ONLINE FIRST

This is a provisional PDF only. Copyedited and fully formatted version will be made available soon.

Rheumatology Forum

OFFICIAL JOURNAL OF THE POLISH SOCIETY OF RHEUMATOLOGY

ISSN: 2720-3921

e-ISSN: 2720-3913

Subglottic stenosis of the larynx in granulomatosis with polyangiitis. A case report and review of the available literature

Authors: Ewelina Machura-Porębska, Przemysław Kotyla, Robert Pieczyrak, Magdalena Kopeć-Mędrek, Barbara Buc-Piorun, Klaudia Palka

DOI: 10.5603/rf.93385

Article type: Case report

Submitted: 2022-12-26

Zaakceptowane: 2023-10-17

Published online: 2024-01-24

Subglottic stenosis of the larynx in granulomatosis with polyangiitis. A case report and review of the available literature

10.5603/rf.93385

Ewelina Machura-Porębska (0000-0003-3474-5740), Przemysław Kotyla, Robert Pieczyrak, Magdalena Kopeć-Mędrek, Barbara Buc-Piorun, Klaudia Palka

Department of Internal Diseases, Rheumatology and Clinical Immunology, Medical University of Silesia, Katowice, Poland

Address for correspondence: Ewelina Machura-Porębska, Department of Internal Diseases, Rheumatology and Clinical Immunology, ul. Ziołowa 45/47, 40-635 Katowice, email: machuraewelina@gmail.com

Abstract

Granulomatosis with polyangiitis (GPA) is a rare systemic connective tissue disease marked by necrotising granulomatous inflammation and inflammation of small and medium-sized vessels. Due to its varied clinical presentation, GPA presents a major challenge for both clinicians and patients. Subglottic stenosis of the larynx (SGS) is a rare manifestation of GPA and is observed in 16–23% of patients. The aetiopathogenesis of this phenomenon is not fully elucidated. There was no correlation between the presence of airway narrowing (stenosis) and the activity and course of the disease. Subglottic stenosis can be a life-threatening condition with a need for urgent tracheotomy. The treatment of choice is immunosuppressive therapy with follow-up surgical treatment, usually using endoscopic approaches. A case of a 46-year-old female patient with SGS in GPA is presented. The patient reported severe dyspnoea, reduction of exercise tolerance and speech impairment. Intravenous pulses of corticosteroids were administered urgently and current immunosuppressive treatment was intensified, achieving a significant improvement in the patient's general condition.

Keywords: GPA; ANCA; SGS

Case report

In March 2021, a 46-year-old female patient diagnosed with granulomatosis with polyangitis (GPA) was admitted to the rheumatology department due to increased dyspnoea in the course of subglottic stenosis of the larynx (SGS). The patient presented with steroid-induced diabetes, lipid disorders, osteoarthritis of the spine, history of cholecystectomy and caesarean section.

The diagnosis of GPA was made in July 2020, at which time the patient presented with mixed hearing loss, peripheral facial nerve paresis and destruction of the right temporal bone. In the following months, disease activity was assessed. Magnetic resonance imaging (MRI) of the head revealed signs of bilateral otitis media, more severe on the right side, without central nervous system (CNS) disease. Other than that, there were no abnormalities in the results of basic laboratory tests, imaging tests or pulmonary function tests (spirometry and measurement of carbon monoxide transfer in the lung). Initial treatment included high-dose corticosteroids, followed by intravenous infusions of cyclophosphamide. In September 2020, treatment with cyclophosphamide was discontinued due to significantly increased indicator liver enzymes and urinary tract infection.

Following the normalisation of liver parameters in October 2020 due to the SARS-CoV-2 pandemic, treatment with oral cyclophosphamide was continued. The total dose of intravenous cyclophosphamide was 4.0 g and the total dose of oral cyclophosphamide was 2.5 g.

In March 2021, the patient presented to the hospital emergency department due to worsening exertional dyspnoea and speech impairment for a fortnight. In addition, the patient had right hearing loss, hoarseness and epistaxis. The patient denied other complaints, including fever and other infectious symptoms. Laboratory results revealed slight leucocytosis [leucocytes (WBC) 10.6 x 10^3/ul], inflammatory markers within normal limits [C-reactive protein (CRP) < 5 mg/l, erythrocyte sedimentation rate (ESR) 7 mm/1 h], normal levels of aminotransferases, normal renal excretory function. The general urine test revealed haematuria without proteinuria [urine albumin-creatinine ratio (UACR) < 30 mg/g]. Antineutrophil cytoplasmic antibodies (ANCA) were absent in blood serum. No genetic material of SARS-CoV-2 virus was detected by polymerase chain reaction (PCR). An urgent computed tomography (CT) scan of the neck was performed, showing thickening of the mucosa in the subglottic region of the larynx, ranging from approximately 18 mm to 6 mm in length. The laryngeal lumen at this level measured the smallest at 7 x 6.2 mm 1). The diagnosis was extended to include MRI of the neck. The examination found a circular

thickening of the subglottic laryngeal mucosa measuring approximately 18 mm in length. The mucous membrane thickened to 6–7 mm and demonstrated uniform post-contrast enhancement, suggesting an inflammatory condition (Fig. 2). Contrast-enhanced CT of the chest revealed no significant abnormalities. The ENT examination revealed swelling in the subglottic region of the larynx. The patient did not consent to tracheotomy. Treatment included intravenous pulses of methylprednisolone (total dose of 1500 mg), broad-spectrum antibiotic therapy with levofloxacin and trimethoprim-sulfamethoxazole preparation. There was a gradual improvement in the patient's general condition, including a reduction in the severity of dyspnoea, weakness and improved exercise tolerance. ENT consultation showed regression of laryngeal mucosal oedema. The patient was discharged from the department with the recommendation to continue immunosuppressive treatment, including oral prednisone, intravenous infusions of cyclophosphamide and regular follow-up at the rheumatology clinic.

