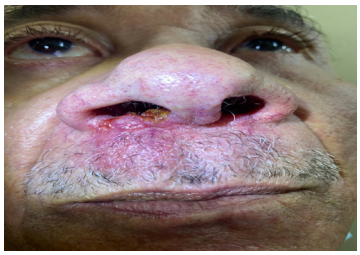

Figure 8 - Physical examination showing the presence of a granulomatous lesion with reddish edges

RESULT

EGPA

A total of 64 articles were found, of which only 2 were considered relevant upon analysis as they contained current diagnostic information for EGPA.

Various criteria for the diagnosis of EGPA have been developed over the years using different methods. In 1984, *Lanham et al.* established criteria that gained widespread use and in 1990, the American College of Rheumatology created classification criteria for EGPA and other vasculitis[4], which were updated in 2022. According to the new classification, a diagnosis of EGPA requires the presence of small- or medium-vessel vasculitis and

a minimum score of 6 points in seven items, including 3 clinical and 2 laboratory criteria, each with its own assigned score (Table 1). The clinical criteria include obstructive airway disease (+3 points), nasal polyps (+3 points), and mononeuritis multiplex (+1 point). Laboratory criteria include eosinophils in blood sample ≥ 1 x 109/liter (+ 5 points), biopsy showing eosinophilic predominant inflammation (+ 2 points), positive test for C-ANCA or anti-PR3 (-3 points), and hematuria (-1 point)[5].

Table 1 – 2022 American College of Rheumatology classification criteria for eosinophilic granulomatosis with polyangiitis.

Clinical Criteria	Score	Laboratory criteria	Score
Obstructive airway disease	+ 3 points	Eosinophils in blood sample ≥ 1 X 10^9/L	+ 5 points
Nasal polyps	+ 3 points	Biopsy showing eosinophilic predominant inflammation	+ 2 points
Mononeuritis multiplex	+ 1 point	Positive test for C-ANCA or anti-PR3	- 3 points
		Hematuria	- 1 point

Source: Grayson PC, et al 2022 [5]

Tuberculosis

A total of 108 articles were found, of which 12 were considered relevant upon analysis, as they specifically addressed the diagnosis of tuberculosis in the nasal region.

Nasal tuberculosis is extremely uncommon, accounting for only 0.1% of cases, with the majority (75%) being secondary to pulmonary tuberculosis[6-12]. The condition is diagnosed through histopathological and microbiological examination of a biopsy sample[6,10,11,13,14]. The histopathological finding pathognomonic for the condition is the presence of granulomatous inflammatory infiltrate along with giant Langhans cells and caseous necrosis[6,10-14]. Isolation of acid-resistant bacilli and culture of Mycobacterium tuberculosis can be found, but are extremely difficult[12,13]. The PCR amplification technology called GeneXpert can be used to enhance diagnostic accuracy in cases where there is uncertainty regarding the detection of *M. tuberculosis* DNA[8].

Histoplasmosis

A total of 8 articles were found, of which 4 were considered relevant upon analysis, as they addressed cases of histoplasmosis specifically involving the nasal and nasosinusal regions, as well as the diagnostic methods used in the case report in question.

Histoplasmosis is rare in otorhinolaryngology, especially in the nasal and nasosinusal regions, and it often goes overlooked[18,19]. Therefore, it is important to consider histoplasmosis as a potential differential diagnosis in cases involving lesions in the aerodigestive tract[18]. The condition can be diagnosed through culture and identification of the fungus in tissue sections, smears using staining techniques such as Gomori Methenamine Silver (GMS) or Periodic Acid Schiff (PAS), and serological tests[18,20,21]. The gold standard for diagnosis is the histopathological identification of the fungus using Periodic Acid-Schiff staining (PAS)[18]. Culture is not the preferred method as, despite its high specificity, it has limitations such as its sensitivity in patients with HIV, which can vary between 75% and 85-95%[19]. Histopathological examination typically shows chronic noncaseating granulomatous inflammation, and PAS staining confirms the identity of the microorganism by revealing *Histoplasma capsulatum* type yeasts[18,19]. Additional diagnostic tools include antigenemia and antigenuria tests, which can also be used for treatment monitoring[20]. These antigens are present at high levels, especially in patients with the human immunodeficiency virus (HIV) in the immunosuppressive phase, where these tests can reach up to 95% sensitivity[20].

Leishmaniasis

A total of 28 articles were found, of which 7 articles specifically focused on the subject of interest, discussing diagnostic methods for leishmaniasis, particularly in the nasal and nasosinusal regions.

