Review

Respiratory and otolaryngologic manifestations of giant cell arteritis

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Abstract

Objective. The classical presentation of giant cell arteritis (GCA) includes the new onset of headache, scalp tenderness, facial pain or jaw claudication in an older patient. Many patients with GCA have features consistent with the diagnosis of polymyalgia rheumatic (PMR) and nearly all have elevated markers of inflammation such as the erythrocyte sedimentation rate (ESR) or the serum C-reactive protein (CRP). Respiratory and ear-nose-throat (ENT) signs and symptoms such as cough, tongue infarction, trismus, hearing loss and facial swelling are less commonly described, yet they may be the initial presentation of GCA.

Our aim was to review the published literature on the topic of respiratory and otologic manifestations of GCA.

Methods. A literature search was performed on PUBMED and MEDLINE using the following keywords: GCA, temporal arteritis, pulmonary, respiratory, ENT, cough, tongue necrosis.

Results. The upper and lower airways manifestations of GCA include a wide variety of conditions that could be caused by ischaemia due to the vasculitis.

Conclusions. It is important to recognise these atypical presentations because they may be the sole initial manifestation of the disease. Early suspicion and confirmation of the diagnosis of GCA can help to prevent more catastrophic consequences of unrecognised disease, including stroke and blindness.

Introduction

Giant cell arteritis (GCA) is an ancient disease. One of the first descriptions of GCA can be found in Ali Ibn Isa’s Tazkiratul-Kahhaleen, Notebook of the Oculist, published in the tenth century AD. Ibn Isa describes migraines, headaches in patients with chronic eye disease and “acute, sharp, catarrhal affections, including those showing heat in and inflammation of the temporal muscles” and that these conditions may lead to vision loss (1). In the English literature, one of the earliest descriptions of GCA is attributed to Sir Jonathan Hutchinson, who, in 1890, described a patient who had “red streaks on his head” which were painful and prevented him from wearing his hat. These red streaks were thought to be swollen temporal arteries (2). Horton et al. characterised GCA as being a systemic illness (3). They observed tenderness over the scalp, painful nodules along the temporal arteries, headaches, and weight loss and jaw stiffness in two patients. In 1938, the observation of an increased erythrocyte sedimentation rate was first noted (4) and a decade later striking improvement of symptoms after steroid treatment was first reported (5).

Headache is the most common symptom, occurring in about 70% of patients with GCA. The headache may be variable in location, intensity and quality. However, it is often of new onset. Jaw claudication occurs due to ischaemia of the masseter muscles, leading to pain when chewing tough foods. Visual symptoms such as vision loss and diplopia may develop in about a third of patients. The most concerning complication is blindness due to its irreversible nature. Other manifestations entail large vessel involvement including aortic aneurysm and dissection, aortic arch syndrome, and limb artery stenosis (6, 7).

Respiratory symptoms involving the upper and lower airways are occasionally observed. These include dry cough, throat and tongue pain and hoarseness. Patients may present with otolaryngologic symptoms such as...
tongue necrosis, dysphagia, and submandibular swelling. The presence of these symptoms may be overlooked in some patients, further delaying the diagnosis. Given the risk for permanent visual loss and other major morbidities, identifying the link between the respiratory tract, otolaryngologic manifestations and other more classical features of GCA can help to expedite the diagnosis and initiate appropriate therapy. Glucocorticoids are a highly effective therapy for GCA and should be initiated early and utilised for the shortest period of time, to avoid long-term adverse effects (8). This review is intended to increase clinicians’ awareness of the less commonly seen respiratory and otolaryngologic symptoms of GCA.

Methods
A literature review using the PUBMED and MEDLINE databases was performed with the following keywords: giant cell arteritis, temporal arteritis, pulmonary, respiratory, ear-nose-throat, cough, and tongue necrosis. Case reports, controlled studies, retrospective studies and review articles were included. Studies published in languages other than English were excluded. Table I lists these sources.

