Short Report

Giant cell arteritis: A clinical and pathological study

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ABSTRACT

Background. Giant cell arteritis is a vasculitis affecting large- and medium-calibre vessels. It is not uncommon in the West and there are many large series in the literature. However, there are very few reports of giant cell arteritis among Indian patients.

Methods. We did a retrospective study of 9 Indian patients (5 men and 4 women; age range 59–81 years [mean and median 70 years]) who had had a temporal artery biopsy for suspected giant cell arteritis at a tertiary care hospital.

Results. Eight patients had biopsy-proven giant cell arteritis. The common presenting features were pyrexia of unknown origin (4), headache (6) and blurring of vision (2). The erythrocyte sedimentation rate was elevated and ranged from 25 to 120 mm at the end of the first hour (mean 96, median 105). The C-reactive protein level, which was available in 5 cases, was raised. Giant cells and inflammatory cells were seen in 7 of 8 temporal artery biopsies; a transmural lymphocytic and neutrophil infiltrate without giant cells was present in 1 case. All patients were treated with steroids and they responded well.

Conclusion. Temporal arteritis is probably under-recognized in India. Pyrexia is a common presenting feature of the disease; temporal arteritis should be considered in the differential diagnosis of elderly patients with pyrexia of unknown origin.

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INTRODUCTION

Giant cell arteritis (GCA) or temporal arteritis is a systemic granulomatous arteritis affecting large- and medium-sized arteries, especially the extracranial branches of the carotid arteries. GCA has a wide spectrum of clinical manifestations, such as claudication of the jaw, blindness, polymyalgia rheumatica, stroke, pyrexia, headache and constitutional symptoms, including loss of weight and anorexia.[1–8] The laboratory results include a high erythrocyte sedimentation rate (ESR), raised levels of C-reactive protein and fibrinogen, and thrombocytosis.[9] The diagnosis is confirmed by demonstration of giant and inflammatory cells in a temporal artery (TA) biopsy. Oral steroids form the mainstay of treatment.

GCA is not uncommon in the West and there are many large series in the literature.[4] However, very few cases have been reported among Indian patients.[7,8,10–12] We document a series of 9 Indian patients with GCA. Of these, 8 were biopsy-positive and one was biopsy-negative.

METHODS

This retrospective study was done over a period of 8 years (2000 to 2008). The biopsy slides and clinical and laboratory data of all 13 patients who had a TA biopsy done for a suspected diagnosis of GCA during this period were reviewed. Twelve patients had undergone a unilateral TA biopsy and 1 had had a bilateral biopsy. Four of these patients were excluded—2 patients with a normal unilateral TA biopsy because on re-evaluation, they showed clinical and pathological features inconsistent with GCA; 1 patient with the bilateral TA (review of the slide showed features of microscopic polyangiitis); and 1 patient who showed features of GCA on biopsy, but there was a lack of clinical details, including follow up, at the time of writing this paper.

RESULTS

The demography, clinical presentation, laboratory analysis and treatment of the 9 patients covered are shown in Table I. The age of the patients ranged from 59 to 81 years (mean 70) with 5 men and 4 women. The duration of illness ranged from 1 to 20 weeks (mean 7.4, median 4). All of them were treated with oral steroids and the response, as assessed clinically, was good.

The length of the excised artery ranged from 5 to 15 mm. The sections were cut at 3 μm thickness. All were examined at multiple levels by staining with haematoxylin–eosin, and some with Periodic-acid Schiff and elastic van-Gieson stain. The morphological changes evaluated included the presence and type of inflammatory infiltrates, multinucleate giant cells and fragmentation of elastic lamina.

Eight patients had features of GCA on TA biopsy, while in one patient the biopsy was normal.

Histology of the affected arteries showed a dense transmural infiltrate of lymphocytes and neutrophils in 8 patients and multinucleate giant cells in 7 (Fig. 1). Calcification of the artery was seen in 1 biopsy and fragmentation of the media was noted in 4. Intimal proliferation was present in 7 patients. Periarteriolar lymphocytic infiltrates (PALI) were seen in 5 patients (Fig. 2) and thrombi in 2. There was no necrosis in any of the biopsies.

One patient had normal morphology of the TA and there was no PALI or calcification even on multiple-level examinations.

