Case 17
Scalp ulceration and visual loss in an elderly man

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Patient: A 78-year-old Thai man from Bangkok

Chief complaint: Bilateral visual loss for 2 weeks

Present illness:
Three weeks earlier, the patient complained of a new-onset headache and small painful red lumps on both temporal areas. Later, these painful lumps became ulcerated and filled with pus.

Two weeks earlier, he experienced a sudden visual loss involving both eyes with spontaneous recovery. He also developed difficulty walking due to severe pain on the hips.

One week earlier, the visual loss became persistent and progressive resulting in difficulties with activities such as recognizing faces. Besides, he also suffered from jaw pain on chewing and talking.

Past history:
- Hypertension, dyslipidemia and chronic kidney disease for 10 years
- Diabetes mellitus type 2 for 4 years
- Hepatocellular carcinoma treated with partial hepatectomy 4 years ago
- No history of smoking

Current medications: Amlodipine 10 mg/d, metoprolol 100 mg/d, doxazosin 4 mg/d, metformin 500 mg/d, simvastatin 20 mg/d

Skin examination:
- Two deep ulcers covered with necrotic debris and pus distributed in a linear pattern over the left frontotemporal area
- Two crusted erosions also distributed in a linear pattern over the right frontotemporal area
- Temporal arteries were not palpable

Eye examination:
- Visual acuity: Hand motion both eyes
- Fundus examination: Papilledema both eyes
Investigation:
Laboratory tests
CBC: Hct 34.1%, WBC 13,080 (N83%, L11%, M5%, E1%),
   Plt 487,000/mm³
BUN 21 mg/dL, Cr 0.68 mg/dL
ESR 100 mm/hr, CRP 122.19 mg/L
Anti-HIV: negative
VDRL and TPHA: non-reactive
ANA: fine-speckled, nucleolar and nuclear dot titer > 1:1280
RF 7.7 IU/mL (<15)
p-ANCA and c-ANCA: negative
HbA1C 6.78%, FBS 150 mg/dL
HBsAg: negative, anti-HBS: positive, anti-HCV: negative

Imaging studies
MRI and MRA of brain and orbit:
- Atrophic change of bilateral optic nerves indicating optic neuropathy
- Thin plaque at the left carotid bulb
- Visualized carotid and superficial temporal arteries
 Orbit angiography: Colloidal drop out

Microbiology tests
- Pus for gram stain: Gram positive cocci in cluster with numerous PMNs
- Pus for aerobe culture: Staphylococcus aureus

Histopathology: (S13-24493, left temporal artery)
- There is a dense inflammatory cell infiltrate of neutrophils, lymphocytes, histiocytes and varying number of giant cells within the lumens and the wall (the intimal and media) of large artery
- AFB, GMS and PAS stains are negative

Diagnosis: Giant cell arteritis
(with superimposed bacterial wound infection)

Treatment:
- Intravenous pulse methylprednisolone 1 gm/day for 5 days followed by prednisolone 1 mg/kg/day
- Methotrexate 7.5 mg weekly as a steroid-sparing agent
- Tocilizumab (anti-IL-6 receptor antibody) 8 mg/kg on the first month and 4 mg/kg on the second month
- Clindamycin 300 mg orally three time a day for 7 days
- Chloramphenical ointment apply ulcers and erosions three time a day

Discussion:
Giant cell arteritis (GCA), also known as temporal arteritis, is a systemic granulomatous vasculitis affecting medium-sized to large-sized arteries, leading to luminal occlusion and therefore presenting as ischemic sequelae. GCA occurs almost exclusively in patients aged over 50 years with a peak incidence in the eight decade of life and showing a female predominance. 

GCA most frequently affects the superficial temporal artery, hence the term temporal arteritis, followed by ophthalmic artery and posterior ciliary artery. Moreover, large vessels also can be involved in about 25% of patients with GCA, commonly aorta and its main branches. Involvement of extra-aortic large vessels, including major arteries of upper and lower extremities, is somewhat less frequent. 

In terms of pathophysiology, inappropriate activation of dendritic cells residing in the arterial wall is suggested to be the earliest step to initiate the pathogenic cascade, including recruitment of T cells and macrophages to form granulomatous infiltration. Infectious organisms are suspected to be a main factor in the triggering of dendritic cells in an individual with genetic predisposition. Effector cytokines released into the arterial wall targets endothelial cells, vascular smooth muscle cells and fibroblasts, resulting in intimal hyperplasia and luminal obstruction. Among various cytokines and inflammatory mediators, interleukin-6 (IL-6) appears to play an important role in the induction of acute phase response. 

Clinical presentations of GCA can be mainly grouped into systemic inflammation on one hand and ischemic sequelae on the other hand. Systemic inflammation usually manifests as polymyalgia rheumatic (PMR), symmetric proximal myalgias combined with laboratory abnormalities, occurring in about half of patients. Fever, malaise and weight loss are also common symptoms. 

