Case Report

Two cases of Giant Cell Arteritis with unusual presentations - diagnosis and management

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Abstract

Giant Cell Arteritis (GCA) is a diagnostic challenge in the Indian population as it is an uncommon disease with varied presentations. Thorough clinical examination and a systematic approach are necessary for making a diagnosis. A high index of suspicion is required to recognize GCA and commence treatment early to prevent disabling complications. We report 2 cases of GCA with atypical presentations. The approach to diagnosis and management of these cases is highlighted.

Key-words: Giant Cell Arteritis, Large Vessel GCA, Fever of unknown origin (FUO), Arm claudication, Positron emission tomography (PET)

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Introduction

Giant Cell Arteritis (GCA) or temporal arteritis is a chronic vasculitis of large and medium sized vessels reported rarely in the non Caucasian population.[1]Though vessel inflammation may be generalized, patients with GCA often present with headache, jaw claudication, or visual disturbances secondary to the involvement of cranial arteries. We report two cases of GCA who presented to us with Fever of Unknown Origin (FUO).

CASE ONE

A 65 year old lady presented to us with a one month history of fatigue and evening rise of temperature along with progressive left upper limb pain suggestive of claudication over the last 4 months. She also complained of anorexia and significant weight loss during this period.

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On examination, she had pallor. Her left radial and brachial pulses were weaker than those on the right side. Her left upper limb blood pressure was 90/70 mm Hg as compared to 120/80 mmHg on the right. Fundus examination was normal. The rest of the systemic examination was unremarkable.

The patient's investigations revealed a normocytic anaemia and elevated inflammatory markers (Table 1). Other investigations including liver function tests, creatinine, calcium, phosphorus, malarial parasite smear, Widal and urine analysis, chest X-ray and ultrasound abdomen were normal (Table 1). A transthoracic echocardiography ruled out endocarditis, blood cultures were sterile and bone marrow examination with appropriate cultures was inconclusive. CT imaging of the thorax and abdomen revealed diffuse circumferential thickening of the wall of ascending, arch and thoracic aorta measuring up to 9 mm. There was diffuse thickening of the left subclavian artery (Figure 1a) and the abdominal aorta.

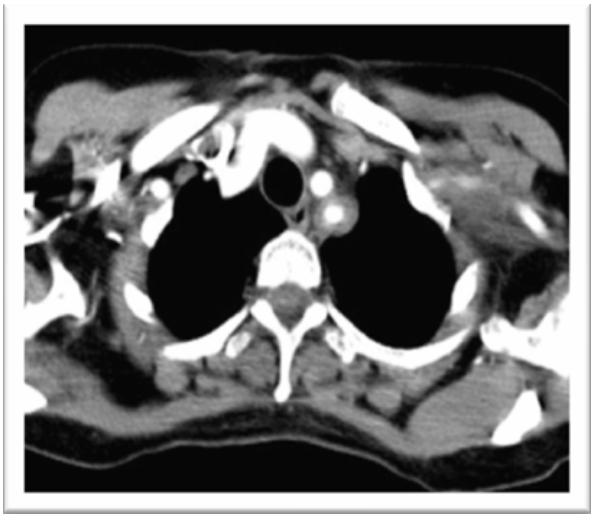
Although she did not fulfill the American College of Rheumatology criteria[4], she was diagnosed to have Large Vessel GCA based on her symptoms, laboratory and radiological findings. Temporal artery biopsy was not performed as the patient did not give consent. The patient was

empirically started on prednisolone 0.75 mg/kg body weight. The dose was tapered after 4 weeks based on a good clinical response and improved laboratory parameters. While on 15 mgs per day of prednisolone, she had a relapse and methotrexate was initiated as a glucocorticoid sparing agent. The steroids were then tapered and continued at 5mgs per day.