DISCUSSION

There is little data on GCA from India. There are only 4 solitary case reports of GCA in Indian patients.[7,8,10,12] Further, Joshi and Mittal have epidemiological data that GCA forms about 3.4% of vasculitis in India.[11]

The American College of Rheumatology (ACR) has established a 5-point scoring system, which gives equal importance to each of the following parameters: age ≥50 years; localized headache of recent onset; TA tenderness; ESR >50 mm at the end of the first

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TABLE I. Demography, clinical presentation and investigation of patients with giant cell arteritis

Age (years)	Sex	Clinical history	Investigations	
			ESR*	Others
81	F	Headache, blurring of vision on left side, TA tenderness (1 week)	110	—
66	M	Subacute proximal girdle pain, TA cord-like (5 months)	25	CRP raised
72	M	PUO (4 months), aneurysm of ascending aorta	100	CRP raised, cANCA-negative
70	F	Occipital headache, loss of weight and appetite (4 months)	120	CRP raised
65	M	Recurrent compressing headache, loss of weight and appetite (1 month)	116	CRP raised
77	M	PUO, headache, neck ache (2 weeks)	78	—
59	F	PUO, blurring of vision, jaw claudication (2 weeks)	110	—
77	M	PUO, headache (2 weeks)	100	CRP raised
64†	F	Bitemporal headache, jaw claudication (1 month)	105	—

* ESR erythrocyte sedimentation rate in mm at the end of the first hour † Biopsy-negative case TA temporal artery
PUO pyrexia of unknown origin CRP C-reactive protein cANCA antineutrophil cytoplasmic antibody

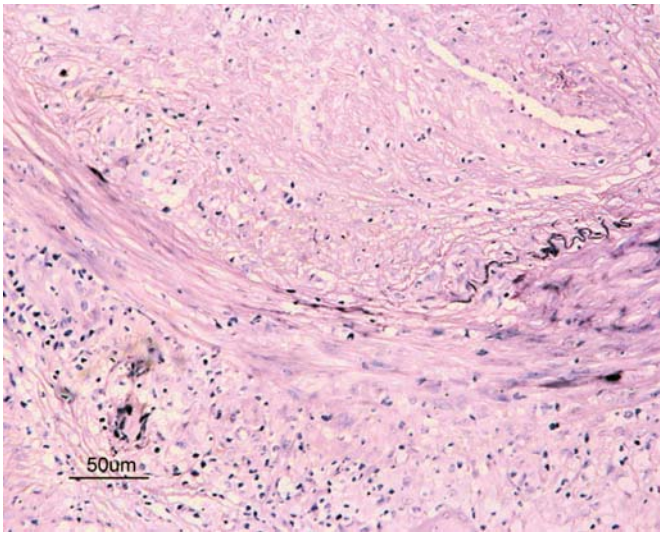

FIG 1. Temporal artery revealing fragmentation of internal elastic lamina and mural inflammatory infiltrate. Note multinucleate giant cell in tunica media (above the scale bar, EVG stain, ×20).

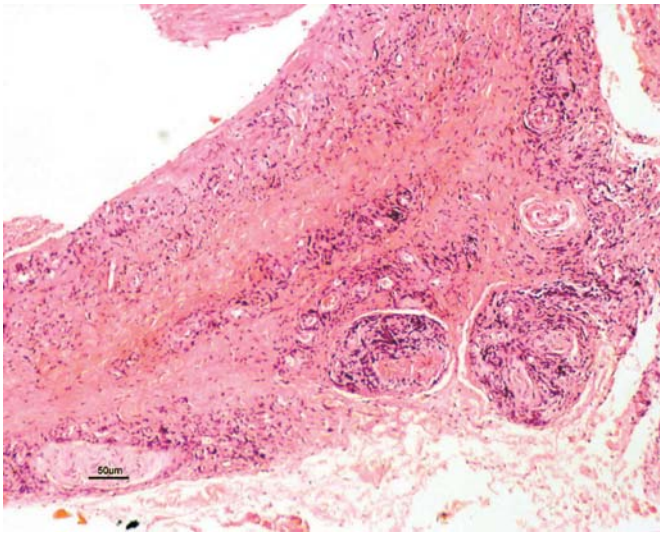

FIG 2. Low-power view of temporal artery revealing transmural inflammatory infiltrates involving tunica intima, media and adventitia. Tunica adventitia shows foci of lymphocytic infiltrates around vasa vasorum and nerve twigs (HE stain, ×10).

hour; and a positive histology on TA biopsy. A score of ≥3 is highly suggestive of GCA (sensitivity 93.5%; specificity 91.2%).[5]

The classical presentation is that of temporal headache, jaw claudication and TA tenderness. However, patients may also present with pyrexia of unknown origin (PUO), myalgia, stroke or cough.[1–8,13] Blindness is the most catastrophic complication and hence, it is imperative that the condition be suspected early.

