
Neurologic manifestations of giant cell arteritis

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ABSTRACT

Neurological manifestations are common in giant cell arteritis. Both the central and peripheral nervous system can be involved. The most dreaded manifestations are visual loss and stroke. Both frequently have premonitory symptoms, such as amaurosis fugax, blurry vision, diplopia, transient ischemic attacks, and jaw claudication. Although most of these manifestations occur prior to steroid therapy, they may also develop during the early phase of therapy, or during tapering of the dose of steroids. Earlier diagnosis, close monitoring and improving the treatment protocols may prevent mortality and improve morbidity in these cases.

Introduction

Giant cell arteritis (GCA) commonly involves the nervous system. GCA can involve the central nervous system, the cranial nerves, and the peripheral nerves (Table I). The neurologic manifestations are the result of vasculitis in the nutrient arteries, or extension of the inflammation from the arterial walls to adjacent nerves.

Central nervous system involvement

Headache is a common presenting symptom of GCA. The origin of the pain is believed to be the inflamed arteries,

hence the pain is mostly in the temporal areas, but can be occipital or widespread. The occurrence of headaches have decreased in recent years. Between 1950-1969, 96% of the patients diagnosed at the Mayo Clinic presented with headaches, compared to only 71% of patients diagnosed between 1980-85 (1). A similar trend was reported in Israeli patients, where the occurrence of headaches decreased from 81% (during 1960-77) to 66% (during 1980-92) (2). This decreasing frequency of headaches is probably related to the increasing rate of diagnosing patients with an "atypical" GCA presentation (2).

Cerebrovascular accidents (CVA) such as strokes and transient ischemic attacks (TIA) are uncommon. In a large-scale study of 166 consecutive biopsy-proven cases, TIA were reported in 6%, and strokes in 3% of the cases (3). However, given the frequent occurrence of these manifestations in the elderly population, it is difficult sometimes to decide whether the ischemic event is related to GCA or to atherosclerotic vascular disease. Involvement of the vertebro-basilar system is relatively more common in GCA, where 40-60% of the strokes occur in the vertebro-basilar territory, compared to atherosclerotic strokes, where only 15-20% of the strokes develop in that territory. Involvement of the vertebro-basilar system results in strokes of the cerebellum, occipital lobe and brain stem, leading to ataxia, cortical blindness, and compromise of vital functions. Stroke is one of the leading causes of GCA-related morbidity and mortality, and is probably the most common cause of early deaths in GCA (4, 5).

It should be noted that strokes may develop shortly after starting steroid treatment or while tapering the dose. In one report of 6 GCA patients with fatal strokes, the ischemic event occurred in only one patient prior to therapy, in 2 patients within the first 2 weeks of treatment, and in 3 cases while tapering the dose to 10 mg/d or less (4). Similarly in a recent report, out of 8 GCA patients

Table I. Neurologic manifestations of giant cell arteritis.

1. Central nervous system

Transient ischemic attacks
Stroke
Neuropsychiatric manifestations
Myelopathy

2. Cranial neuropathies

Optic neuropathy
Oculomotor disorders
Vestibulo-auditory manifestations
Lingual nerve involvement

3. Peripheral neuropathies

Mononeuropathy/mononeuropathy multiplex
Polyneuropathy
Radiculopathy
Brachial plexopathy

with CVA, the ischemic events developed in 7 cases after starting steroid therapy (median time on treatment was 10 days) (6). Two of the patients died as a result of the stroke (both had vertebral-basilar stroke). CVA were more common in patients with visual loss (odds ratio 7.6) and jaw claudication (odds ratio 3.5) (6). It is possible that addition of antiplatelet or anti-coagulant therapy at the initiation of steroid treatment, or increasing the initial steroid dose in high-risk patients, may decrease the occurrence of early strokes in GCA.

Neuropsychiatric manifestations were reported in 3% of GCA patients (3). The various symptoms include dementia (disorientation, cognitive and memory impairment), mood disorders (mostly depression), and psychotic features. Visual hallucinations have also been reported but these are probably not "true" psychiatric manifestations, and are always associated with visual loss (see below). It is important to note that GCA is one of the treatable causes of dementia, and in such cases treatment with steroids can improve symptoms or result in stabilization (7). Steroid therapy in patients with psychosis initially worsens the psychotic manifestations, and should be combined with anti-psychotic drugs. In addition, some GCA patients may develop psychosis or depression as adverse effects of steroids during therapy (3). Involvement of the spinal cord, in the form of transverse myelopathy, is very rare, occurring in less than 1% of patients (3).

