CASE REPORTS

Giant cell arteritis of the female genital tract with temporal arteritis

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Abstract

The clinical and pathological features of a patient with giant cell arteritis of the uterus and ovaries are described. A 61 year old woman had fever and weight loss over a period of eight months. A hysterectomy with bilateral salpingo-oophorectomy was performed for a large cystic ovarian mass. Histological examination showed a benign ovarian cyst and unexpected giant cell arteritis affecting numerous small to medium sized arteries in the ovaries and myometrium. The diagnosis of temporal arteritis was confirmed by a random temporal artery biopsy, despite the absence of symptoms of temporal arteritis. This observation is compared with previously reported cases and the relation between granulomatous arteritis of the genital tract and temporal arteritis is discussed. The main differential diagnosis in this localisation was represented by Wegener's granulomatosis and periarteritis nodosa.

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Giant cell arteritis is a systemic vasculitis that primarily affects large and medium sized arteries. The most characteristic clinical features of giant cell arteritis are seen when the cranial arteries, particularly the temporal arteries, are affected. Occasionally, giant cell arteritis may affect the aorta and its branches,¹ but the pelvic arteries

are rarely affected by the inflammatory process.² Most examples of giant cell arteritis of the genital tract are incidental findings in samples removed during operations. We describe here the clinical and pathological features of giant cell arteritis, fortuitously discovered in the uterus and ovaries, and preceding the diagnosis of temporal arteritis which was proved by taking a biopsy sample. In view of similar cases reported previously, we discuss the relation between giant cell arteritis of the female genital tract, temporal arteritis, and polymyalgia rheumatica.

Case report

A 61 year old white woman was referred to us in January 1991 because of a fever of unknown origin and a five month history of declining general health. Her past medical history was not unusual. Menopause had occurred in 1980. She was in good health until five months earlier, when she consulted her doctor because of fever, major asthenia, anorexia, and weight loss. On admission, a physical examination was normal. Laboratory results were as follows: haemoglobin 103 g/l; white blood cell count $7.8 \times 10^9/l$ (60% neutrophils, 6% eosinophils, 30% lymphocytes, and 4% monocytes); erythrocyte sedimentation, 112 mm/hour; fibrinogen 9.14 g/l; haptoglobin 8.7 g/l; alkaline phosphatase 494 IU/l (normal range <220 IU/l). A chest radiograph was normal. An ultrasound examination of the abdomen and pelvis showed the presence of a cystic left ovarian mass, 8×9 cm, without evidence of intracystic vegetations. A computed tomographic scan of the pelvis disclosed a well circumscribed rounded mass of low attenuation, 10×10 cm, in the posterior and middle portion of the pelvis (fig 1). A left temporal artery biopsy sample was normal. A diagnosis of ovarian malignancy was suspected and a laparotomy was performed on 13 March 1991. The left ovarian mass was cystic, without adherence to the parietal peritoneum and uterus. The uterus and the right ovary appeared normal, and no other abnormalities were found. A bilateral salpingo-oophorectomy and hysterectomy were performed. Microscopic examination of the left ovarian mass showed it to be a benign cyst. The uterus presented several benign uterine leiomyomas. Extensive giant cell arteritis of the small to medium sized arteries was found unexpectedly in the uterus and both ovaries (figs 2 and 3).

Recovery after the operation was uneventful, and the patient progressively improved. One month after the hysterectomy, a biopsy sample

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Figure 1 Computed tomography scan of the abdomen and pelvis showing a well circumscribed rounded mass of low attenuation, 10×10 cm, in the posterior and middle portion of the pelvis.

Figure 2 Extensive giant cell arteritis of small to medium sized arteries of the ovarian hilus. Also seen are intimal fibrotic narrowing of the lumen and a dense granulomatous infiltrate with giant cells affecting part of the media and the adventitia. Haematoxylin-eosin stain.

Figure 3 Giant cell arteritis of the ovary. The media of this medium sized artery was infiltrated with lymphocytes, histiocytes, and giant cells, abutting against the fragmented internal elastic lamina. Haematoxylin-eosin stain.

from the right temporal artery was taken which showed the characteristic pathological features of giant cell arteritis. Treatment with prednisone (0.7 mg/kg daily) was then started.

Pathological findings

The removed uterus weighed 58 g and measured 10 cm in length. Three uterine leiomyomas, 1–2 cm in diameter, were found in the corpus. Examination of the left ovary disclosed a unilocular cyst measuring 10 cm in diameter and filled with a yellowish necrotic material. The cyst wall was smooth without papillations. No epithelial lining was found, and no precise diagnosis could be made for the ovarian benign cyst. The right ovary and fallopian tubes were normal.

The microscopic examination showed a widespread and active giant cell arteritis affecting numerous small to medium sized arteries of the uterus and ovaries. In most of the affected arteries, a dense inflammatory infiltrate, predominantly composed of lymphocytes, histiocytes and rare plasma cells, was seen mainly in the media, extending to the adventitia. The granulomatous inflammation was often focal, affecting a localised area of the media, but in some arteries the media was replaced circumferentially by granulomatous tissue. Multinucleated giant cells often abutted against the fragmented internal elastic lamina. Elastic tissue stains underlined the focal disruption and loss of elastic fibres. An intimal fibrosis resulted in luminal narrowing and thromboses were rarely seen. Fibrinoid necrosis was noted in a

Clinical and pathological features of 19 women with genital tract giant cell arteritis

Reference	Age (years)	Symptoms	Pelvic organs affected by giant cell arteritis	Temporal artery biopsy sample results	Treatment and follow up
7	82	Weakness, weight loss, polymyalgia rheumatica	Uterus	Not performed	Prednisone (30 mg/day); improvement (8 mo)
8		Weight loss, fever, metrorrhagia	Uterus, ovaries	Temporal arteritis	Prednisone; improvement
9	66	Shoulder pain, tiredness, vaginal spotting, prolapsed uterus	Uterus	Not performed	No treatment; improvement (one year)
	79	Prolapsed uterus	Uterus	Not performed	No treatment; improvement
10	66	Ovarian cyst, symptoms of temporal arteritis	Ovary	Temporal arteritis	Prednisone; improvement
11	78	Resection of a residual cervix, symptoms of temporal arteritis	Cervix		
12	61	Endometrial adenocarcinoma, polymyalgia rheumatica	Uterus, cervix ovaries, fallopian tubes	Not performed	Aspirin; improvement
13	76	Ovarian cyst, polymyalgia rheumatica	Uterus, ovaries, fallopian tubes		Prednisone; improvement
14		Polymyalgia rheumatica, cervical carcinoma	Ovaries, cervix, fallopian tubes, myometrium	No temporal arteritis	—
15	78	Fatigue, weight loss, fever, ovarian cyst (CT scan)*	Left ovary, mesosalpinx, fallopian tubes	Not performed	Prednisone (50 mg/day); improvement (one year)
	75	Polymyalgia rheumatica, benign leiomyoma of the uterus	Uterus, ovaries, fallopian tubes	Not performed	Prednisone; improvement (six years)
16	80	Fatigue, anaemia, weakness, ovarian cyst (CT scan)*	Ovarian cyst, ovaries, myometrium, fallopian tubes, cervix	Not performed	Prednisone (20 mg/day); improvement
17	64	Fatigue, lower abdominal mass, ovarian fibromas	Ovaries, fallopian tubes	Not performed	No treatment; improvement (17 years)
	57	Fever, weight loss, abdominal mass (left ovarian cyst)	Cyst wall, right ovary, fallopian tubes, mesosalpinx	Not performed	No treatment, dissecting aneurysm of aorta (seven years)
18	73	Prolapsed uterus and bleeding from cervical polyps, bilateral axillary arteritis (angiogram)	Myometrium	Not performed	Prednisolone (60 mg/day); improvement
19	68	Unexplained fever, left ovarian cyst (CT scan)*	Cervix, myometrium, ovaries, broad ligaments	Bilateral temporal arteritis	Prednisone (1 mg/kg daily); improvement
20	65	Polymyalgia rheumatica, abdominal pain, left ovarian cyst	Myometrium, parametrium, ovaries	Not performed	Prednisolone; improvement (one year)
21	69	Cystocele, postoperative fever, temporal pain	Myometrium	Temporal arteritis	—
This paper	61	Fever, fatigue, weight loss, ovarian cyst (CT scan)*	Uterus, ovaries	Temporal arteritis	Prednisone (0.7 mg/kg daily); improvement

*CT=computed tomography.

few affected myometrial arteries. Venules and veins were normal.

The temporal artery biopsy sample showed the same inflammatory changes, occurring mainly in the media, with multinucleated giant cells lying adjacent to the fragmented elastic internal lamina. These features are in agreement with the diagnosis of granulomatous and giant cell arteritis.

Discussion

These pathological findings led us to question the possible relation between granulomatous and giant cell arteritis of the uterus and ovaries, and temporal arteritis.

Giant cell arteritis, first described by Hutchinson³ and later by Horton *et al*,⁴ is a disease of the elderly that typically affects the cranial arteries. In 1946, however, Cooke *et al*⁵ described two patients with temporal granulomatous arteritis also affecting multiple medium and large sized arteries at necropsy.⁵ Since then, involvement of other extra cranial medium and large sized arteries has been described in four to 14% of patients with giant cell arteritis,^{1 2 6} supporting the idea that temporal arteritis and giant cell arteritis are manifestations of a systemic arterial disease.

Localisation of giant cell arteritis in the female genital tract has rarely been reported. The first case of giant cell arteritis affecting the cervix and corpus of the uterus was described by Polasky *et al* in an 82 year old woman with polymyalgia rheumatica.⁷ Including our patient, 19 cases⁷⁻²¹ have been reported and these are summarised in the table. All cases were postmenopausal women ranging in age from 57 to 82 years (average 70). None of the patients had pelvic symptoms that could be attributable to the vasculitis and, in most instances, the genital organs were removed for gynaecological lesions unrelated to giant cell arteritis. Nine of the 19 women had abnormal ovarian tissue: seven had simple cysts,^{10 13 16 17 19 20} one had a paratubal cyst,¹⁵ and one had ovarian fibromas.¹⁷ For the remaining women, hysterectomies were performed for benign or malignant uterine tumour,^{12 14 15 18} prolapsed uterus,^{7 9 18} incarcerated pessary,¹¹ and cystocele.²¹ The vascular lesions were incidental findings noted at microscopic examination. Most of the patients had systemic symptoms. Seven of the 19 patients had symptoms suggestive of polymyalgia rheumatica,^{7 8 12-15 20} and three patients had symptoms of temporal arteritis,^{10 11 21} but giant cell arteritis was never diagnosed before surgery. Seven patients,^{8 15-17 19} including the one reported here, were in deteriorating general health with minor⁸ or no gynaecological symptoms,^{15-17 19} and a hysterectomy was performed after the discovery of a uterine or ovarian mass to exclude malignancy. The absence of specific signs and symptoms of temporal arteritis is well known during giant cell arteritis and its onset can be insidious. In 30 of 74 patients with giant cell arteritis proved by taking a biopsy sample and reported by Healey and Wilske,²² the cardinal manifestations of temporal headache, blindness, or polymyalgia

rheumatica were absent. Twelve of these patients presented with fever, and like our patient, seven had a 'malignoid' syndrome of malaise, anorexia, low grade fever, weight loss and, in five patients, increased alkaline phosphatase. In a retrospective study of the histories of 100 patients with giant cell arteritis proved by taking a biopsy sample, Calamia and Hunder²³ described 15 patients who had fever of undetermined origin, in a similar manner to our patient. Other extragenital localisations of the giant cell arteritis were found in six patients. A temporal artery biopsy sample was taken six times following the finding of giant cell arteritis of the reproductive tract. In five instances, temporal arteritis was found,^{8 10 19 21} without any cranial symptoms in three cases.^{8 19} One had bilateral axillary artery stenosis which was seen on the angiogram,¹⁸ with clinical symptoms of ischaemia of the arms. In some cases,^{9 15-17} in the absence of symptoms of temporal arteritis or polymyalgia rheumatica, giant cell arteritis affecting the female genital tract may be limited to this area.

Treatment and follow up studies of patients with giant cell arteritis of the female genital tract have not been reported in detail. Ten of the previously described patients^{7 8 10 13 15 16 18-20} improved symptomatically after treatment with steroids. Four asymptomatic patients^{9 17} were not treated with steroids and did not develop systemic manifestations, even after a follow up of 17.5 years in one patient.

Pathologically, giant cell arteritis is characterised by an inflammatory granulomatous infiltrate of the arterial wall, fibrous intimal proliferation, and fragmentation of the internal elastic lamina often associated with multinucleated giant cells. Fibrinoid necrosis of the media is rare. Segments of the blood vessels are commonly affected. Histological examination of genital samples disclosed the same lesions, affecting predominantly the media of small to medium sized arteries. The organs affected in the vascular process were the uterus (13 patients), the ovaries (13 patients), the fallopian tubes (seven patients), and the cervix (four patients). Eight women had a benign adnexal cyst.^{10 13 15-17 19 20}

The differential diagnosis of genital giant cell arteritis includes rare patients with the genitals affected by other forms of vasculitis, namely Wegener's granulomatosis and polyarteritis nodosa.^{24 25} In addition to its distinctive clinical symptoms and types of vessels affected, giant cell arteritis differs from other necrotising and granulomatous vasculitides, by the presence of giant cells and the absence of vascular fibrinoid necrosis and eosinophilic infiltrates. In Wegener's granulomatosis, histological features include extensive necrosis and granulomatous inflammation affecting the arteries and the surrounding parenchyma. Polyarteritis nodosa typically shows prominent fibrinoid necrosis and a mixed inflammatory infiltrate, with eosinophils and no giant cells. In our patient the histological aspect of the ovarian and uterine vasculitis and the discovery of temporal arteritis provided solid arguments for the diagnosis of giant cell arteritis.

In most instances of female genital tract giant cell arteritis the presence of systemic manifestations and classical symptoms of polymyalgia rheumatica or temporal arteritis underlines the systemic nature of the vasculitis but, in some patients, the female genital tract may be the only area affected. Preoperative diagnosis of genital tract giant cell arteritis is difficult in the absence of specific morphological lesions. The discovery of giant cell arteritis in the genital tract led us to take a biopsy sample of the temporal artery to determine the extent of the vasculitis and the indications for systemic treatment.

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