A UNIQUE CASE OF OVARIAN MANIFESTATION OF SYSTEMIC VASCULITIS THAT MIMICS OVARIAN CANCER

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Abstract. Heading objectives: Granulomatosis with polyangiitis (GPA) is an antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) that may involve any organ. Rarely, clinical manifestation of inflammatory changes may resemble tumours, which, combined with untypical ovarian localization, may cause misdiagnosis and treatment delay. Case report: In this paper, we present the case of ovarian tumour-like lesion being the first manifestation of GPA and mimicking ovarian cancer. Conclusion: In case of a patient presenting with a tumour of untypical features, differential diagnosis should include inflammatory processes, including vasculitis. (Sarcoidosis Vasc Diffuse Lung Dis 2020; 37 (2): 179–183)

Key words: granulomatosis with polyangiitis, ovarian cancer, systemic vasculitis, Wegener’s granulomatosis

Introduction

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are a group of necrotizing systemic autoimmune diseases, affecting small-and medium-sized blood vessels, such as capillaries, arterioles and venules. As immune complex deposits within the inflammatory changes are scarce (or even absent), the process is commonly described as pauci-immune vasculitis. A number of predisposing factors (for example genetic or environmental factors, infections, drugs) can cause the production of autoantibodies active against myeloperoxidase (MPO-ANCAs) or proteinase 3 (PR3-ANCAs), both present in azurophilic granules of neutrophils. When neutrophils primed by proinflammatory cytokines are activated by interacting with ANCA, they tend to accumulate within the walls of the vessel, causing a number of inflammatory processes ended with the death of the cell, which causes injury of the surrounding tissue. Coagulation factors and serum proteins drawn to the injured epithelium cause fibrinoid necrosis (1).

AAV may involve any organ, such as the lungs, kidneys, gastrointestinal tract, brain, heart, skin, eyes, pancreas, liver, testicles or ovaries (1–5). Due to its many possible localizations and its pathogenesis, there’s a vast variety of signs and symptoms that may occur – from non-specific symptoms of inflammation (fever, weight loss, fatigue, anaemia), local organic damages (for example rashes, petechiae, purpura) to multi-organ involvement of often rapidly progressing course. The ACR/EULAR (American College of Rheumatology/ European League Against Rheumatism) 2017 provisional classification criteria for GPA include bloody nasal discharge, ulcers, crustling or sinonasal congestion, nasal polyps, hearing loss or reduction, cartilaginous involvement, red or painful eyes, C-ANCA or PR3-ANCA, eosinophilia, nodule, mass or cavitation on chest im-
aging and granuloma on biopsy (6). Typical findings include upper respiratory tract involvement and often renal disorder (1,4,7). Rarely, clinical manifestation of inflammatory changes may resemble tumours, which, combined with an untypical localization (for example within the reproductive system), can cause misdiagnosis and improper treatment (4).

**Case Presentation**

A 48-year-old woman was hospitalized due to severe pain in the lumbosacral region, hydronephrosis of the left kidney with dilation of the left ureter (abdominal part) caused by outside infiltration (CT and MRI were performed). During her stay at the urology ward, she had fever, increased CRP (C-reactive protein) (161 mg/l) and PCT (procalcitonin) (0,1 ug/ml). Both urine and blood culture examination were carried out and the results came back negative four times. Despite that, owing to the high CRP level, she was empirically treated with antibiotics, without any outcome. Blood pressure was normal. Renal parameters were gradually increasing but the function of the kidneys was preserved. The patient underwent gastroscopy, colonoscopy and non-contrast abdominal CT and some fluid in pleural, pericardial and abdominal cavity were found. Moreover, the CT revealed a large tumour (dimensions 34x27x51 mm with 5 mm calcification) possibly infiltrating the left internal obturator and iliopsoas muscle (as showed in Figure 1). The size and location of the tumour, together with ROMA (the Risk of Ovarian Malignancy Algorithm, using CA125 and HE4 concentration in patient’s serum) score of 96,7%, raised the suspicion of disseminated ovarian cancer and inclined the need for gynaecological consultation. Small erythrocyturia revealed in urinalysis was firstly associated with cancerous infiltration of the urinary tract.

Nephrostomy of the left kidney was performed with no urine outflow. Due to the lack of diuresis, primary renal diseases, rather than obstruction of the ureter, were investigated and, after a nephrological consultation, additional laboratory tests, such as MPO-ANCA and PR3-ANCA, were carried out. Due to acute kidney injury (increasing renal parameters: creatinine 5,99 mg/dl, urea 87 mg/dl), the patient was transferred to the Nephrology Clinic, where a haemodialysis catheter was placed. After haemodialysis, patient’s general state improved but

![Fig. 1. CT multiplanar reconstruction showing a tumour (34x27x51 mm with 5 mm calcification) suspected of being an ovarian cancer. The arrows point out the lesion](attachment:image.png)
kidney function wasn’t retrieved. Meanwhile, the patient underwent diagnostic laparoscopy with removal of left uterine appendages. Due to the size of the tumour, it came as a surprise that the peritoneum was intact and with no signs of infiltration.