Clinical manifestations
Orofacial manifestations
Since GCA has a predilection for involvement of cranial arteries, it should not be surprising to observe orofacial signs and symptoms in some patients. These can be divided into two distinct groups: those that are associated with ischaemia and those that demonstrate features of localised inflammation. In the former category, one can observe temporal and scalp pain, jaw pain and complaints of claudication. Jaw claudication is elicited in about half of patients. Tongue or scalp necrosis has been rarely observed, yet GCA is the most common cause of tongue necrosis (9). It is often localised to small areas of the tongue mucosa due to an extensive collateral blood supply network in the tongue (10).

Some patients complain of dysphagia, which is due to involvement of the pharyngeal vessels (11). In the second category, one may observe non-specific facial swelling (9, 12). In one prospective study of 345 patients with GCA, the frequency of facial oedema was 12% (13). Similarly, a chart and literature review of 260 patients with GCA found 37 cases (14%) of head and neck swelling that lasted at least one day (13). Head and neck swelling appeared to be a transient but heralding feature, preceding the development of GCA. The swelling mainly involved the orbital region, the lower part of the cheeks and maxillae. Periorbital pain has also been described as a presenting feature of GCA (14). Less commonly, oedema was noted in the lateral and anterior aspects of the neck, the tongue and the supraclavicular space. The swelling typically resolves following with therapy and in some patients it may spontaneously remit over time (13). Tongue pain may be tested by assessing for repetitive rapid protrusion of the tongue, which may produce pain, burning or fatigue (10). The tongue has a rich blood supply; thus necrosis is rare and indicates extensive vascular involvement. The presence of tongue necrosis portends a worse prognosis as these patients tend to be older and also have a higher incidence of vision loss. However, the non-specific swelling may be mistaken for other diagnoses including sinusitis and angioedema.

As noted earlier, jaw claudication, is the most specific non-neurological sign of GCA and may be misdiagnosed as a temporomandibular joint disorder (15). However, trismus or reduction in jaw opening, is much less recognised. One retrospective analysis of 88 patients, noted six to have reduction in jaw opening. These patients had a more acute presentation with shorter time to diagnosis (average of four weeks versus twelve weeks), and there was a high correlation with eye involvement in about half of the patients (16).

Submandibular swelling has also been noted to be an initial manifestation of giant cell arteritis (14, 17, 18). Ruiz-Masera et al. reported a case of a 75 year-old woman who presented with a submandibular mass, ultimately requiring resection of the gland. The diagnosis of GCA was made following a review of the histopathology of the mass (17). Other less commonly reported symptoms include necrosis at the tip of the nose, lip necrosis, paresthesias felt over the chin, glossitis, and dental pain (19).

Audiovestibular manifestations
One of the earliest links of deafness with GCA was provided by Cook et al., who described seven patients who developed unilateral, and subsequently bilateral deafness which improved spontaneously (20). A later study found that 5 out of 68 patients with GCA had bilateral sensorineural deafness, which did not improve after steroid therapy (21). Progressive hearing loss as an initial manifestation of GCA has also been reported in a handful of cases, with improvement of hearing loss noted in some patients (21). Whether or not the hearing loss is reversible and to what extent, may depend on how early the corticosteroid treatment is initiated. Audiovestibular manifestations may occur prior to other symptoms of GCA (22). Thus, early recognition of these signs is important since the treatment of this condition with corticosteroids may be quite different than the more watchful approach that is often used in the management of patients with these issues. In addition, missing the diagnosis of GCA and the opportunity to initiate appropriate therapy may lead to even more dire consequences. Thus, in a patient with PMR and new audiovestibular symptoms, the clinical suspicion of underlying GCA should be considered and higher doses of corticosteroids may need to be instituted (4).

Spontaneous ear pain has been described as an initial manifestation of GCA (23). In addition, a recent prospective study with 44 patients with GCA showed that audiovestibular dysfunction was significantly more common in patients with GCA than among age-matched controls (4). A patient was defined as having abnormal vestibular tests if any of these three findings were noted: spontaneous nystagmus, head-shaking nystagmus, or an abnormal caloric test. Using these criteria, audiovestibular manifestations such as hearing loss, tinnitus, vertigo, and diz-
Table I. Patient characteristics, initial presentation and diagnosis.