Discussion

Subglottic stenosis of the larynx (SGS) can be acquired, congenital or idiopathic. This narrowing most commonly develops following intubation, tracheotomy, mechanical trauma, thermal burns of the airway or in the course of systemic connective tissue diseases [1]. The subglottis is a particularly vulnerable region of the larynx. This region is the junction of two embryological sites and is vascularised by two microcirculatory sites [2]. Laryngeal stenosis is usually located at this junction with the glottal cords unoccupied by the disease process and the portion of the larynx above and below the stenosis [2]. The most common symptoms of SGS include hoarseness of voice, dyspnoea, cough, haemoptysis, stridor and whistling rale [3].

Computed tomography (CT), MRI and endoscopies are used to diagnose airway stenosis. It is essential to exclude coexisting gastroesophageal reflux disease. Pulmonary function testing, including measurement of forced expiratory volume in the first second (FEV1) and peak expiratory flow (PEF), appear to be useful in assessing the effectiveness of ongoing treatment [4, 5]. Laryngeal biopsy provides information on the severity of inflammation. Its complication is the risk of bleeding and increased fibrotic processes with the formation of adhesions within the upper airway [6]. Positron emission tomography (PET) scanning is also used to assess the inflammatory process degree, e.g. in the course of systemic connective tissue diseases [7].

Granulomatosis with polyangitis (GPA) is an autoimmune disease of undetermined aetiology, marked by necrotising granulomatous inflammation and inflammation of small and medium-sized vessels [8]. The disease affects patients of all ages, and is most commonly diagnosed at 40-50 years of age. Men and women are affected with similar frequency [9], with a limited form of the disease more common in women. The prognosis is severe [8]. Granulomatosis with polyangitis (GPA) is associated with the presence of ANCA in serum [10].

The clinical picture is varied, most commonly with upper and lower respiratory tract and renal involvement [11, 12]. Jennings et al. estimated the prevalence of otolaryngological symptoms in GPA to be 80% [13]. In clinical practice, GPA is usually diagnosed based on the clinical picture, the presence of ANCA in the blood serum and the histopathological result (Tab. 1) [10, 12]. The BVAS (Birmingham Vasculitis Activity Score) scale is a tool for assessing disease activity (Tab. 2).

Studies conducted by the European Vasculitis Society (EUVAS) have made it possible to classify the disease according to location, severity of the disease process and development of management regimens. A distinction was made between localised, early systemic, generalised, severe and refractory forms of the disease (Tab. 3) [16–18]. In the localised form, a positive serum ANCA titer is present in approximately 60% of cases [20]. Accurate assessment of the prevalence of the limited form of GPA is difficult, not least because of the lack of specific symptoms. Infectious and inflammatory diseases, including sarcoidosis, eosinophilic granulomatosis with polyangiitis (EGPA), as well as the use of intranasally administered drugs such as cocaine, should be considered in the differential diagnosis [21, 22].

Upper airway stenosis is one of the rare manifestations of GPA, with an estimated incidence of 17.5% [23]. Bilateral main bronchial stenosis represents 11.4% of airway stenosis, of which 60% of cases are asymptomatic [23, 24]. Supraglottic laryngeal stenosis is observed very rarely [25]. The most common area of stenosis, which is observed in approximately 16% of patients, is the subglottic region of the larynx [26]. This complication is more common in patients under 20 years of age, often with a refractory course of treatment [27].

The aetiopathogenesis of airway stenosis in GPA remains unexplained. A chronic inflammatory process that increases the susceptibility of the laryngeal mucosa to injury with a subsequent increase in fibrotic processes is most likely to be involved [3]. Findings

regarding serum ANCA titres are inconclusive. Langford et al. described higher titres of cytoplasmic ANCA (c-ANCA) compared to perinuclear ANCA (p-ANCA) [26, 28], while Quinn et al. found a frequent absence of ANCA antibodies in the serum of SGS patients [29]. Both acute and chronic inflammatory processes contribute to airway stenosis [3]. Airway stenosis can occur in 50-75% of patients in remission [24, 30].

Diagnosis of SGS in GPA patients is frequently difficult. It may represent the only symptom of the disease, often without characteristic abnormalities in laboratory findings and without the presence of serum ANCA antibodies [31]. Suspicion of SGS should be raised in young GPA women presenting with symptoms of severe, destructive nasal sinus lesions without concomitant renal involvement [32].

Endoscopy is considered the gold standard for the diagnosis of laryngeal stenosis [33]. The Myer-Cotton and McCaffrey classifications are the most widely used classification systems for laryngotracheal stenosis, which are also useful in assessing patient prognosis [27]. The management of airway stenosis in GPA has not been developed. Based on few available data, it appears that a CT scan and upper airway endoscopy should be performed in every patient with suspected SGS [1, 35].

Most available treatments for airway stenosis include invasive procedures. As a life-threatening condition, laryngeal stenosis may require an emergency tracheotomy [28, 36]. Aggressive immunosuppressive therapy is used to reduce GPA activity. This therapy as a single treatment only achieves improvement in 20-26% of patients [11, 37]. Surgical procedures [23], usually endoscopic airway dilatation with local administration of corticosteroids and mitomycin C, are used in addition to causal treatment [38]. A higher remission rate was found in patients treated with rituximab compared to cyclophosphamide therapy [24]. There are reports in the literature of favourable results from the use of sirolimus as an adjunct to conventional SGS therapies in GPA and IgG4-associated disease [39].

Procedural interventions include mechanical dilatation of the airway, laser surgery for dilatation of the airway, cryotherapy, argon plasma coagulation and open surgery methods. During surgical procedures, it is important to minimise tissue damage to reduce the risk of exacerbation of stenosis. The appropriateness of performing invasive procedures during the high-activity phase of the underlying disease remains controversial [40], e.g. insertion of a stent to dilate the airway lumen may increase inflammatory processes contributing to exacerbation of GPA [16].

Currently available treatments have reduced the need for tracheostomies and airway stenting [23]. Disease activity, the presence of serum ANCA antibodies and other signs of GPA do not appear to affect the efficacy of treatment [7].