Regarding ischemic sequelae, the presentation will depend on the territory, which the affected artery supplies to. Temporal arteritis typically presents with headache, scalp tenderness, jaw claudication, thickened temporal artery and tender nodules; nonetheless, it sometimes manifests as scalp ulceration and necrosis. Indeed, scalp necrosis appears to be a poor prognostic factor as it is associated with increased mortality and a higher incidence of visual loss. When the artery supplying to the optic nerve is affected, it can result in ischemic optic neuropathy, the true emergency in GCA by the reason of leading to permanent visual loss in about 15% of patients. Visual manifestations in GCA patients widely range from transient diplopia, amaurosis fugax to sudden visual loss. 

Turning to large-vessel GCA, the most common presentation of upper or lower extremity vasculitis is limb claudication while occasionally digital necrosis may be seen in patients with GCA of upper extremities. In contrast, when GCA affects the aorta, it does not cause obstruction, but aortic dilatation and aneurysm formation, which are often asymptomatic. In view of the prognosis, GCA is now recognized as a chronic condition. The longevity is generally not reduced by GCA unless having severe complications from aortitis. 

Although the diagnosis of GCA remains clinical, when possible it should be confirmed by histopathology, typically showing inflammatory infiltration with giant cell formation in the arterial wall, fragmentation of elastic lamina and intimal hyperplasia causing luminal occlusion. Temporal artery biopsy has long been the gold standard for diagnosing GCA; however, duplex ultrasonography of temporal artery has emerged as a valid alternative. In fact, the sensitivity of
temporal artery biopsy is about 90%\(^3\); hence, a negative biopsy does not entirely exclude the diagnosis of GCA. The negative biopsy might be explained by the focal and segmental nature of inflammation, so-called skip lesion\(^6\), or the fact that GCA does not involve the temporal artery in every case.

Diagnosis of large-vessel GCA, in particular aortitis, generally requires imaging studies. Computed tomographic angiography (CTA) and magnetic resonance angiography (MRA) have been taking place to be the reference standard while traditional angiography is now reserved for planning revascularization procedures.\(^1\)

Marked elevations in the level of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are commonly found in GCA patients, giving a greater specificity when combined testing. Only 4% of patients with confirmed GCA had a normal level of both ESR and CRP.\(^7\) Anemia and thrombocytosis are also often demonstrated.

High-dose corticosteroids are the mainstay in the GCA treatment. Therapy is usually initiated with prednisolone at a dose of 1 mg/kg/day or intravenous pulse therapy in an individual having unstable supply of blood to the eyes or central nervous system.\(^1,2\) The treatment duration is highly variable, with most of patients being able to discontinue corticosteroids after 1-2 years. As the more adverse events occur in parallel to the longer use of corticosteroids, there have been numerous attempts to identify the effective steroid-sparing agents in GCA therapy. Unfortunately, there are no other immunosuppressive agents that improve therapeutic efficacy or safety, compared to the use of corticosteroids alone.\(^2\) Among the sparing agents with disappointing results, methotrexate appears to be a potential adjunct as it can reduce the relapsing rate and the cumulative dose of corticosteroids, but it cannot reduce corticosteroid-related side effects.\(^8\)

Tumor necrosis factor-\(\alpha\) (TNF-\(\alpha\)) levels have been reported to express at high levels in the serum of patients with GCA, as well in the granulomatous infiltrates. Thus, TNF-\(\alpha\) inhibitors seem to be a theoretical rationale for the treatment of GCA. However, infliximab and etanercept fail to establish their effectiveness for GCA treatment.\(^9\) Recently, the promising results have been revealed in GCA patients treated with tocilizumab, anti-IL-6 receptor antibody, either when using with corticosteroid therapy or using alone. Its effectiveness has also been shown in GCA patients with newly diagnosed, relapsing or refractory disease. However, follow-up was short in all cases and controlled trials are needed to confirm its benefits.\(^9\)

Our patient is another classic case of GCA in an elderly man who chiefly presents with ischemic sequelae from vasculitis affecting temporal artery and perhaps posterior ciliary artery. The histopathological findings of temporal artery biopsy were not typical for diagnosing GCA possibly due to interfering from superimposed bacterial infection. Therapy was initiated with intravenous pulse therapy of corticosteroids, which appeared to be very effective. Apart from abated clinical signs and symptoms, the therapy also yielded a marked improvement in patient’s visual acuity, turning from hand motion to 20/50 in the right eye. Besides, tocilizumab was also given in addition to the ongoing treatment to improve the therapeutic efficacy. Unfortunately, patient eventually died due to severe sepsis after 3 months of treatment.

References: