Case report

Giant-cell arteritis of the female genital tract associated with occult temporal arteritis and FDG-PET evidence of large-vessel vasculitis

G. Bajocchi, G. Zamorani, [1]A. Cavazza, N. Pipitone, [2]A. Versari, L. Boiardi, C. Salvarani

Unità Operativa di Reumatologia,[1]Unità Operativa di Anatomia Patologica, and [2]Unità Operativa di Medicina Nucleare, Arcispedale S. Maria Nuova, Reggio Emilia, Italy.

Gianluigi Bajocchi, MD; Giovanna Zamorani, MD; Alberto Cavazza, MD; Nicolò Pipitone, MD; Annibale Versari, MD; Luigi Boiardi, MD; Carlo Salvarani, MD.

Please address correspondence and reprint requests to: Dr. Gianluigi Bajocchi, Servizio di Reumatologia, Arcispedale S.Maria Nuova, V.le Risorgimento N80, 42100 Reggio Emilia, Italy.
E-mail: baiocchi.gianluigi@asmn.re.it

Received on June 27, 2006; accepted in revised form on December 15, 2006.

Clin Exp Rheumatol 2007; 25 (Suppl. 44): S36-S39.

Key words: Giant cell arteritis, female genital tract, positron emission tomography, temporal artery biopsy.

ABSTRACT

We describe a case of giant cell arteritis (GCA) of the female genital tract. Fluorine-18-fluorodeoxyglucose positron emission tomography ([18]F-FDG PET) and CT-scan showed evidence of large-vessel vasculitis involving the thoracic aorta and its branches, while temporal artery biopsy showed arteritis despite the absence of clinical manifestations suggestive of GCA. We review the literature and discuss the relationship between "cranial" GCA, large-vessel GCA and female genital GCA.

Introduction

We describe a case of giant cell arteritis (GCA) of the female genital tract, fortuitously discovered in the uterus. Fluorine-18-fluorodeoxyglucose positron emission tomography ([18]F-FDG PET) and CT-scan showed evidence of large-vessel vasculitis involving the thoracic aorta and its branches, while temporal artery biopsy showed arteritis despite the absence of clinical manifestations suggestive of GCA. We review the literature and discuss the relationship between "cranial" GCA, large-vessel GCA and female genital tract GCA.

Case report

In May 2004, a 63-year-old woman was referred to the Gynaecological Department for a programmed hysterectomy because of a uterine prolapse. Surprisingly, on routine histology the vessel walls of some medium myometrial arteries were infiltrated by mononuclear cells. Giant cells and fibrinoid necrosis were also present (Fig. 1). In August of the same year she was referred to our Department for elevated acute phase reactants (C-reactive-protein: 12.70 mg/dl, normal values < 0.5 mg/dl; ESR: 120 mm/hour) raising the suspect of an occult vasculitis.

No recent constitutional symptoms (in particular fever, anorexia, weight loss) or musculoskeletal manifestations were reported. The patient denied cranial symptoms (in particular headache, jaw claudication, and loss of vision) and limb claudication. Physical examination was normal. Both superficial temporal arteries were normal on palpation. Bruits were not heard on auscultation over the carotid, subclavian, axillary, and brachial arteries. Pulses in the neck and arms were normal. In addition to elevated acute phase reactants, a mild chronic-disease type anaemia (Hb 11.9 g/dl, MCV 78.2 fl) was present.

The rest of the laboratory studies including WBC, platelet count, serum chemistry and protein electrophoresis was unremarkable. A diagnosis of temporal arteritis was suspected even in absence of cranial and systemic manifestations. A temporal artery biopsy was thus performed which showed a prevalently inflammatory infiltrate in the adventitia (vasa vasorum) and presence of fibrinoid necrosis.

To evaluate the extension of the vasculitis a [18]F-FDG PET was performed. A vascular high grade uptake along the wall of the thoracic aorta was evident (Fig. 2). An angio-CT scan of the thoracic aorta and its branches was also performed. The thoracic aorta and supra-aortic vessels revealed wall thickness of 2-3 mm (with the same intensity of signal of soft tissue), which had the same anatomical distribution of FDG uptake.