Fever is not an uncommon presenting feature and 15% of patients in one large western series presented with PUO.[2] Four of our 8 biopsy-proven patients presented with PUO. Given that PUO is a common symptom, we suggest that GCA be a part of the differential diagnosis of PUO in all patients over 50 years of age. Gonzalez-Gay *et al*. observed visual complications in 26.1% and irreversible blindness in 14.9% of their biopsy-proven patients.[14]

An ultrasound evaluation should be done before a TA biopsy to confirm that the TA is not the collateral artery to the brain.[6] As scalp necrosis, facial nerve injury and stroke are complications of the biopsy procedure,[15] Allsop and Gallagher suggest that the biopsy be omitted and replaced by a trial of steroid therapy.[16] However, Drehmer *et al*. state that most physicians prefer biopsy as the comfort level of the treating physician increases.[17] In our series, 4 patients would have met the ACR criteria even before the biopsy was done. Conversely, 1 patient with a negative biopsy met the ACR criteria with a score of 3.

There is no gold standard for the diagnosis of GCA, as Chakrabarty and Franks state; however, the TA biopsy is close to it.[18] Biopsy reveals a vasculitic process characterized by a predominance of mononuclear infiltrates or granulomas, usually with multinucleate giant cells. The artery shows fragmentation of the internal elastic lamina, along with intimal hyperplasia and a lymphocytic infiltrate in the wall/intima. Necrosis is uncommon in GCA[19,20] and other forms of vasculitis merit consideration if it is present.[1]

Positive results may be obtained in 18%–82% of TA biopsies.[15] Eight of our 9 patients were positive on TA biopsy. We excluded 2 patients in whom GCA was suspected initially. However, after the biopsy was interpreted as negative for GCA, the patients were re-evaluated clinically and it was retrospectively realized that they had been clinically misdiagnosed as cases of GCA. Eosinophils were present in the biopsy of the patient with the bilateral biopsy; this was consistent with microscopic polyangiitis.[21]

The factors which determine the presence of giant cells in the biopsy include the size of the artery, a bilateral biopsy, presence or absence of skip lesions, use of immunohistochemistry, and number of levels studied.[15,18] The incidence of skip lesions

determined on actual biopsies ranges from 0% to 28%. Biopsy-negative GCA comprises 15% of clinically suspected patients.[22] A normal TA biopsy does not exclude the diagnosis, since the lesions are often focal or patchy. Longer specimens are more likely to be useful and immunohistochemistry for LCA and CD15 can be used to identify the inflammatory infiltrate in skip lesion segments.[23] A close differential diagnosis of GCA is Takayasu's arteritis. It is characterized by inflammatory cells and giant cells, and there is full thickness cicatrization, including that of the intima, a feature which is uncommon in GCA. Further, it is usually seen in young women, whereas GCA is seen in patients over 50 years of age.[6,20] It is also essential to recognize the mimics of GCA and not to over-diagnose the condition. Fragmentation of the internal elastic lamina devoid of inflammatory infiltrate is a common feature of old age change.[22] PALI may represent an aging change or may be part of the vasculitic process.[18] Thus, merely the presence of lymphocytes or calcification or internal lamina fragmentation must not be interpreted as GCA. Finally, not all patients of GCA show multinucleate giant cells: one of our patients was initially labelled as biopsy-negative. A retrospective review during this study showed that there was a dense lymphoid and neutrophilic infiltrate in the arterial wall and that the features were strongly suggestive of the diagnosis of GCA.

If the TA biopsy is negative, either it is a biopsy-negative GCA, or the physician needs to consider other possible diagnoses. Finally, occasionally a TA biopsy shows some other pathology, such as microscopic angiitis, as in our experience and that of Guerin *et al*.[21]

GCA is treated with prednisolone at a dosage of 30–40 mg/day in the absence of ocular symptoms. Referral to a specialist needs to be considered in the case of patients with visual symptoms. Such patients are treated with prednisolone at a dosage of 1 mg/kg/day (60–80 mg). Intravenous methylprednisolone is sometimes used in patients with impending loss of vision. The reason for treating these patients aggressively is to prevent loss of vision in the contralateral eye, which has a 20%–50% chance of becoming affected within a short period of time. The dosage of steroids is gradually tapered down by 5–10 mg every 2 weeks, until it reaches 20 mg per day, and is then tapered down more slowly. The duration of treatment is 1–3 years.[6,24]

In conclusion, GCA is probably under-recognized in India, going by the published literature. Pyrexia and headache were common presenting features of GCA in our series and we feel that physicians should consider GCA in the differential diagnosis of all patients with PUO over the age of 50 years. The TA biopsy confirms the diagnosis.

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