<table>
<thead>
<tr>
<th>Author (Year)</th>
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<tbody>
<tr>
<td>Huston et al. (1978)</td>
<td>Retrospective</td>
<td>Temporal arteritis: a 25 year epidemiologic, clinical and pathologic study</td>
<td>-Mayo Clinic patients Olmsted county, MN 1950-1974</td>
<td>-Headache: 90%</td>
<td>Either positive temporal artery biopsy or -Classic manifestations of temporal arteritis including ESR, and at least 4 of: tender, swollen temporal artery, jaw claudication, blindness, PMR and response to corticosteroids</td>
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<tr>
<td>Cohens et al. (1982)</td>
<td>Case report</td>
<td>Facial swelling and giant cell arteritis</td>
<td>-62-year-old white woman</td>
<td>Severe facial swelling, glossitis, odynophagia</td>
<td>Temporal artery biopsy positive</td>
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<td>Pedersen et al. (1983)</td>
<td>Case report</td>
<td>Lingual infarction in giant cell arteritis</td>
<td>-77-year-old woman</td>
<td>-3 weeks of left tongue &amp; jaw pain; unable to speak or swallow</td>
<td>-Symptoms reversed with corticosteroid therapy</td>
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<tr>
<td>Bradley et al. (1984)</td>
<td>Case report</td>
<td>Giant cell arteritis with pulmonary nodules</td>
<td>-59-year-old woman</td>
<td>-Left arm, bilateral foot and ankle pain for 6 months</td>
<td>-Left temporal artery biopsy showed GCA</td>
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<td>Pedersen et al. (1983)</td>
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<td>Lingual infarction in giant cell arteritis</td>
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Table I continues
## Respiratory manifestations of GCA / T.F. Imran et al.