A diagnosis of large vessel GCA involving thoracic aorta was made.

Despite the fact that the patient was asymptomatic prednisone was started

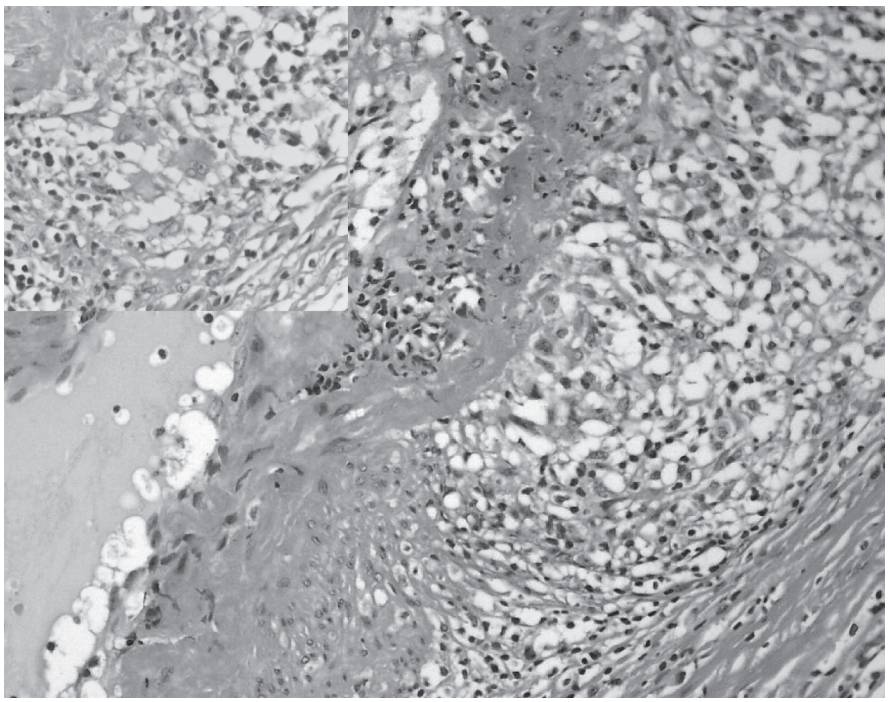

Fig. 1. Myometrial biopsy. Medium-sized vessel with heavy transmural mixed inflammation and fibrinoid necrosis. (Hematoxylin and eosin stained; original magnification X 200).
Two giant cells are shown in the insert. (Hematoxylin and eosin stained; original magnification X 600).