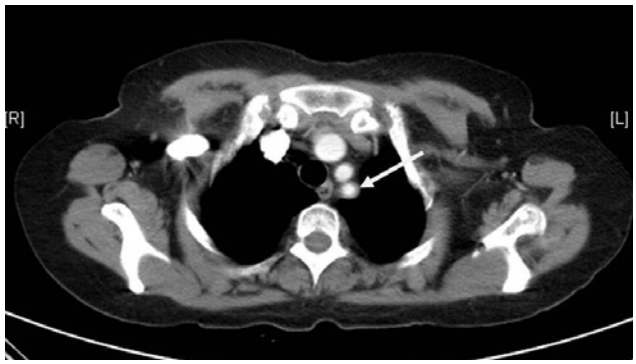
Table 1. Lab investigation at presentation of the two patients

Investigations	Results of case no 1	Results of case no 2	Normal Ranges
Haemoglobin	8.4 gm%	10.7 gm%	12 – 16 gm%
MCV	80.0	87.0	80 – 96 femtoL
Reticulocyte	1.51	1.82	
Platelet	505000/ cu mm	451000/cu mm	1.5 – 4 lakhs/ cumm
WBC count	10800/ cu mm	10600/cu mm	4000 – 12000/ cumm
Differential count			
Neutrophils	69%	60%	
Eosinophils	2%	2%	
Basophils	0%	1%	
Monocyte	8%	15%	
Lymphocyte	21%	22%	
ESR(1 hr)	100 mm	94 mm	< 35mm/hr
CRP	100 mg/L	30.3 mg/L	<5 mg/L
Creatinine	0.8 mg%	1.14 mg%	0.5 – 1.4 mg%
Liver Function Test			
Total Bilirubin	0.5 mg%	0.4 mg%	0.5 – 1.0 mg%
Direct Bilirubin	0.2 mg%	0.1 mg%	
Total Protein	7.7 gm%	6.9 gm%	6.0 – 8.5 gm%
Albumin	3.5 gm%	3.0 gm%	3.5 – 5.0 gm%
SGOT	19 U/L	40 U/L	8 – 40 U/L
SGPT	13 U/L	42 U/L	5 – 35 U/L
Alkaline Phos	151 U/L	76 U/L	40 – 120 U/L
Urine Analysis	Normal	Normal	
LDH	420 U/L	359 U/L	225 – 460 U/L
Uric Acid	4.7 mg%	4.1 mg%	4.0 – 7.0 mg%
TSH	0.61 micro U/L	1.37 micro U/L	0.3 – 4.5 micro U/L
Calcium	9.2 mg%	9.2 mg%	8.3 – 10.4 mg%
Phosphorus	4.3 mg%	2.8 mg%	2.5 – 4.6 mg%
Malarial Smear x 3	Negative	Negative	
Blood Culture x 2	No Growth	No Growth	
Stool Occult Blood x 2	Negative	Negative	

Till her last follow up 1 month back, there was no recurrence of symptoms and her inflammatory markers continued to remain normal. A repeat CT scan done after two years of treatment showed significant reduction in vessel wall thickness of the aorta and the left subclavian artery (Figure 1b).



1a



1b.

Figure 1a. CT thorax image at presentation showing vessel wall thickening of left subclavian artery. **Figure 1b.** CT thorax after 2 years showing reduction of wall thickening of left subclavian artery (arrow)

CASE TWO

A 65 year old man, a known hypertensive and dyslipidemic presented with a history of low grade fever for one month. He also complained of bifrontal headache, with loss of weight and appetite. There was no history suggestive of a connective tissue disorder.

He had undergone extensive investigations in his local hospital which included CT imaging of the chest and abdomen, multiple blood and urine cultures, serologies for brucella and typhoid, tests for malaria and tuberculosis that were inconclusive. However, his inflammatory markers were persistently elevated.

On examination in our hospital, he did not have pallor, peripheral pulses were normal, and there was no thickening or tenderness of temporal artery.

Investigations revealed elevated inflammatory markers (Table 1); bone marrow studies and cultures were inconclusive. A clinical possibility of GCA was considered in view of the persistent headache. Temporal artery doppler and biopsy were normal. Repeat CT thorax and abdomen scan showed mild diffuse circumferential wall thickening and scattered calcifications along the thoracic and abdominal aorta, with no significant stenosis or aneurysmal dilatation. PET images revealed abnormal FDG uptake (SUV 7.07) along the wall of the thoracic and abdominal aorta and few of its branches suggesting a large vessel vasculitis (Figure 2). He was diagnosed to have large vessel GCA and was initiated on a tapering dose of prednisolone and methotrexate. At follow up 6 months later, he had significantly improved and the inflammatory markers had normalised.