Conclusions

Subglottic stenosis (SGS) is a relatively rare but life-threatening manifestation of GPA. The uncharacteristic clinical picture makes a correct diagnosis significantly more difficult. Delay in the use of targeted treatment may lead to death of the patient by severe airway obstruction. The management of patients remains a significant therapeutic challenge, involving a multidisciplinary approach. Due to poor response to immunosuppressive treatment, multiple endoscopic procedures are often necessary, as well as surgery and tracheostomy in a few cases.

References

1. Szyfter W, Wierzbicka M, Gawecki W, et al. [The reasons of laryngo-tracheal stenosis: a review of literature and analysis of 124 patients]. Otolaryngol Pol. 2009; 63(4): 338–342, doi: 10.1016/S0030-6657(09)70137-4, indexed in Pubmed: 19999751.
2. Eliachar I, Chan J, Akst L. New approaches to the management of subglottic stenosis in Wegener's granulomatosis. Cleve Clin J Med. 2002; 69 Suppl 2: SII149–SII151, doi: 10.3949/ccjm.69.suppl_2.sii149, indexed in Pubmed: 12086256.
3. Ugan Y, Doğru A, Aynalı G, et al. A clinical threat in patients with granulomatosis polyangiitis in remission: Subglottic stenosis. Eur J Rheumatol. 2018; 5(1): 69–71, doi: 10.5152/eurjrheum.2017.16025, indexed in Pubmed: 29657878.
4. Jagpal N, Shabbir N. Subglottic Stenosis. In: Shabbir N. ed. StatPearls [Internet]. StatPearls Publishing, Treasure Island (FL) 2022.
5. Smith MM, Cotton RT. Diagnosis and management of laryngotracheal stenosis. Expert Rev Respir Med. 2018; 12(8): 709–717, doi: 10.1080/17476348.2018.1495564, indexed in Pubmed: 29969925.
6. Klink T, Holle J, Laudien M, et al. Magnetic resonance imaging in patients with granulomatosis with polyangiitis (Wegener's) and subglottic stenosis. MAGMA. 2013; 26(3): 281–290, doi: 10.1007/s10334-012-0351-6, indexed in Pubmed: 23086288.
7. Terrier B, Dechartres A, Girard C, et al. French Vasculitis Study Group. Granulomatosis with polyangiitis: endoscopic management of tracheobronchial stenosis: results from a multicentre experience. Rheumatology (Oxford). 2015; 54(10): 1852–1857, doi: 10.1093/rheumatology/kev129, indexed in Pubmed: 26001634.
8. Kur-Zalewska J, Tłustochowicz W. In: Puszczewicz M. ed. Reumatologia. Wyd. II. Medical Tribune, Warszawa 2016: 211–235.

9. Rottem M, Fauci AS, Hallahan CW, et al. Wegener granulomatosis in children and adolescents: clinical presentation and outcome. J Pediatr. 1993; 122(1): 26–31, doi: 10.1016/s0022-3476(05)83482-1, indexed in Pubmed: 8419611.

10. Wojciechowska J, Krajewski W, Krajewski P, et al. Granulomatosis With Polyangiitis in Otolaryngologist Practice: A Review of Current Knowledge. Clin Exp Otorhinolaryngol. 2016; 9(1): 8–13, doi: 10.21053/ceo.2016.9.1.8, indexed in Pubmed: 26976020.

11. Pajor AM, Kwiatkowska S, Kroczyńska-Bednarek J, et al. Acute laryngeal dyspnea as first presentation of granulomatosis with polyangiitis. Pneumonol Alergol Pol. 2015; 83(3): 216–219, doi: 10.5603/PiAP.2015.0035, indexed in Pubmed: 26050983.

12. Guardiani E, Moghaddas HS, Lesser J, et al. Multilevel airway stenosis in patients with granulomatosis with polyangiitis (Wegener's). Am J Otolaryngol. 2015; 36(3): 361–363, doi: 10.1016/j.amjoto.2014.12.010, indexed in Pubmed: 25630847.

13. Jennings CR, Jones NS, Dugar J, et al. Wegener's granulomatosis--a review of diagnosis and treatment in 53 subjects. Rhinology. 1998; 36(4): 188–191, indexed in Pubmed: 9923063.

14. Robson JC, Grayson PC, Ponte C, et al. DCVAS Investigators. 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for granulomatosis with polyangiitis. Ann Rheum Dis. 2022; 81(3): 315–320, doi: 10.1136/annrheumdis-2021-221795, indexed in Pubmed: 35110333.

15. Zimmermann-Górska I, Tuchocka-Kaczmarek A, Goncerz G. Choroby reumatyczne. In: Gajewski P, Tuchocka-Kaczmarek A, Goncerz G. ed. Interna Szczeklika. Medycyna Praktyczna, Cholerzyn 2022: 2117.

16. Gottschlich S, Ambrosch P, Kramkowski D, et al. [Wegener's granulomatosis in the head and neck region]. HNO. 2004; 52(10): 935–45; quiz 946, doi: 10.1007/s00106-004-1118-9, indexed in Pubmed: 15309321.

17. Millet A, Pederzoli-Ribeil M, Guillevin L, et al. Antineutrophil cytoplasmic antibody-associated vasculitides: is it time to split up the group? Ann Rheum Dis. 2013; 72(8): 1273–1279, doi: 10.1136/annrheumdis-2013-203255, indexed in Pubmed: 23606701.

18. Smith RM, Jones RB, Jayne DRW. Progress in treatment of ANCA-associated vasculitis. Arthritis Res Ther. 2012; 14(2): 210, doi: 10.1186/ar3797, indexed in Pubmed: 22569190.

19. Kur-Zalewska J, Tłustochowicz W. Zapalenia małych naczyń. In: Puszczewicz M, Tłustochowicz W. ed. Reumatologia. Wyd. II. Medical Tribune, Warszawa : 211–235.

20. Wiik A. Rational use of ANCA in the diagnosis of vasculitis. Rheumatology (Oxford). 2002; 41(5): 481–483, doi: 10.1093/rheumatology/41.5.481, indexed in Pubmed: 12011368.