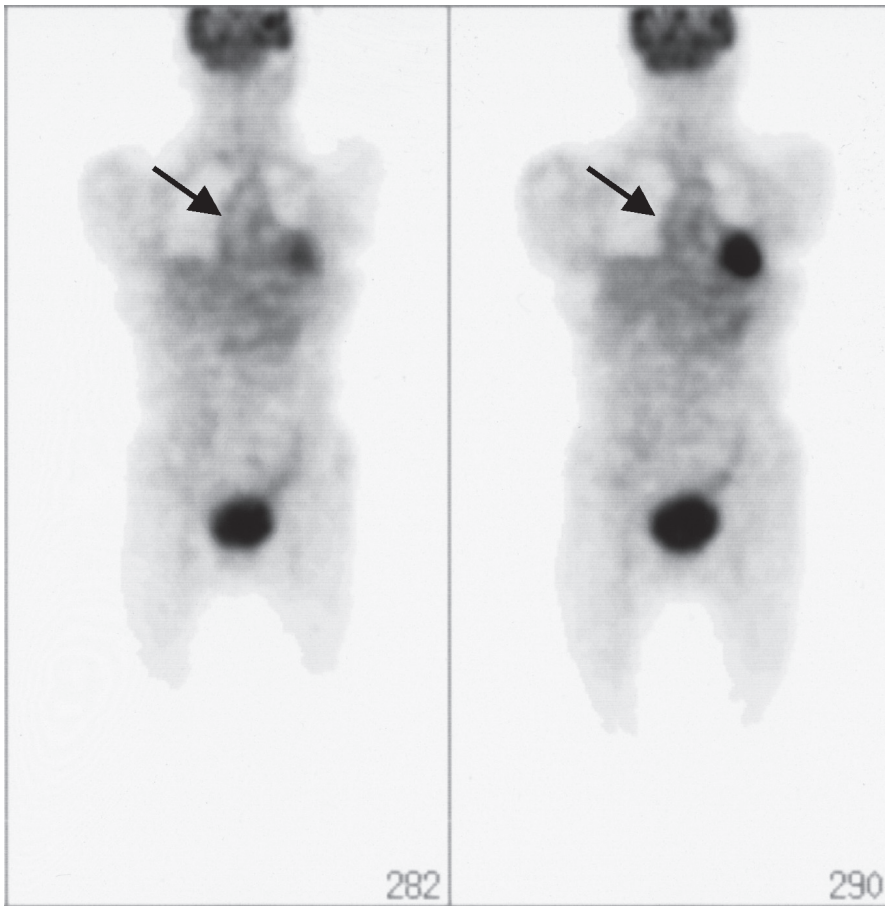

Fig. 2. ^{18}F-FDG PET in coronal section. Increased FDG uptake in the thoracic aorta (arrows).

at 37.5 mg daily and then tapered after 3 months to 20 mg. After 20 days of treatment ESR and CRP decreased to 50 mm/hour and 1.66 mg/dl, while after 3 months ESR and CRP were 22 mm/hour and 1.23 mg/dl, respectively. After one year of follow-up the patient is still asymptomatic and ESR is normalized. Prednisone was stopped after 10 months of treatment.

Discussion

Most GCA patients present with clinical manifestations that are the result of vascular involvement. Because of that, a diagnosis of GCA in these patients is relatively straightforward. However, a variable proportion of patients may present without obvious vascular manifestations (1). ^{18}F-FDG PET imaging is a new technique that may be particularly helpful in the diagnosis of GCA of large arteries in patients with atypical manifestations of the disease, or, as in the present case, in patients with "occult-silent" GCA (2, 3).

GCA of the female genital tract was first reported by Ritawa in 1951 (4). Including our patient, at the best of our knowledge, 47 cases have since been reported and their characteristics are summarised in Table I (4 - 15). In almost all published cases the diagnosis of vasculitis was made by chance on histologic examination of surgically removed genital organs for gynaecological reasons unrelated to GCA. Histopathologic involvement has been demonstrated in virtually any genital organ such as uterus (myometrium, cervix), tube, ovary and parametrium.

Our patient lacked clinical evidence of cranial, systemic and PMR musculoskeletal manifestations. Therefore, GCA affecting the female genital tract was apparently limited to this area. However ^{18}F-FDG PET showed increased vascular uptake in the thoracic aorta suggestive of inflammatory involvement. CT-scan confirmed the presence of a large-vessel vasculitis affecting the thoracic aorta and its branches. Large-vessel GCA has been described in approximately 15% of patients with GCA and it is characterized by the presence of angiographically defined stenoses or occlusions of the subclavian/axillary

arteries (16, 17). Upper extremity vascular insufficiency dominates the clinical presentation of patients with large-vessel GCA.

However, inflammatory involvement of large arteries could be more frequent in GCA patients at diagnosis, although most of the patients will not develop stenosis or occlusion and related signs/symptoms during the disease course. Recently Blockmans *et al*. (18) performed ^{18}F-FDG PET in a consecutive series of 35 GCA patients at diagnosis before steroid treatment was started. Vascular FDG uptake was observed in 83% of patients, especially in the subclavian arteries (74%), but also in the aorta (> 50%). Unfortunately, ^{18}F-FDG PET for its limited resolution is not suitable for evaluating the presence of inflammation in small diameter vessels such as pelvic/uterine arteries.

Brack *et al*. have attempted to identify the characteristics that distinguish the patients with large-vessel GCA from those with cranial GCA (17). The patients with female genital tract GCA have findings common to both main variants of GCA. The distinctive characteristics of the 3 variants of GCA are summarized in the Table I. For comparison the characteristics of total GCA patients derived from a population-based study were also reported (17, 19, 20).

