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Peripheral T-cell lymphoma mimicking granulomatosis with polyangiitis

Elif Durak Ediboğlu[1] · Dilek Solmaz[2] · Sermin Özkal[3] · Nezahat Karaca Erdoğan[4] · Servet Akar[2]

[1] Hatay Research and Training Hospital, Hatay, Turkey
[2] Department of Internal Medicine, Division of Rheumatology, Izmir Katip Celebi University, Izmir, Turkey
[3] Department of Pathology, Dokuz Eylül University, Izmir, Turkey
[4] Department of Radiology, Izmir Katip Celebi University, Izmir, Turkey

Abstract

Upper respiratory tract involvement is common in patients with granulomatosis with polyangiitis (GPA), but malignancies should be kept in mind in the differential diagnosis. A 68-year-old man was referred to rheumatology to investigate for GPA after nasal excisional biopsy. After careful radiologic and pathologic assessment, he was diagnosed with peripheral T-cell lymphoma, nasal type. This is a rare case of T-cell lymphoma in a patient who was referred as GPA.

Keywords
Granulomatosis with polyangiitis · Lymphoma, T-Cell · Neoplasms · Biopsy · Pathology

Introduction

Granulomatosis with polyangiitis (GPA) is a type of systemic small vessel vasculitis and may affect upper and lower respiratory tracts, the kidneys, and other systems. Upper tract involvement is common in patients with GPA [1] but physicians should be careful regarding differential diagnosis. In this report, we present a patient with peripheral T-cell lymphoma mimicking GPA.

Case report

A 68-year-old Turkish man with a history of Sezary's syndrome for 17 years presented in March 2019 with a 9-month history of purulent and bloody nasal discharge, postnasal drip, nasal blockage, and a 1-month history of red and swollen eyelids. He had undergone functional endoscopic sinus surgery for nasal polyposis 8 months and 1 month prior to presentation. The first time he was operated on for nasal polyposis, he was told that his pathology was benign and he had no need for treatment. One month ago, his nasal excisional biopsy specimens showed histologic findings of chronic inflammation of nasal mucosa and granulomatous necrosis. He was referred to rheumatology to investigate for GPA. He had a history of 8 kg weigh loss in 1 year but did not have night sweats or fever. He did not have cough, shortness of breath, hemoptysis, or a history of proteinuria, hematuria, or renal insufficiency. Liver, spleen, and lymph nodes were unremarkable on physical examination. Baseline laboratory examination revealed serum creatinine 0.96 mg/dl, erythrocyte sedimentation rate (ESR) 42 mm/h, C-reactive protein (CRP) 5.82 mg/dl, white blood cell 10.99×10^9/L (66.9% neutrophils, 23.7% lymphocytes, 7.7% monocytes, and 1.2% eosinophils), hemoglobin 11.9 g/dl, and platelets 311×10^9/L. The cytoplasmic pattern of antineutrophil cytoplasmic antibody (cANCA) and perinuclear pattern of antineutrophil cytoplasmic antibody

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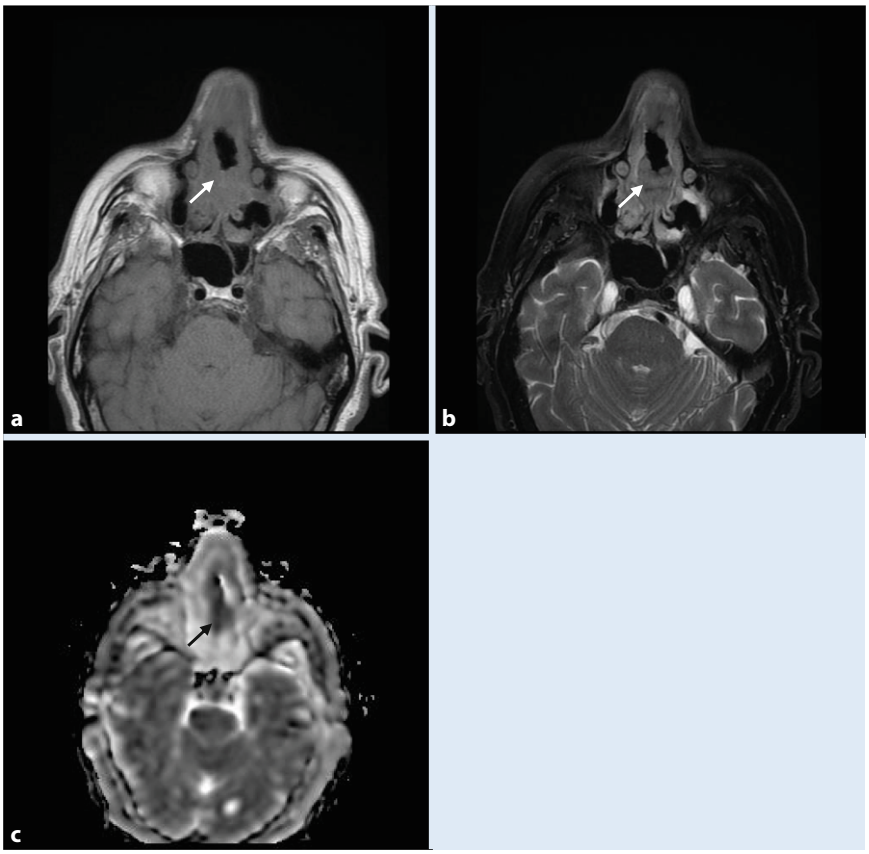

Fig. 1 ◀ The maxillofacial magnetic resonance image (MRI) of the patients. *White arrows* show a minimally enhancing mass after low-signal IV contrast agent in T1 (**a**) and T2 (**b**) sequences. The mass was obliterating the nasal passage in the perpendicular lamina. The *black arrow* depicts marked diffusion restriction (apparent diffusion coefficient: 0.6×10^{-3}; **c**)

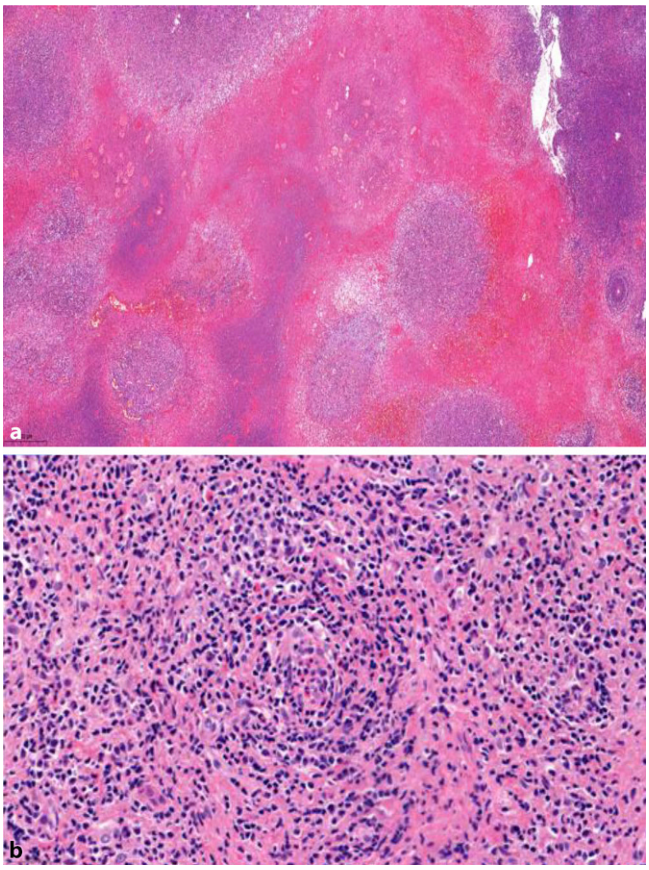

Fig. 2 ◀ Histopathologic examination of biopsies taken from nasal cavity. Nasal cavity, lymphoid infiltrate infiltrating the vessel wall and showing an angiocentric array

(pANCA) were negative. Serum LDH and liver function parameters were normal. The urinalysis revealed no proteinuria, hematuria, or casts. Computed tomography (CT) of the chest was normal, CT of the paranasal sinuses showed inflammation of the paranasal sinuses, septal erosion, mucosal thickening, bony destruction; the comment of radiologist on these findings was "these findings are seen in GPA but nasal extranodal lymphoma should be regarded as a differential diagnosis." Maxillofacial magnetic resonance imaging (MRI) was performed and showed a minimally enhancing mass after low-signal IV contrast agent in both (T1 and T2) sequences. There was a large defect in the nasal septum. The mass involved localized tissue destruction in the nasal septum, infiltrating the mucosal area in a band-like manner, involving lymphoid tissue in the nasopharynx, deep tissues on the left side, and palatal tonsils caudally in both sequences. In addition, it was obliterating the nasal passage in the perpendicular lamina and showed marked diffusion restriction (apparent diffusion coefficient: 0.6×10^{-3}; ◘ **Fig. 1**). After maxillofacial MRI, the patient underwent repeat endoscopic paranasal sinus biopsy. In the sections prepared from the consultation block of the biopsy taken from the nasal cavity, diffuse necrotic areas in the fragmented tissues were observed, as well as lymphoid infiltrate infiltrating the vessel wall and showing an angiocentric array (◘ **Fig. 2**). Occasional apoptosis was evident. The cells forming this infiltrate were positively stained with CD3 and CD7. In addition, most of these cells were CD5 and CD2 positive, and some were CD4 and TIA-1 positive. Staining for TDT, CD57, CD56, ALK, and CD30 was negative. Ki-67 proliferative activity was estimated to be approximately 50–75%. In addition to CD20-positive B lymphocytes that formed aggregates from time to time, CD68-positive histiocytes were seen. The