The detection of mucocutaneous leishmaniasis, including involvement of the nasal and nasosinusal regions, can be challenging due to its resemblance to other infectious and malignant conditions[22]. The condition can be diagnosed through biopsy and tissue staining using Giemsa or hematoxylin and eosin (H&E) to visualize the parasite on the slide[23]. However, mucosal lesions tend to have few amastigote forms due to the hyperergic-pauciparasitic reaction, which can make diagnosis by staining challenging, requiring confirmation through immunohistochemistry and/or polymerase chain reaction (PCR)[23-25]. Therefore, due to its higher diagnostic sensitivity, most studies consider biopsy with molecular detection of the parasite's DNA by PCR as the gold standard for diagnosis[26]. This technique has a specificity of 100% and improves diagnostic accuracy from 55% to 70% in the mucosal form of the disease when compared to conventional techniques, except in cases in which DNA is partially degraded or contains inhibitory components[23,24]. Other complementary diagnostic tests

include parasite culture, immunofluorescence, animal inoculation, direct smear, serological assays, and the Montenegro skin test[23,27]. Bezermer JM et al. found that a combination of clinical criteria (male gender, ulcer of the nasal mucosa, age > 15, and symptom duration > 4 months) leads to a diagnostic accuracy similar to the Montenegro skin test, offering a rapid, cheap, and feasible alternative that could be implemented in resource-limited endemic regions[28].

Table 2 - Diagnostic methods used in the clinical cases.

Clinical case	Sex	Age	Etiological diagnosis	Diagnostic methods used
1	F	43	EGPA	American College of Rheumatology classification criteria
2	M	34	Tuberculosis	Histopathology GeneXpert MTB/RIF Rapid Test
3	F	41	Histoplasmosis	Serology Antigenemia
4	M	70	Leishmaniasis	Molecular detection of DNA by PCR Immunohistochemistry Microscopy Bezermer JM et al. clinical criteria

Source: Elaborated by the authors

DISCUSSION

In case number 1, according to the literature review, the patient met the diagnostic criteria for EGPA established by the American College of Rheumatology and updated in 2022. Among the clinical criteria, the patient reported nasal obstruction, which added 3 points, and the fiberoptic nasolaryngoscopy revealed nasal polyposis, adding another 3 points. Only the mononeuritis multiplex criterion was not fulfilled. Regarding the laboratory criteria, the patient presented eosinophils in the blood sample ≥ 1 x 10^9 /L, which added 5 points, and the biopsy demonstrated an intense eosinophilic predominant inflammation, which added 2 more points. The C-ANCA test was negative. Only 1 point was deducted due to the presence of hematuria. The total score reached 12 points, surpassing the cutoff point of ≥ 6 and confirming the diagnosis.

In case number 2, the patient underwent a biopsy, which revealed an immunohistochemical finding of a necrotizing granulomatous inflammation, which is the histological finding pathognomonic for the condition, according to the literature. The rapid GeneXpert MTB/RIF test was used as an adjunctive tool and detected genetic material from Mycobacterium tuberculosis in the secretion, thereby enhancing diagnostic accuracy.

In case number 3, the histopathology study revealed non-specific chronic inflammation, and the serology for histoplasmosis was positive. Special PAS staining, the gold standard diagnostic method recommended by the literature, was not performed to confirm the identity of the microorganism. Additionally, *Histoplasma capsulatum* antigen was detected, which is commonly used as a diagnostic adjunct, as stated by Singh A et al.

In case number 4, both molecular biology testing (molecular detection of DNA by PCR), which is considered the gold standard according to the literature, due to its 100% specificity, and immunohistochemistry were performed, confirming the presence of the parasite *Leishmania sp*. Microscopy was also used as diagnostic adjunct and yielded positive results. Additionally, considering the clinical criteria described in a study by Bezermer JM et al., the patient met all four criteria, including male gender, ulcer of the nasal mucosa, age > 15, and symptom duration > 4 months.

CONCLUSION

Although rare, granulomatous inflammations of the nose can cause significant morbidity and pose diagnostic challenges. It is important to consider these conditions in patients with persistent nasal or sinus inflammation that does not respond to conventional treatments. We believe that the use of the diagnostic script outlined in this concise review can result in a significant enhancement in diagnostic precision.

Participation of the authors: Mariana Ignacio Gomes - obtaining information from the medical records, reviewing medical literature, acquiring patient authorizations, writing the text and adapting it to the journal's standards. Eliane Maria Dias von Sohsten Lins - providing guidance on topics for the literature review, and reviewing the article. Marcela Giorisatto Dutra- diagnosing, managing the evolution, and treating some of the described clinical cases and providing information for the report. Mariana Aguiar Bianco de Abreu - conducting the bibliographic review and assisting in the formatting of the article. Carlos Eduardo Cesário de Abreu - performing the surgical procedure on the patient in case 1 and contributing to the literature review. Edson Monteiro - outpatient monitoring of patients.

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Received: 2022, November 02
Accepted: 2023, June 14