21. Fuchs HA, Tanner SB. Granulomatous disorders of the nose and paranasal sinuses. Curr Opin Otolaryngol Head Neck Surg. 2009; 17(1): 23–27, doi: 10.1097/MOO.0b013e32831b9e58, indexed in Pubmed: 19225301.

22. Trimarchi M, Bussi M, Sinico RA, et al. Cocaine-induced midline destructive lesions - an autoimmune disease? Autoimmun Rev. 2013; 12(4): 496–500, doi: 10.1016/j.autrev.2012.08.009, indexed in Pubmed: 22940554.

23. Martinez Del Pero M, Jayne D, Chaudhry A, et al. Long-term outcome of airway stenosis in granulomatosis with polyangiitis (Wegener granulomatosis): an observational study. JAMA Otolaryngol Head Neck Surg. 2014; 140(11): 1038–1044, doi: 10.1001/jamaoto.2014.2430, indexed in Pubmed: 25321076.

24. Girard C, Charles P, Terrier B, et al. Tracheobronchial Stenoses in Granulomatosis With Polyangiitis (Wegener's): A Report on 26 Cases. Medicine (Baltimore). 2015; 94(32): e1088, doi: 10.1097/MD.0000000000001088, indexed in Pubmed: 26266344.

25. Belloso A, Estrach C, Keith AO. Supraglottic stenosis in localized Wegener granulomatosis. Ear Nose Throat J. 2008; 87(7): E11–E14, indexed in Pubmed: 18633919.

26. Langford CA, Sneller MC, Hallahan CW, et al. Clinical features and therapeutic management of subglottic stenosis in patients with Wegener's granulomatosis. Arthritis Rheum. 1996; 39(10): 1754–1760, doi: 10.1002/art.1780391020, indexed in Pubmed: 8843868.

27. Aravena C, Almeida FA, Mukhopadhyay S, et al. Idiopathic subglottic stenosis: a review. J Thorac Dis. 2020; 12(3): 1100–1111, doi: 10.21037/jtd.2019.11.43, indexed in Pubmed: 32274178.

28. Gluth MB, Shinners PA, Kasperbauer JL. Subglottic stenosis associated with Wegener's granulomatosis. Laryngoscope. 2003; 113(8): 1304–1307, doi: 10.1097/00005537-200308000-00008, indexed in Pubmed: 12897550.

29. Quinn KA, Gelbard A, Sibley C, et al. Subglottic stenosis and endobronchial disease in granulomatosis with polyangiitis. Rheumatology (Oxford). 2019; 58(12): 2203–2211, doi: 10.1093/rheumatology/kez217, indexed in Pubmed: 31199488.

30. Schokkenbroek AA, Franssen CFM, Dikkers FG. Dilatation tracheoscopy for laryngeal and tracheal stenosis in patients with Wegener's granulomatosis. Eur Arch Otorhinolaryngol. 2008; 265(5): 549–555, doi: 10.1007/s00405-007-0518-3, indexed in Pubmed: 18000676.

31. Costantino CL, Niles JL, Wright CD, et al. Subglottic Stenosis in Granulomatosis With Polyangiitis: The Role of Laryngotracheal Resection. Ann Thorac Surg. 2018; 105(1): 249–253, doi: 10.1016/j.athoracsur.2017.07.026, indexed in Pubmed: 29100647.

32. An J, Song JW. Life-Threatening Subglottic Stenosis of Granulomatosis with Polyangiitis: A Case Report. Medicina (Kaunas). 2021; 57(5), doi: 10.3390/medicina57050423, indexed in Pubmed: 33925546.

33. Henes FO, Laudien M, Linsenhoff L, et al. Accuracy of Magnetic Resonance Imaging for Grading of Subglottic Stenosis in Patients With Granulomatosis With Polyangiitis: Correlation With Pulmonary Function Tests and Laryngoscopy. Arthritis Care Res (Hoboken). 2018; 70(5): 777–784, doi: 10.1002/acr.23332, indexed in Pubmed: 28772006.

34. Alam DS, Seth R, Sindwani R, et al. Upper airway manifestations of granulomatosis with polyangiitis. Cleve Clin J Med. 2012; 79 Suppl 3: S16–S21, doi: 10.3949/ccjm.79.s3.04, indexed in Pubmed: 23203639.

35. McDonald TJ, DeRemee RA. Head and neck involvement in Wegener's granulomatosis (WG). Adv Exp Med Biol. 1993; 336: 309–313, doi: 10.1007/978-1-4757-9182-2_49, indexed in Pubmed: 8296624.

36. Taylor SC, Clayburgh DR, Rosenbaum JT, et al. Clinical manifestations and treatment of idiopathic and Wegener granulomatosis-associated subglottic stenosis. JAMA Otolaryngol Head Neck Surg. 2013; 139(1): 76–81, doi: 10.1001/jamaoto.2013.1135, indexed in Pubmed: 23329095.

37. Hernández-Rodríguez J, Hoffman GS, Koening CL. Surgical interventions and local therapy for Wegener's granulomatosis. Curr Opin Rheumatol. 2010; 22(1): 29–36, doi: 10.1097/BOR.0b013e328333e9e9, indexed in Pubmed: 19910793.

38. Almuhanna A, Almahboob A, Alhussien A, et al. Current Therapeutic Approaches to Subglottic Stenosis in Patients With GPA: A Systematic Review. Ear Nose Throat J. 2021 [Epub ahead of print]: 1455613211036246, doi: 10.1177/01455613211036246, indexed in Pubmed: 34392732.

39. Poo SX, Pepper RJ, Onwordi L, et al. Sirolimus use in patients with subglottic stenosis in the context of granulomatosis with polyangiitis (GPA), suspected GPA, and immunoglobulin G-related disease. Scand J Rheumatol. 2021; 50(1): 52–57, doi: 10.1080/03009742.2020.1777324, indexed in Pubmed: 32865088.