Cranial neuropathies

Anterior ischemic optic neuropathy (AION), the main cause of visual loss, is relatively common in GCA. Its frequency has decreased in the last 20 to 30 years, probably due to increasing awareness of physicians and earlier diagnosis of GCA patients, but it still involves 6-15% of the patients (1-3). Less common causes of visual loss are central retinal artery occlusion, posterior ischemic optic neuropathy and cortical blindness. Most cases occur prior to initiation of steroid therapy; however, AION may develop during tapering of the dose, and rarely even during treatment with full-dose steroids. AION re-

sults from involvement of the posterior ciliary arteries (PCA) - branches of the ophthalmic artery which supply the optic nerve head and the choroid. An autopsy study described vasculitic involvement of the PCA in 75% of GCA cases (8). Thus it seems that PCA involvement is common, but clinically silent in most cases.

Visual loss in GCA has been considered to be sudden and without warning symptoms. However, recently Font *et al.* reported that 65% of GCA patients with irreversible loss of vision had premonitory visual symptoms (9). The most common was blurry vision (43% of cases), followed by amaurosis fugax (33%), hemifield loss and diplopia. These premonitory symptoms lasted 1-10 days prior to the loss of vision. Blurry vision possibly results from choroidal ischemia which precedes AION (10). Such gradual visual deterioration may also cause visual hallucinations (Charles Bonnet syndrome): in sane elderly individuals decreasing visual stimuli to the visual cortex may lead to increased autonomous cortical activity, resulting in release phenomena: visions which are formed (i.e., have shapes of certain figures such as animals, flowers, etc.) that are pleasant and vivid, and superimposed on the existing visual environment (11). The patients are aware of the unreal nature of the visions, but are frequently reluctant to disclose them, fearing they would be labeled as "psychotic". Those visions precede the visual loss and cease within 2 weeks (12, 13).

Amaurosis fugax must also be considered a medical emergency in this context of GCA: 64% of GCA patients with transient visual loss developed irreversible visual loss within a short period of time. This was mostly due to AION, while some cases developed central retinal artery occlusion or posterior ischemic optic neuropathy (14). Prompt treatment with steroids might prevent the development of such complications.

Visual loss is irreversible in most cases when it occurs in GCA. Early treatment with high-dose steroids has been suggested in such cases; however its beneficial effect has not been proven. The only hope to preserve vision in GCA patients is by awareness to the various pre-

monitory symptoms. Hopefully imaging modalities such as fluorescein angiography and color Doppler ultrasonography of the ocular vessels will enable us to monitor the degree of ophthalmic involvement, as a guide to therapy (10, 14, 15).

Diplopia, resulting from the involvement of the oculomotor, abducens or trochlear nerves is uncommon. It has been reported in 2% of GCA patients (3).

Vestibulo-auditory manifestations have been reported in 7% of GCA patients (3). A review of the English literature of the last 45 years has identified 33 cases. The most common symptom was hearing loss (bilateral in 16 and unilateral in 7), followed by vertigo in 12 cases and tinnitus in 6. Some patients experienced a combination of hearing loss and vertigo or tinnitus. The effect of steroid therapy was reported in 15 of these cases: treatment resulted in improvement in 7 of the patients.

Peripheral neuropathies

Peripheral mononeuropathies and peripheral polyneuropathy each occur in 7% of GCA patients (3). The pathogenesis of this type of neuropathy probably involves vasculitis of nutrient arteries, or extension of the inflammatory process from adjacent arteries. Most cases were diagnosed prior to, or at the time of GCA diagnosis, but some neuropathies developed following diagnosis and treatment. Review of the English literature of the last 40 years disclosed 50 cases: 40% had polyneuropathy, which was usually symmetric. The others had mononeuropathies, including mononeuropathy multiplex. The most commonly involved nerve was the median (12 cases), followed by brachial plexopathy with involvement of the upper part of the plexus (C5-C6 roots). This part of the plexus is adjacent to the subclavian artery. The brachial plexus lesion typically presents with weakness of the deltoid muscle, which is quite difficult at times to differentiate from C5 radiculopathy. Other nerves, such as the ulnar or peroneal, were less commonly involved.

Response of the peripheral neuropathy to steroid therapy was reported in 35 of those 50 cases: 26 of them improved (74%), while the others had no change

or became worse.

Neurological manifestations are common in GCA patients. Some may cause mortality or severe morbidity. Earlier diagnosis and close monitoring during treatment, possibly with the use of newer imaging modalities or serologic tests, and advances in treatment protocols, may enable us to prevent some of these complications and improve the outcome of GCA patients.

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