Mediastinal mass in a patient with granulomatosis with Polyangiitis

Teixeira CEG[1], Fernandes DA[2], Reis F[3], Sachetto Z[4]

[1] Department of Internal Medicine, Rheumatology, School of Medical Sciences, University of Campinas (UNICAMP). Campinas, São Paulo, Brazil
ORCID: https://orcid.org/0000-0002-5340-6894

[2] Department of Radiology, School of Medical Sciences, University of Campinas (UNICAMP). Campinas, São Paulo. Brazil.
ORCID: https://orcid.org/0000-0001-8138-1316

[3] Department of Radiology, School of Medical Sciences, University of Campinas (UNICAMP). Campinas, São Paulo. Brazil.
ORCID: https://orcid.org/0000-0003-2256-4379

[4] Department of Internal Medicine, Rheumatology, School of Medical Sciences, University of Campinas (UNICAMP). Campinas, São Paulo, Brazil.
ORCID: https://orcid.org/0000-0003-1216-9690

Correspondence to

Carlos Eduardo Garcez Teixeira

E-mail: carlosgarcezt@gmail.com

Submitted: 27/08/2023

Accepted: 03/10/2023

Dear Editor,

We report a 49-year-old male with granulomatosis with polyangiitis (GPA) who developed facial plethora and arterial blood pressure asymmetry. The patient had been diagnosed with GPA for 15 years for ear and nose manifestations, including sensorineural hearing loss, mastoiditis, episcleritis, and nasal granulomatous inflammation with necrotizing vasculitis on nasal biopsy. At diagnosis, no renal or lower respiratory tract involvement, constitutional symptoms, or joint involvement were observed. Antineutrophil cytoplasmic (ANCA) antibodies were negative, while inflammatory markers were elevated (erythrocyte sedimentation rate [ESR] of 58 mm/h, C-reactive protein [CRP] of 4.95 mg/dL).

The patient had a background of recurrent tracheitis, managed previously with methotrexate (MTX), azathioprine (AZA), and oral cyclophosphamide (CYC). However, due to adverse reactions (urticarial skin reaction to oral CYC and gastric intolerance to MTX and AZA), they were switched to mycophenolate sodium (MS) at a dose of 2,160mg/day followed by 1,440mg/day. Tracheostomy was performed because of subglottic stenosis.

Following three years of maintenance treatment with MS, the patient developed facial plethora upon positional changes, arterial blood pressure asymmetry, arthralgia, epistaxis, and a 10 kg weight loss, necessitating hospitalization. Thorax angiotomography revealed inferior vena cava obstruction, aortic branch stenosis, moderate stenosis in both the pulmonary artery trunk and right pulmonary artery, and mild stenosis in the left pulmonary artery. Additionally, an extrinsic mediastinal mass with fibrosing pattern was found, characterized by infiltrative soft tissue, compressing mediastinal fat planes that encased adjacent structures, including large vessels. The mass was not calcified and affected several mediastinal compartments (Figure 1).

Bronchoscopy identified 40% tracheal stenosis without bronchial tree involvement or active inflammation. Mediastinal and pericardial biopsies indicated chronic inflammation with fibrosis, scarce lymphoid infiltration, and microcalcifications. Morphological and immunohistochemical assessments ruled out malignancy, sarcoidosis, lymphoma, thymoma, diving goiter, or teratoma. Nephrological evaluation demonstrated a urine protein-creatinine ratio of 700 mg and dysmorphic hematuria, suggesting renal involvement. Kidney biopsy was not performed after discussion with nephrology team. Treatment involved methylprednisolone 1 g/day (3 days), followed by prednisone tapering and rituximab for induction (375mg/m^2 x 4 weekly doses) and maintenance (500mg every 6 months). Surgery was contraindicated due to mass's proximity to vital structures. Although symptoms improved, the mediastinal mass remained unchanged during two years of follow-up.

GPA is a rare systemic small-vessel vasculitis with necrotizing granulomatous inflammation involving upper and lower respiratory tract[1]. GPA is associated with ANCA, targeting myeloperoxidase (MPO) and proteinase 3 (PR3) antigens, exhibiting cytoplasmic or perinuclear staining patterns[2,3]. However, ANCA sensitivity and specificity can reach 78% and 93%, respectively, and may occasionally be undetectable[3].

GPA can present with central airway compromise, impacting the subglottic trachea with parietal thickening and stenosis. The principal, lobar and segmental bronchi may also be involved[4]. For accurate assessment, tomographic evaluation with thin slices (1 mm) and multiplanar reconstructions is recommended. As presented by our patient, juxta-vertebral injuries also represent an uncommon manifestation of GPA[5].

Although uncommon, GPA patients may develop tumor-like masses[6, 8]. In this context, malignancies and infections should be excluded given their prognostic implications. In a cohort involving 302 GPA patients, 2% exhibited mediastinal or hilar involvement[6]. Mediastinal compartment divisions are just didactic, lacking strict anatomical delimitations, and often allowing a lesion to extend to a contiguous compartment. Besides the pericardial sac, mediastinal compartments interconnect, making it more practical to evaluate masses in two forms: those originating from primary mediastinal structures and those impacting the mediastinum while originating from non-mediastinal structures[7].

Glucocorticoids and immunosuppressants are standard GPA treatments, yet they may not affect mass lesions[8,9]. The mechanisms behind this unresponsiveness involving residual fibrotic tissue remain unclear. When drug therapies fail, surgery or radiotherapy can mitigate complications in refractory GPA masses[10].