40. Nouraei SAR, Obholzer R, Ind PW, et al. Results of endoscopic surgery and intralesional steroid therapy for airway compromise due to tracheobronchial Wegener's granulomatosis. Thorax. 2008; 63(1): 49–52, doi: 10.1136/thx.2007.078915, indexed in Pubmed: 17573443.

Table 1. The 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology — classification criteria of granulomatosis with polyangiitis [14, 15]

Before applying the criteria:
the criteria indicated for patients with a diagnosis of small or medium-sized vasculitis should be used

- other diagnoses that may cause symptoms of vasculitis should be excluded

Clinical criteria:
nasal involvement: bloody discharge, ulceration, scabbing, sensation of congestion, obstruction damage or perforation of the nasal septum
+3

cartilage involvement: auricular chondritis or nasal chondritis, hoarseness or stridor, bronchial involvement or saddle nose
+2

conductive or sensorineural hearing loss
+1

Laboratory, imaging, histological criteria
c-ANCA or anti-proteinase 3 antibodies (PR3-ANCA)
+5

nodules, tumours or cavities in the lungs
+2

granuloma, extravascular granulomatous inflammation or giant cells
+2

inflammation, opacity or fluid in the nasal cavity or paranasal sinuses, or mastoiditis
+1

pauci-immune glomerulonephritis
+1

p-ANCA or myeloperoxidase antibodies (MPO-ANCA)
-1

blood eosinophil count ≥1000/μl
-4

The results of the 10 categories must be summed to obtain a score. The score ⩾ 5 is required to meet the classification criteria.

Table 3. **CAPTION [17-19]**

Disease form	Definition	Induction of treatment	Maintenance therapy
Localised	Disease confined to the upper or lower respiratory tract	Co-trimoxazole	Co-trimoxazole
Early systemic	Systemic disease without threat to organ function, not life-threatening for the patient	MTX or CYC + GC	Co-trimoxazole
Generalised	Disease with deterioration of renal or other organ function, creatinine levels < 500 μmol/l	CYC+ GC or RTX + GC or MMF + GC	AZA + GC or MTX + GC or Leflunomide or AZA or MMF + GC
Severe	Disease with deterioration of renal or other organ function, creatinine levels > 500 μmol/l	CYC or RTX + GC or PEX	AZA or MMF + GC
Refractory	Progressive disease despite treatment with GCS and cyclophosphamide	IVIg, RTX, DSG, MMF, ATG, IFX, HSCT, ALM	No consensus
In the course of testing		Ocrelizumab, afatumumab, epratuzumab, belimumab, abatacept	

ALM — alemtuzumab; ATG — anti-thymocyte globulin; AZA — azathioprine; CYC — cyclophosphamide; DSG — gusperimus; EUVAS — European Vasculitis Society; GC — glucocorticosteroids; HSCT — hematopoietic stem cell transplantation; IFX — infliximab; IVIg — intravenous immunoglobulin; MMF — mycophenolate mofetil; MTX — methotrexate; PEX — plasmapheresis; RTX — rituximab