Similarly to large-vessel GCA cranial symptoms are often absent, as they were observed in only 27.6% of patients with female genital GCA. However, differently from large-vessel GCA, a high proportion of patients with female genital tract GCA had positive findings on temporal artery biopsy (58% versus 93.7%) and systemic manifestations (34% versus 57.4%). Arm claudication, present in most patients with large-vessel GCA, has been reported in only 2% of patients with female genital tract GCA (7).

The absence of systemic and/or cranial manifestations raises the possibility that inflammatory vascular changes in some patients with female genital tract GCA may be restricted to the pelvic area. However, a more extensive recourse to temporal artery biopsy and/or ^{18}F-FDG PET in these patients could show, as evidenced in our patient, a clinically silent inflammation of temporal arteries and/or of large arteries in some or most of them.

Table I. Comparison of the characteristics of patients with female genital tract GCA, large-vessel GCA and cranial GCA.

Characteristics	Female genital tract GCA	Large-vessel GCA	Cranial GCA	Total GCA
Mean age at diagnosis, years	68	66[a]	72[a]	75.6[b]
Cranial signs/symptoms (%)	27.6	22-29[a]	73-80[a]	54-72[c]
Systemic manifestations (%)	57	34[a]	70[a]	55[c]
Arm claudication (%)	2	78[a]	0[a]	0.6[b]
Polymyalgia rheumatica (%)	28	41[a]	46[a]	51[c]
Mean ESR at diagnosis, mm/h	99	61[a]	84[a]	82.5[b]
Temporal artery biopsy positivity (%)	93.7	58[a]	100[a]	90[c]

Cranial signs/symptoms: headache, visual disturbances, jaw claudication, abnormalities of temporal artery at inspection; systemic manifestations: fever, weight loss, anorexia; ESR: erythrocyte sedimentation rate. [a]Brack *et al*. (14); [b]Nuenninghoff *et al*. (17); [c]Salvarani and Hunder (16).

Similarly to the findings observed in large vessel GCA, patients with female genital tract GCA had a slightly younger age at diagnosis compared to that observed in patients with GCA (68 years versus 75.6 years) (20) .

The high ESR values observed at diagnosis in the patients with genital tract GCA are more similar to the values observed in "cranial" GCA, compared to the lower values observed in the patients with large-vessel involvement. PMR appears to be independent from the pattern of arterial involvement and its frequency in patients with genital tract GCA is similar to that observed in patients with "cranial" GCA and in those with large vessel involvement.

Female genital tract GCA may be a variant of GCA different from "cranial" GCA and large-vessel GCA. It is probably underdiagnosed in the clinical practice because the vasculitic involvement of female genital tract does not apparently cause local clinical manifestations.

In patients with signs/symptoms suggestive of GCA and/or PMR, the additional finding of GCA of female genital tract does not pose diagnostic or therapeutic problems. In these patients treatment with corticosteroids is mandatory. In patients without systemic, cranial and musculoskeletal manifestations the unexpected finding of GCA of the female genital tract should prompt the clinician to perform a temporal artery biopsy to confirm the diagnosis of GCA. In case of a negative biopsy we suggest that ^{18}F-FDG PET be performed for its capacity to reveal an "occult" inflammation of large arteries, as shown in our patient.

In the case of GCA limited exclusively to the female genital tract the usefulness of corticosteroids remains unclear. Although treatment and follow-up of patients with GCA of female genital tract have not been reported in detail, we reviewed all the available data (4-15). Eight patients were not treated with corticosteroids, 4 of them were asymptomatic at diagnosis. Seven untreated patients did not develop GCA-related complications, while one presented during the follow-up aortic aneurysm with dissection.

In conclusion, we feel that female genital tract GCA is a variant of GCA, which may be underdiagnosed in the clinical practice because it is usually clinically silent. In a group of patients the vasculitic process seems to be limited to the female genital tract. However, temporal artery biopsy and/or ^{18}F-FDG PET should be considered in these patients to identify coexisting asymptomatic systemic GCA which requires corticosteroid treatment.