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<tr>
<td>Ginzburg et al. (1992)</td>
<td>Case report</td>
<td>Lingual infarction: a review of the literature</td>
<td>79-year-old woman</td>
<td>-Tongue necrosis -3 month history of right facial and jaw pain -Acute right ocular blindness -1 month prior: fatigue, lethargy, tongue swelling with inability to eat</td>
<td>-Patient refused biopsy -Clinical diagnosis -Improvement with glucocorticoid therapy</td>
</tr>
<tr>
<td>Mangenelli et al. (1992)</td>
<td>Case report</td>
<td>Trismus and facial swelling in a case of temporal arteritis</td>
<td>71-year-old woman with euthyroid goiter</td>
<td>-Left temporal headache, fever, malaise, anorexia -3 weeks later: masseter spasm, painful chewing -Lower facial swelling -One episode of amaurosis fugax</td>
<td>Biopsy of left temporal artery -Oedema improved with 4-6 weeks of steroid therapy</td>
</tr>
<tr>
<td>Romero et al. (1992)</td>
<td>Case series</td>
<td>Pleural Effusion as manifestation of temporal arteritis</td>
<td>67-year-old woman 71-year-old woman</td>
<td>Patient 1: -3 month history of malaise, weight loss, shoulder pain, frontoparietal headache, jaw clausication, cough, scanty sputum, and left pleuritic chest pain -Pleural effusion: exudates with high protein Patient 2: -1 month history of temporal headache, fatigue and jaw claudication -Right pleuritic chest pain, productive cough -Pleural effusion: exudate</td>
<td>-Temporal artery biopsy positive -1 patient had pleural biopsy: atypical mesothelial hyperplasia with inflammatory cells</td>
</tr>
<tr>
<td>Ruiz-Masera et al. (1995)</td>
<td>Case report</td>
<td>Submandibular swelling as the first manifestation of giant cell arteritis</td>
<td>75-year-old woman</td>
<td>-Right submandibular pain and difficulty swallowing for several months</td>
<td>Submandibular mass histopathology confirmed the diagnosis of GCA</td>
</tr>
<tr>
<td>Ghanchi et al. (1996)</td>
<td>Case report</td>
<td>Facial swelling in giant cell (temporal) arteritis</td>
<td>79-year-old Caucasian woman with hypertension</td>
<td>-Sudden, painless blurring of vision -Shoulder pain, malaise, fatigue -“Heavy” feeling on the affected side of the face -A month prior: swelling of face on left and around left eye, pain with chewing</td>
<td>Confirmed later with left temporal artery biopsy</td>
</tr>
<tr>
<td>Hellmann et al. (2002)</td>
<td>Case report</td>
<td>Temporal Arteritis: a cough, toothache and tongue infarction</td>
<td>79-year-old woman</td>
<td>-Blindness in right eye -1 month prior: fatigue, dry cough, then toothache, burning sensation on left side of tongue, weight loss; ESR: 115</td>
<td>Temporal artery biopsy positive</td>
</tr>
<tr>
<td>Amor-Dorado et al. (2003)</td>
<td>Prospective</td>
<td>Audiovestibular manifestations in GCA</td>
<td>44 patients with GCA -10 patients with biopsy negative, isolated PMR</td>
<td>-90% of GCA patients had abnormal vestibular tests compared to patients with isolated PMR</td>
<td>Hearing loss, vestibular function improved after 3 months of therapy in some cases, and in almost all cases with 6 months of therapy</td>
</tr>
<tr>
<td>Forderreuther et al. (2003)</td>
<td>Case report</td>
<td>Giant cell arteritis presenting as a periorbital pain syndrome and a submandibular mass</td>
<td>72-year-old woman</td>
<td>-Intense, gnawing, constant pain around left eye, mild lacrimation -Two years later, the patient developed a submandibular mass</td>
<td>Submandibular mass histopathology -confirmed GCA with transmural inflammation</td>
</tr>
<tr>
<td>Gonzalez-Gay et al. (2005)</td>
<td>Retrospective</td>
<td>GCA: Disease patterns of clinical presentation in a series of 240 patients</td>
<td>Single hospital population of Lugo, Spain, between January 1, 1981, and June 15, 2004</td>
<td>-Headache: 86.4% -Severe ischaemic manifestations: 54.6% - Abnormal temporal artery on exam and anaemia may predict the risk of severe ischaemic complications related to GCA</td>
<td>Temporal artery biopsy positive</td>
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</table>

*Table 1 continues*
The mechanisms of pulmonary involvement in GCA have not been clearly elucidated, and may be related to a primary vasculitis of small and medium-sized vessels (26). Pulmonary symptoms may precede other manifestations of GCA, and thus an evaluation for underlying GCA should be done in an elderly patient who may not have the typical features of GCA and PMR.

Direct involvement of the lung has been reported in a few cases of GCA. Chest radiographs may demonstrate either a diffuse reticular pattern or multiple nodules (29). Patients with GCA, who present with involvement of one of these organs, a high index of suspicion for GCA is required, since any delay in diagnosis could result in serious outcomes. Table I summarises the features of the pulmonary manifestations of GCA, which are less commonly reported but may be equally serious.

**Discussion**

GCA is an inflammatory disease affecting large and medium-sized vessels that is characterised by medial and adventitial inflammation with giant cells, leading to the destruction of the elastic laminae (33). Although the precise etiology is not known, it has been proposed that GCA is T cell dependent and an antigen driven process (26). Though most of the literature on GCA has focused on the visual complications, GCA encompasses a wider spectrum of clinical features, including respiratory and otolaryngologic manifestations, which are less commonly reported but may be equally serious.

Table I summarises the features of the pulmonary involvement noted in prospective and retrospective studies, case series and case reports. When patients present with involvement of one of these organs, a high index of suspicion for GCA is required, since any delay can result in detrimental outcomes.

The head and neck swelling presentation, and jaw claudication symptoms may be explained by involvement of the cervical arteries. Aneurysms were present in about two thirds of patients with GCA. Hearing loss was noted in 27% of patients. About 30% of patients had persistent head-shaking nystagmus that did not resolve after three months of corticosteroid treatment (4). However, vestibular symptoms generally improved after three months of treatment with steroids and some patients may actually compensate over time without any treatment.