Figure 1. Computed tomography (CT): sagittal view

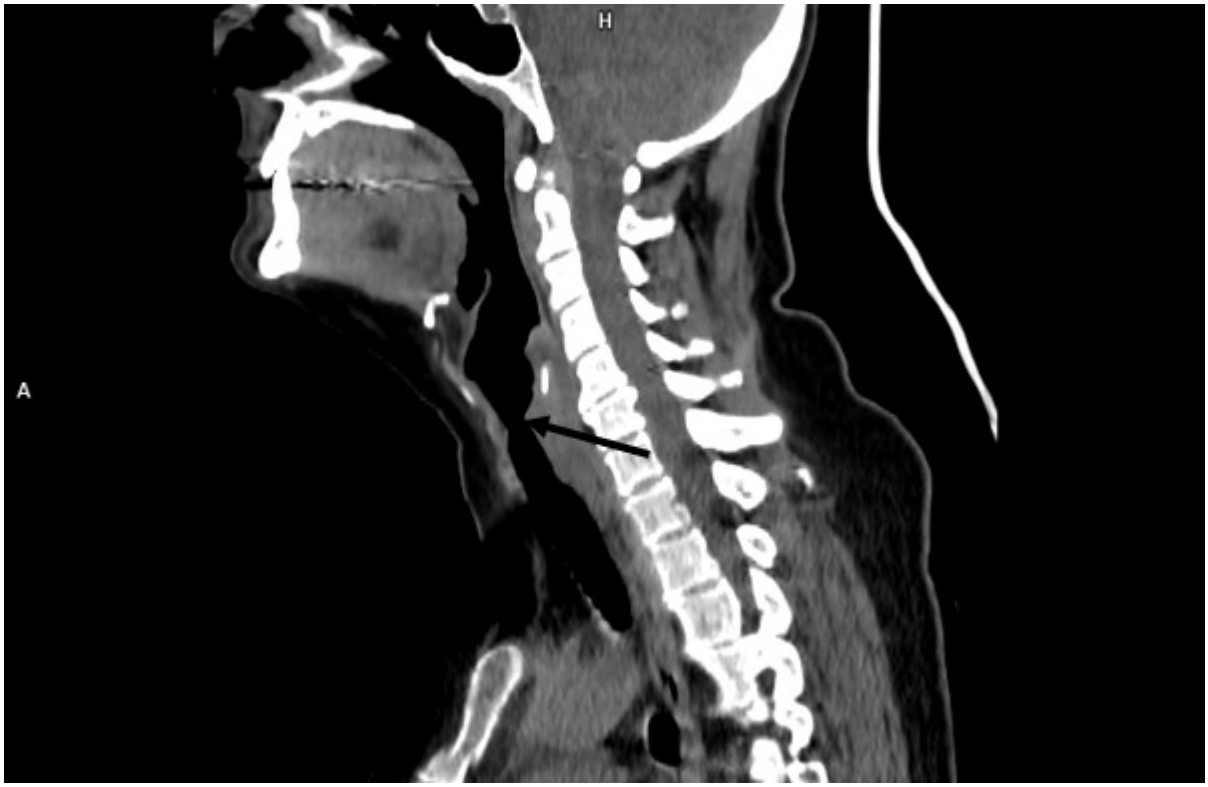


Figure 2. Computed tomography (CT): coronal view

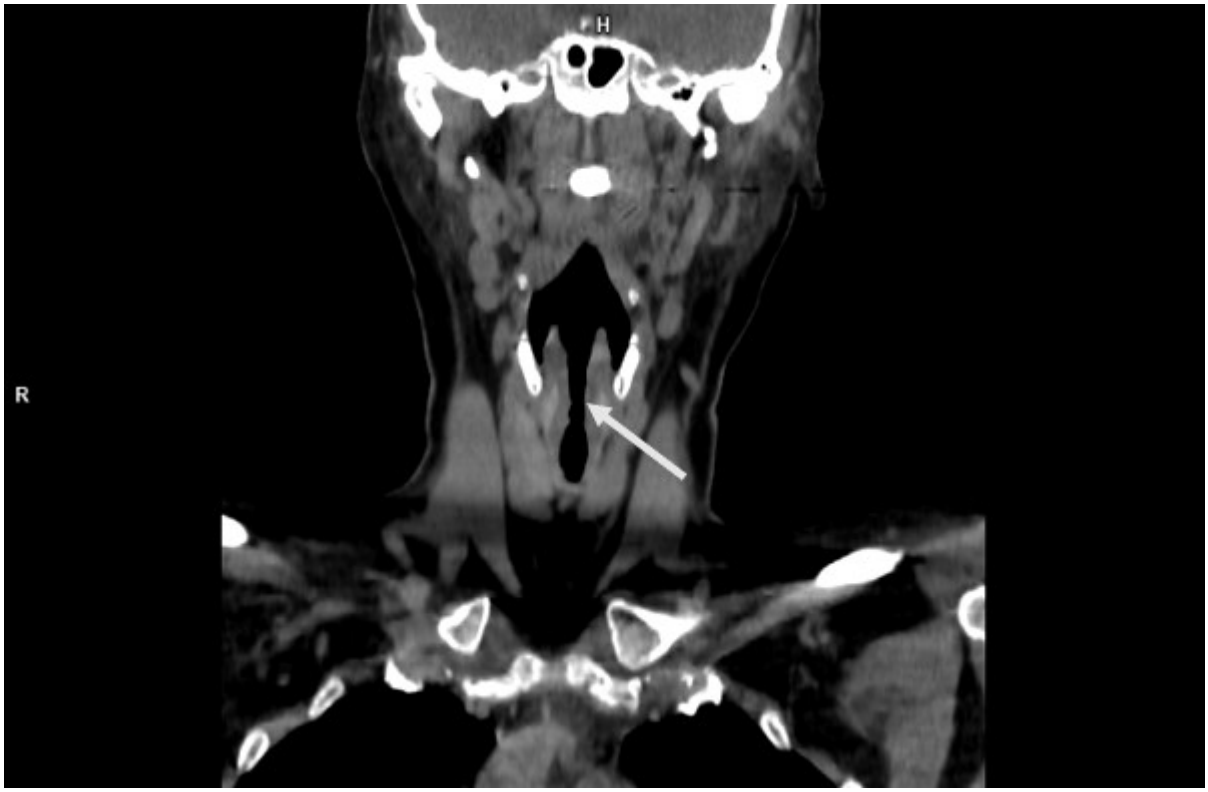