described findings were found to be compatible with peripheral T-cell lymphoma. 18-Fluorodeoxyglucose positron-emission tomography (FDG-PET) findings revealed the tumor to be limited to the nasal cavity. The patient received eight courses of a chemotherapy regimen. Although he had second-line treatment because of nonresponsive disease, he died 1 year after diagnosis.

Discussion

Upper airway involvement is a common manifestation of GPA and 58–90% of patients have nasal and paranasal involvement. Furthermore, upper airway involvement has been reported in up to 40% of patients in few case series [2–5].

In the EULAR (European Alliance of Associations for Rheumatology) recommendation, AAV (anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides) is defined as a chronic disease where infection and malignant tumors are excluded and characteristic histologic findings are shown in biopsy or an ANCA-positive result is obtained [6]. Particularly in cases with atypical presentation, minimal systemic involvement, negative ANCA status, histopathology, or other factors are crucial to support clinical diagnosis. However, diagnosis of localized GPA can be challenging because these patients lack other features of systemic vasculitis and between 17 and 30% of patients are ANCA negative at presentation [7, 8]. In addition, biopsies of many of these lesions are non-accessible or insufficient to demonstrate granuloma and small vessel vasculitis. Thus, diagnosis of localized GPA should be based on strong pathologic or radiologic evidence.

Nasal natural killer (NK)/T-cell lymphoma is a rare disorder and its pathogenesis is poorly understood, although it may be related to Epstein–Barr virus infection of the tumor cells. The large majority of patients present with localized disease resulting in symptoms of nasal obstruction, epistaxis, and a destructive mass of the nose and sinuses, such as patients with localized GPA. In addition to the nasal cavity, extranodal sites such as skin, lung, eye, or soft tissues may be involved and patients may also have constitutional symptoms like fever and weigh loss.

To date, the nasal type of lymphoma has been reported to be important in differential diagnosis of GPA in two cases. In one case, a patient with a 4-year history of GPA had constitutional symptoms and an oropharyngeal lesion. Because of unresponsiveness to steroid therapy, biopsy was performed and the diagnosis was extranodal NK/T-cell lymphoma, nasal type [9]. In the other case the patient had severe periodontitis and was diagnosed as GPA in the first biopsy, but consecutive diagnosis was extranodal nasal-type NK/T-cell lymphoma [10].

This case highlights the multifaceted clinical presentation of extranodal lymphoma that may mimic GPA. Misdiagnosis of a type of lymphoma as GPA cause delayed lymphoma treatment and inappropriate immunosuppressive therapy for vasculitis. Underlying T-cell lymphoma should be considered in patients with suspected localized GPA, in particular in the absence of ANCA positivity. Careful clinical, radiologic, and pathologic assessment is crucial.

Corresponding address

Prof. Dr. Servet Akar
Department of Internal Medicine, Division of Rheumatology, Izmir Katip Celebi University
Izmir, Turkey
servet.akar@gmail.com

Zusammenfassung

Peripheres T-Zell-Lymphom mit Imitation einer Granulomatose mit Polyangiitis

Die Beteiligung des oberen Respirationstrakts tritt häufig auf bei Patienten, die an einer Granulomatose mit Polyangiitis (GPA) leiden, jedoch sollte man bei der Differenzialdiagnose auch an Malignome denken. In der vorliegenden Kasuistik wurde ein 68-jähriger Mann zur Abklärung einer GPA nach nasaler Exzisionsbiopsie an die Rheumatologie überwiesen. Nach sorgfältiger radiologischer und pathologischer Untersuchung wurde bei ihm die Diagnose eines peripheren T-Zell-Lymphoms vom nasalen Typ gestellt. Hiermit handelt es sich um den seltenen Fall eines T-Zell-Lymphoms bei einem Patienten, der wegen GPA überwiesen wurde.

Schlüsselwörter
Granulomatose mit Polyangiitis · Lymphom, T-Zell · Neoplasmen · Biopsie · Pathologie

Declarations

Conflict of interest. E.D. Ediboğlu, D. Solmaz, S. Özkal, N.K. Erdoğan, and S. Akar declare that they have no competing interests.

For this article no studies with human participants or animals were performed by any of the authors. All studies mentioned were in accordance with the ethical standards indicated in each case. For images or other information within the manuscript which identify patients, consent was obtained from them and/or their legal guardians.

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