References

1. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2013;65(1):1-11. https://doi.org/10.1002/art.37715
2. Choi CB, Park YB, Lee SW. Antineutrophil Cytoplasmic Antibody-Associated Vasculitis in Korea: A Narrative Review. Yonsei Med J. 2019;60(1):10-21. https://doi.org/10.3349/ymj.2019.60.1.10
3. Suwanchote S, Rachayon M, Rodsaward P, Wongpiyabovorn J, Deekajorndech T, Wright HL, et al. Anti-neutrophil cytoplasmic antibodies and their clinical significance. Clinical Rheumatology 2018 *37:4*, *37*(4), 875–884. https://doi.org/10.1007/S10067-018-4062-X

4. Sheehan RE, Flint JD, Müller NL. Computed tomography features of the thoracic manifestations of Wegener granulomatosis. *J Thorac Imaging*. 2003;18(1):34-41. https://doi.org/10.1097/00005382-200301000-00005
5. Ramirez GA, Della-Torre E, Campochiaro C, Bozzolo E, Berti A, Praderio L, et al. Juxta-vertebral lesions in granulomatosis with polyangiitis. *Semin Arthritis Rheum*. 2016;46(3):356-360. https://doi.org/10.1016/j.semarthrit.2016.07.009
6. George TM, Cash JM, Farver C, Sneller M, van Dyke CW, Derus CL, et al. Mediastinal mass and hilar adenopathy: rare thoracic manifestations of Wegener's granulomatosis. Arthritis Rheum. 1997;40(11):1992-7. https://doi.org/10.1002/art.1780401111
7. Whitten CR, Khan S, Munneke GJ, Grubnic S. A diagnostic approach to mediastinal abnormalities. Radiographics. 2007;27(3):657-671. https://doi.org/10.1148/rg.273065136
8. Gendelman O, Kuntzman Y, Shovman O, Langevitz P, Tsur AM, Erez D, Levy Y, Amital H. Tumor-like Lesions in Patients with Granulomatosis with Polyangiitis: A Case Series. *Isr Med Assoc J*. 2021;23(6):350-352.
9. Hanzawa S, Noda S, Hosoya T, Kawahara T, Nukui Y. Mass-like Lesions Causing Compression of Large Vessels in Granulomatosis with Polyangiitis: A Case Report [published online ahead of print, 2022 Dec 28]. *Intern Med*. 2022;10.2169/internalmedicine.0561-22. https://doi.org/10.2169/internalmedicine.0561-22
10. Padoan R, Campaniello D, Gatto M, Schiavon F, Doria A. Current clinical and therapeutic approach to tumour-like mass lesions in granulomatosis with polyangiitis. Autoimmun Rev. 2022;21(3):103018. https://doi.org/10.1016/j.autrev.2021.103018

Tables and Figures

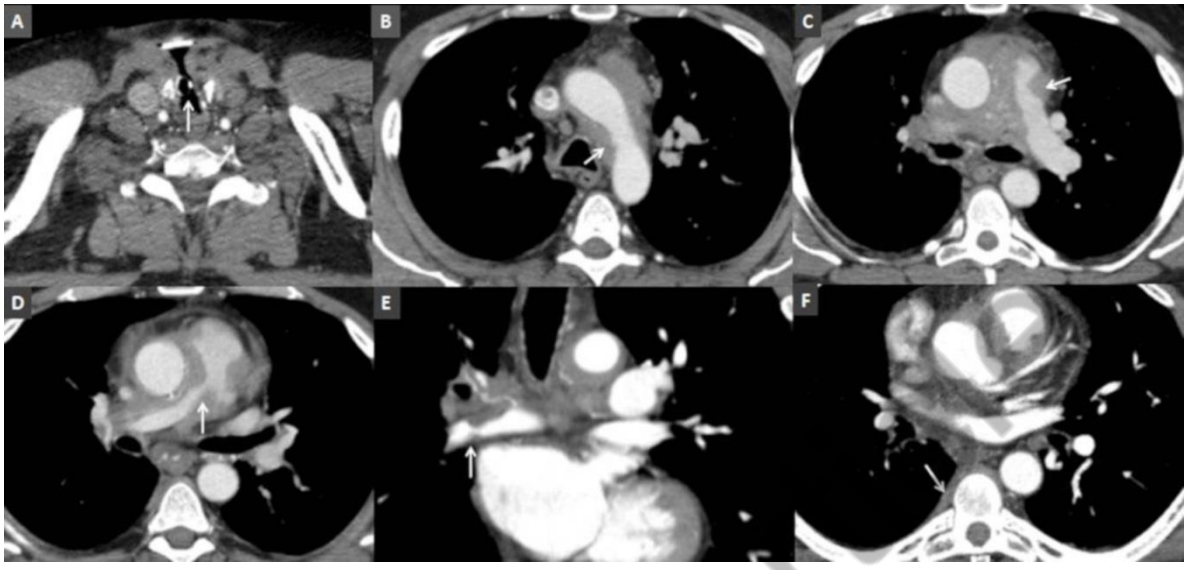

Figure 1- Computed tomography angiography of the chest. Significant stenosis of the subglottic trachea (A), with tracheostomy prosthesis. Mediastinal infiltrative-looking tissue with soft tissue density superiorly and around the aortic arch (B), determining slight irregularities and reduced caliber. It involves the emergence of the branches of the aortic arch. It does not show significant uptake after contrast medium injection. The tissue also infiltrates around the pulmonary artery trunk (C) and its right and left branches, determining significant moderate stenoses in the pulmonary artery trunk and proximal portion of the right pulmonary artery (D) and severe stenosis in the distal portion of the pulmonary artery right (E). There is infiltrative tissue similar to mediastinal poorly delimited located anteriorly to the middle and lower thoracic vertebral bodies (F) between T5 and T11, with a thickness of up to 5 mm.