Figure 3. Magnetic resonance imaging (MRI): T2 image, transversal view

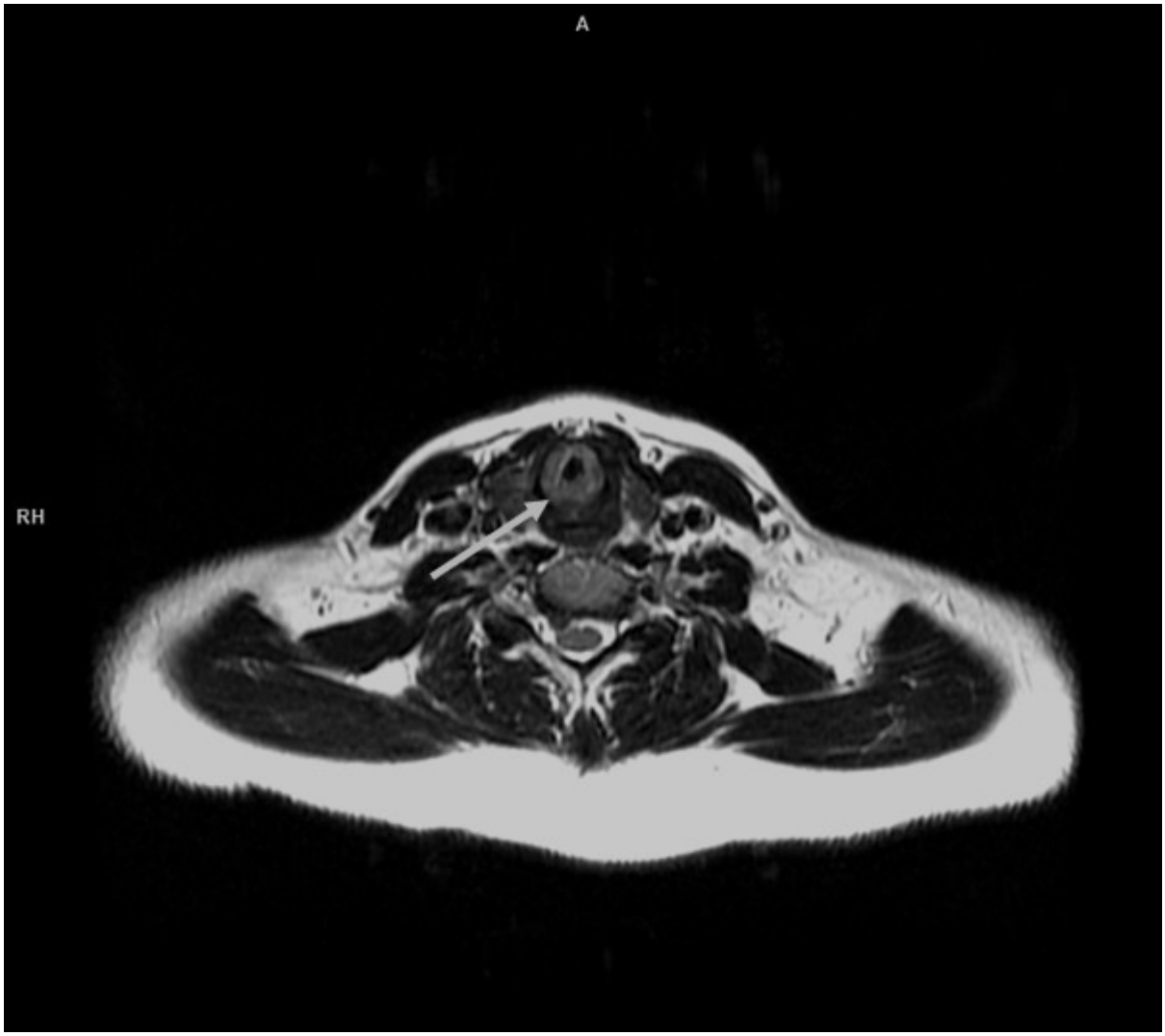


Figure 4. Computed tomography (CT): transversal view

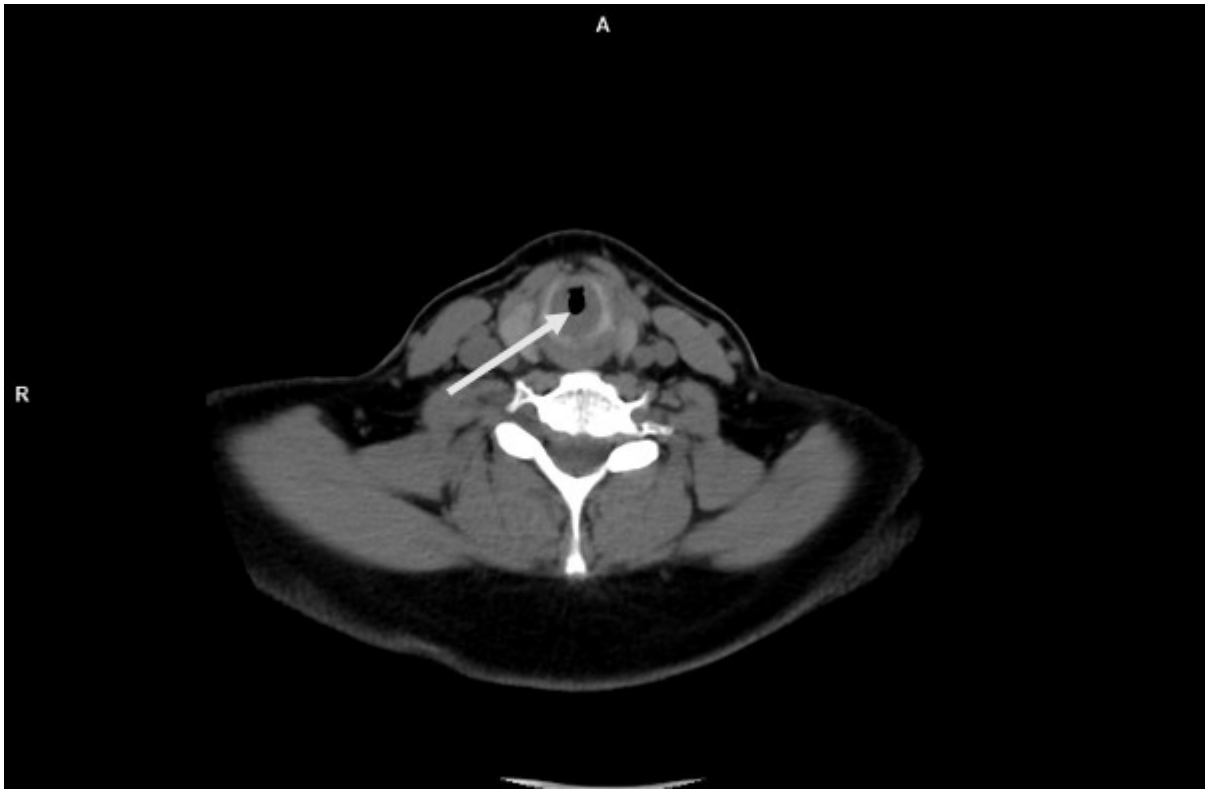