**Respiratory manifestations**

Respiratory symptoms have been reported in up to one third of GCA patients seen at the Mayo Clinic (24). Rarely, the respiratory symptoms may be the initial form of presentation (25).

- **Chronic cough or sore throat**
  A dry non-productive, persistent cough is the most common respiratory manifestation in GCA. It usually improves with steroid treatment (26). It may be associated with fever, and in rare cases may be the initial manifestation of the disease (27, 28). Some patients may have concomitant symptoms such as headache and PMR but may not voluntarily report these symptoms (19). Thus, it is vital to obtain a thorough review of systems to determine the likelihood of GCA as a cause.

- **Imaging of pulmonary involvement**
  The mechanisms of pulmonary involvement of GCA may all be explained by involvement of the cervical arteries. Aneurysms were present in about two thirds of patients with GCA. Hearing loss was noted in 27% of patients. About 30% of patients had persistent head-shaking nystagmus that did not resolve after three months of corticosteroid treatment (4). However, vestibular symptoms generally improved after three months of treatment with steroids and some patients may actually compensate over time without any treatment.

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<tr>
<td>Zadik et al. (2011)</td>
<td>Case report</td>
<td>A 78-year-old woman with bilateral tongue necrosis</td>
<td>-78-year-old woman</td>
<td>-Tongue pain -Pain of right side of head, neck, face and shoulder worse while eating -Fatigue, visual blurring over 2 months, weight loss -ESR: 69, CRP: 6.1</td>
<td>Duplex sonography: occlusion of left artery, compatible with GCA</td>
</tr>
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</table>
of the external carotid artery system. In contrast, since the tongue has a rich blood supply and collateral circulation with the lingual, facial, pharyngeal, and palatine arteries, tongue necrosis may be localised to small areas of the tongue mucosa (10). In addition some patients with GCA may also have show features of a peripheral facial paresis, auditory-vestibular symptoms and dysphagia (4). The exact mechanism(s) of auditory-vestibular dysfunction in GCA remain to be elucidated. However, it is likely that ischaemic complications of the vasculitis, and inflammatory involvement of the vertebobasilar arteries or the terminal branches of the cochleovestibular vasculature are responsible (34). Auditory and vestibular functional areas are supplied primarily by the labyrinthine artery, which branches off of the anterior inferior cerebellar artery (34).

The most common respiratory manifestation of GCA is cough. Its precise etiology is not known. It is thought that cough receptors that are distributed throughout the airways, diaphragm and esophagus may play a role in this manifestation as they become irritated by inflammation of blood vessels. In addition, cough receptors that lie outside the respiratory tract may also be stimulated by the external auditory canals, eardrums, nose, and sinuses (26). In some patients, the disease itself may incite hyper-reactivity of the airways, leading to cough. As an example, arteritis of the bronchial mucosa has also been demonstrated (29). The hoarseness, sore throat, choking sensation, and tenderness of the cervical structures that may occur concurrently with cough may be due to ischaemia or inflammation in the arteries supplying the laryngeal and pharyngeal structures (26). Moreover, GCA can involve the main pulmonary arteries in addition to large and medium pulmonary elastic arteries. In some cases, there may be an overlap in symptoms of GCA with granulomatosis with polyangiitis (GPA) or other ANCA positive vasculitides.

Conclusion

Though uncommon, patients with GCA may present with respiratory, auditory-vestibular, or otolaryngologic symptoms, which may or may not accompany other characteristic symptoms of GCA. Patients are often misdiagnosed with other conditions. The astute clinician should be keenly aware of these features, as timing is critical in establishing the diagnosis of GCA to prevent serious complications such as blindness and stroke. A better understanding of the respiratory and otolaryngologic features of GCA may provide clinicians with a better understanding of the myriad presentations of GCA.

References

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34. GUR H, EHRENFELD M et al.: Pleural effusion