References

1. GONZALEZ-GAY MA, GARCIA-PORRUA C, AMOR-DORADO JC, LORCA J: Giant-cell ar-

teritis without clinically evident vascular involvement in a defined population. *Arthritis Rheum* 2004; 51: 274-7.
2. GONZALEZ-GAY MA, GARCIA-PORRUA C, MIRANDA-FILLOY JA: Giant cell arteritis: diagnosis and therapeutic management. *Curr Rheumatol Rep* 2006; 8: 299-302.
3. DE LEEUW K, BIJL M, JAGER PL: Additional value of positron emission tomography in diagnosis and follow-up of patients with large vessel vasculitides. *Clin Exp Rheumatol* 2004; 22 (Suppl. 36): S21-6.
4. RITAWA V: Temporal Arteritis. *Ann Int Med* 1951; 40: 63-87.
5. MARTINELLI G, BAZZOCCHI F, SERRA L, BORGETTI G: Arterite a cellule giganti dell'utero. *Pathologica* 1981; 73: 263-8.
6. KYLE V, HAMILTON DUTOIT S, ELIAS-JONES J, HAZLEMAN B: Giant cell arteritis of myometrial and axillary arteries and the polymyalgia rheumatica. *Ann Rheum Dis* 1987; 46: 256-8.
7. DUCROIX JP, SEVESTRE H, HUMBERT *et al*.: Localisations génitales de l'artérite à cellules géantes. *G Rev Med Interne* 1990; 11: 285-8.
8. LHOTE F, MAINGUENE C, GRIESELLE-WISELER W *et al*.: Giant cell arteritis of the female genital tract with temporal arteritis. *Ann Rheum Dis* 1992; 51: 900-3.
9. ORMSBY AH, HASKELL R: Giant cell arteritis of the uterus: case report and review. *Pathology* 1997; 29: 227-30.
10. GIL H, CHIROUZE C, MAGJ N *et al*.: Arterité gigantocellulaire de l'ovaire: une localisation rare de la maladie de Horton. *Rev Méd Interne* 1999; 20: 825-6.
11. ORBO A, STEFFENSEN A: Endometrial cancer, vasculitis of the genital tract and occult temporal arteritis. *Histopathology* 2001; 38: 178-9.
12. PACCALIN M, LE MOAL G, ROBLOT P: Giant cell arteritis of the female genital tract. *Ann Intern Med* 2001; 134: 626-7.
13. GANESAN R, FERRYMAN SR, MAIER L, ROLLASON T: Vasculitis of the female genital tract with clinicopathologic correlation: a study of 46 cases with follow-up. *Int J Gynecol Pathol* 2000; 19: 258-65.
14. PIURA B, WOLAK A, RABINOVICH A, YANAI-INBAR I: Giant cell arteritis of the female genital tract. *Clin Exp Obst & Gyn* 2004; XXXI: 31-33.
15. PATEL RK, CARRICK K: Giant cell arteritis of the female genital tract: report of a case and review of the literature. *South Med J* 2005; 98: 469-71.
16. SALVARANI C, CANTINI F, BOIARDI L, HUNDER GG: Polymyalgia rheumatica and giant-cell arteritis. *N Engl J Med* 2002; 347: 261-71.
17. BRACK A, MARTINEZ-TABOADA V, STANSON A, GORONZY JJ, WEYAND CM: Disease pattern in cranial and large-vessel giant cell arteritis. *Arthritis Rheum* 1999; 42: 311-17.
18. BLOCKMANS D, DE CEUNINCK L, VANDERSCHUEREN S, KNOCKAERT D, MORTELMANS L, BOBBAERS H: Repetitive 18-fluorodeoxyglucose positron emission tomography in giant cell arteritis: a prospective study in 35 patients. *Arthritis Rheum* 2006; 55: 131-7.
19. SALVARANI C, HUNDER GG: Giant cell arteritis with low erythrocyte sedimentation rate: frequency of occurrence in a population-based study. *Arthritis Rheum* 2001; 45: 140-6.
20. NUENNINGHOFF DM, HUNDER GG, CHRISTIANSON TJH, MCCLELLAND RL, MATTESON EL: Incidence and predictors of large-artery complication (aortic aneurysm, aortic dissection, and/or large-artery stenosis) in patients with giant cell arteritis. A population-based study over 50 years *Arthritis Rheum* 2003; 48: 3522-31.