Figure 5. Computed tomography (CT): coronal view 1

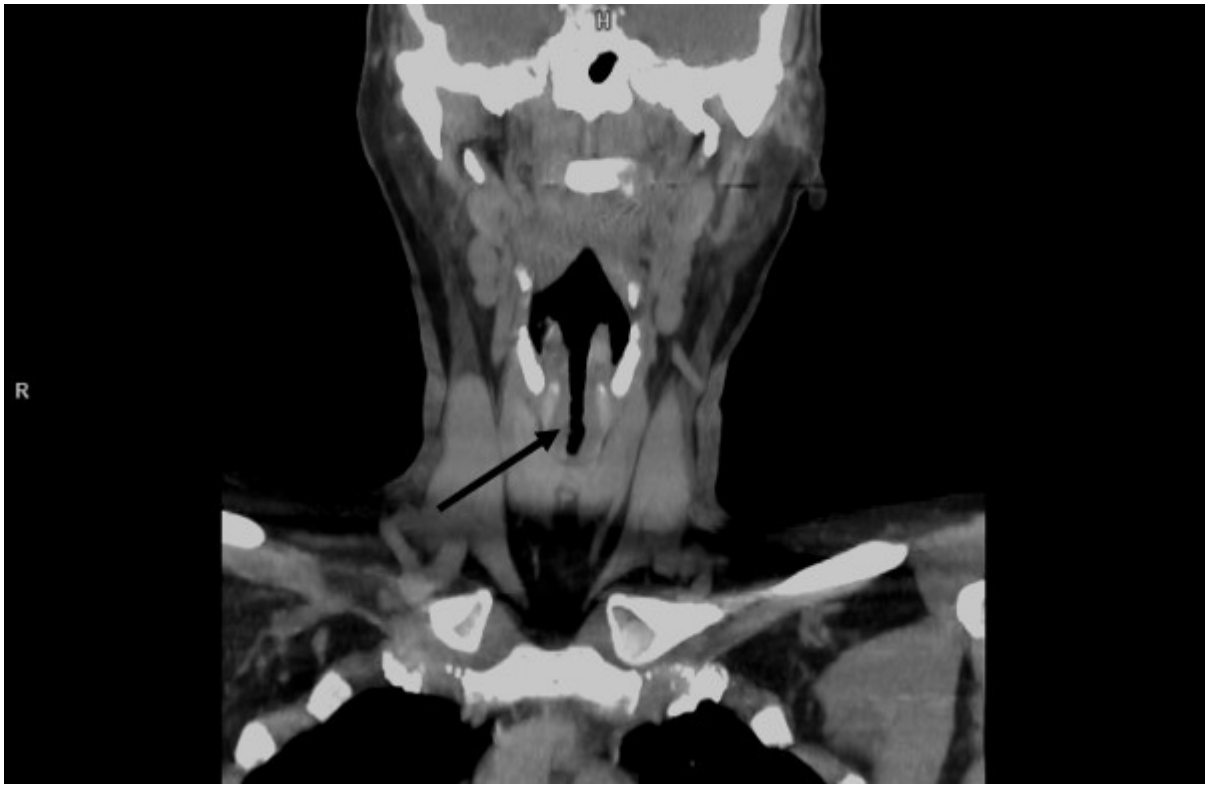
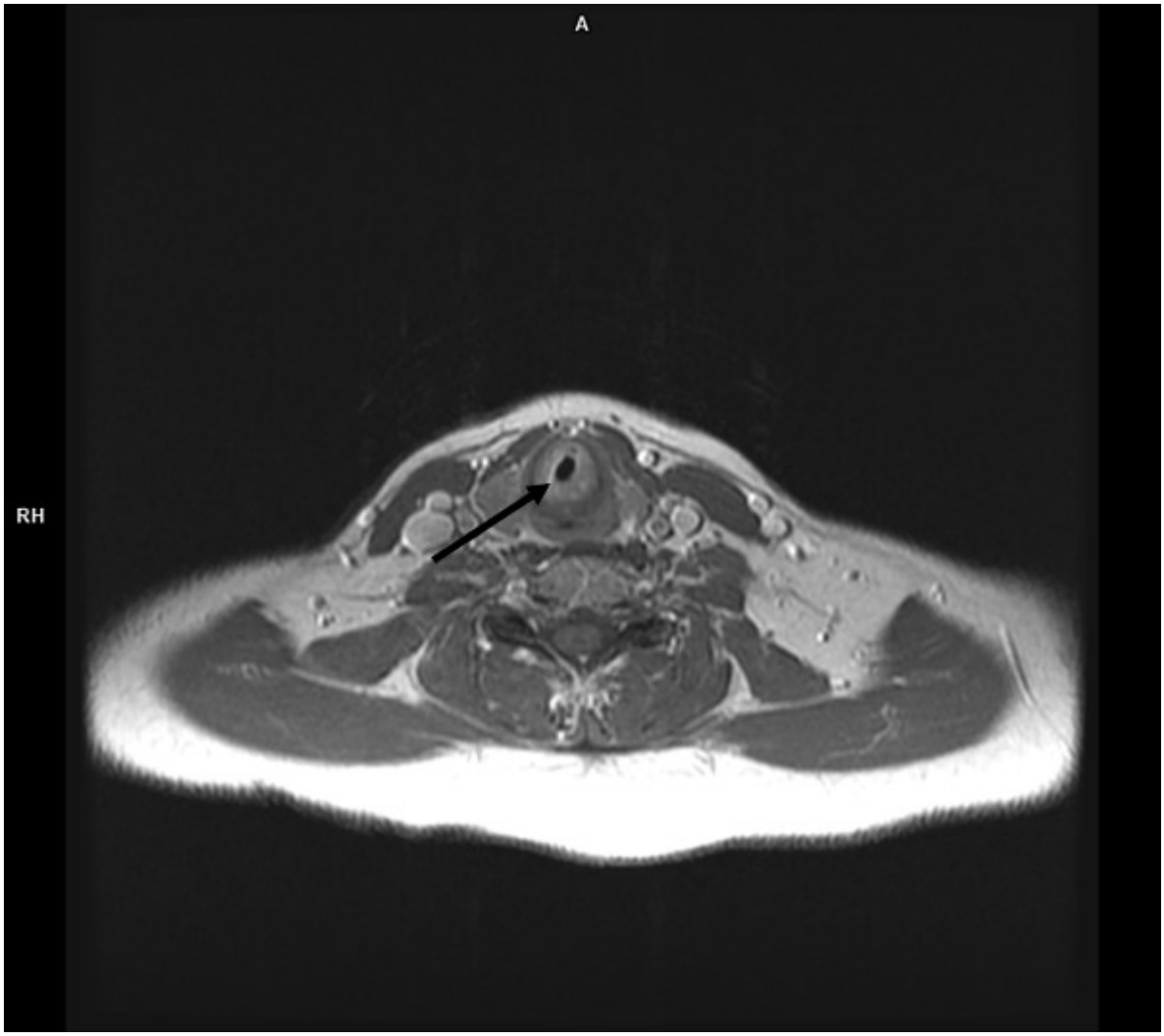


Figure 6. Magnetic resonance imaging (MRI): T1 image, transversal view


A
RH