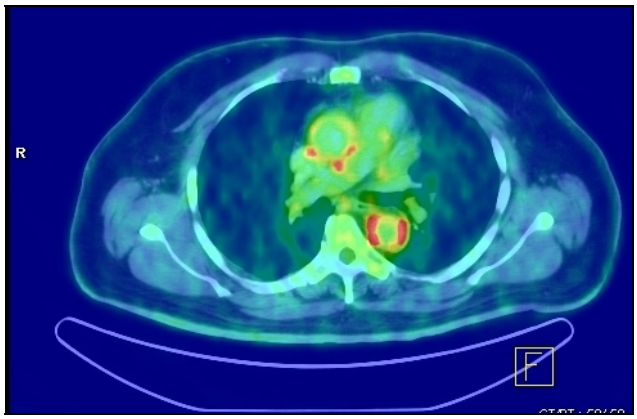


Figure 2. PET image showing Abnormal FDG uptake (SUV 7.07) in descending aorta

Discussion

GCA is a chronic vasculitis of large and medium sized vessels. Vessel inflammation involves the cranial branches of the arteries originating from the aortic arch mainly, but can be generalized. It is thought that a viral infection or other factors triggers monocyte activation leading to systemic involvement and arterial infiltration.[2]

Typically, GCA is a disease of the elderly and commonly observed in Caucasians. It is considered to be a rare occurrence in India. Singh et al in 2010 have published the largest case series of 21 patients with GCA over 15 years.[3] None of the patients had arm claudication as a presenting symptom.[3]

Pathophysiologically, GCA is classified as cranial artery GCA and large vessel GCA (LVGCA).[5,9] The classical presentation of a patient with cranial artery GCA is a new onset headache (60%-70%), with or without visual disturbances, jaw claudication (40%-50%) due to involvement of cranial vessels. It is usually associated with unexplained fever, malaise or anaemia (40%), symptoms of polymyalgia rheumatica and high inflammatory markers.[5,9] In 3 to 15 percent of cases, the aorta and proximal branches of the aortic arch, particularly the subclavian and axillary arteries, become sufficiently narrowed to produce arm claudication as described in the first patient. The second patient presented with constitutional symptoms, as the disease process involved only the large vessels without causing vascular insufficiency. This type of GCA involving aorta and its proximal branches is termed as LVGCA.[5, 9] Patients with LVGCA rarely have headache as a presenting symptom and have very high inflammatory markers and they may need positron emission tomography[8] or magnetic resonance angiography for assessment. Temporal artery biopsy may be inconclusive.[9]

Temporal artery biopsy (TAB) remains the cornerstone for a definitive diagnosis and may remain positive for two to six weeks even after commencement of treatment and should be performed in all patients suspected to have GCA It is pertinent to note that TAB may be negative in patients with LVGCA or due to the presence of skip lesions or because of sub-optimal biopsy specimens. Therefore, patients with negative biopsies should be managed as having GCA if there are typical clinical or neuro-ophthalmic features typical of GCA (e.g. anterior ischaemic optic neuritis) along with laboratory and radiological evidence. Duplex ultrasonography can detect the characteristic appearance of a hypoechoic 'halo', occlusions and stenosis, but this requires a high level of experience and training.[6]

High-dose glucocorticoid therapy should be initiated immediately when there is a clinical suspicion of GCA in order to prevent neuro- opthalmological complications.[6] TAB should not delay the prompt institution of therapy. The initial dose of prednisolone should not be less than 0.75 mg/kg per day and should be continued till the resolution of symptoms and laboratory abnormalities. Subsequently, prednisolone should be tapered till the dose reaches 10 mg daily. It is then decreased by 1 mg every one to two months with cautious surveillance for relapse.[6]

Patients with GCA are well known to suffer relapses and disease flares during steroid tapering periods. In recurrent or resistant GCA, methotrexate or other immunosuppressive (e.g. azathioprine or leflunomide) may be used.[6,7] Addition of low-dose aspirin has also been shown to decrease the rate of visual loss and vascular events in GCA.

Conclusion

A high degree of clinical suspicion, thorough clinical examination and a systematic approach are necessary for making a diagnosis of GCA given its protean clinical manifestations. TAB may not always be confirmatory in the case of LVGCA and may require imaging such as like PET-CT to make a diagnosis. Immediate initiation of high dose of steroids is imperative with close monitoring for disease flares when steroids are being reduced.

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