The results of the laboratory tests came back three days after the surgery and both MPO and PR3-ANCA were found (32 IU/ml and > 200 IU/ml respectively), giving the diagnosis of vasculitis, suggesting GPA. Histopathological examination revealed the involvement of small vessels with necrotizing and granulomatous inflammatory infiltrate predominantly composed of neutrophils as well as lymphocytes and eosinophils and chronic purulent inflammation of the connective tissue surrounding iliac arteries and left ureter, inflammatory tumour of the left ovary with no sign on neoplasm within the uterine appendages, which confirmed the diagnosis of GPA.

Later, the patient complained of recurrent nasal bleeding and laryngological consultation was made. Nasal ulcer was found and then biopsy was performed. Histopathological examination’s result, combined with clinical symptoms revealed the progression of GPA. The patient was treated with 100mg/d oral cyclophosphamide and 3 x 1.0 g intravenous methylprednisone, followed by 40 mg/d oral prednisone. Due to hepatitis B in the past and unknown current level of viral DNA in serum, the patient was disqualified from rituximab treatment. Despite general state’s improvement, renal function wasn’t retrieved. The patient was haemodialyzed 3 times a week and treated with immunosuppressive drugs as above.

The patient was re-hospitalised due to anaemia (4.3 g/dl), haemoptysis and purpura on both lower legs. CT revealed diffuse alveolar haemorrhage (figures 2 and 3). She was given a high dose of cyclophosphamide and overwent seven plasmapheresis complicated by transient leukopenia treated with granulocyte colony stimulating agent (G-CSF). After the treatment, the patient was discharged from hospital in general good condition. After a year of haemodialysis, the patient successfully underwent a kidney transplant.

Fig. 2. CT multiplanar reconstruction showing diffuse alveolar haemorrhage in course of granulomatosis with polyangiitis.
To our best knowledge, no case of GPA with ovarian manifestation as a first symptom has ever been described. On admission, our patient presented with urinary retention and hydronephrosis with preserved renal function. Except for inflammation, there were no systemic signs. Moreover, hypertension, pulmonary changes or other symptoms that could point towards GPA were absent, which additionally delayed the diagnosis. Due to the tumour in the true pelvis, suspected to be a disseminated ovarian cancer (high ROMA, infiltration of the left ureter, muscles and vessels), as well as the lack of response to the antibiotics, the decision was made to operate and perform an intra-operative biopsy. The decrease in renal function, as well as the appearance of respiratory tract symptoms showed only after the resection was performed and thus began the diagnosis of AAV. Positive results of MPO-ANCA and PR3-ANCA, combined with the biopsy results (inflammatory tumour), confirmed the diagnosis of GPA.

Some cases of tumour-like lesions in the female reproductive system were reported in the course of other types of systemic vasculitis: polyarteritis nodosa, giant cell arteritis, EGPA (eosinophilic granulomatosis with polyangiitis) and Takayasu arteritis. In the course of GPA, lesions were observed in other organs but not in the ovary (4). Due to a high suspicion of malignancy, surgical treatment was also adopted but histopathological examination revealed vasculitis with no signs of malignancy in these cases.

Even though the ovary seems to be an extremely rare localisation of an inflammatory process in vasculitis, it is important to remember about it in differential diagnosis of an ovarian cancer, especially in cases of untypical course. In patients diagnosed with vasculitis (especially AAV with systemic symptoms), there is a high probability that observed lesions are non-malignant so in these cases investigation should be more insightful than usual due to a possibility of avoidance of unnecessary operation.

In case of a patient suffering from AAV and presenting with a tumour of rare localisation or untypical radiological features, differential diagnosis of cancer should also include inflammatory tumours. In such a case, the decision of further management, especially an operation, should be taken with caution, as sometimes biopsy of the affected organ could be considered. On the other hand, if the recognition of vasculitis is questionable or the disease gives symptoms in an isolated location, the risk of the cancer progression may be too high to postpone necessary investigations.

**Fig. 3.** Virtual reality 3D reconstruction from CT scan (presented on figure 2) showing diffuse alveolar haemorrhage in course of granulomatosis with polyangiitis.

(2,4,8–10).
treatment (resection of the lesion). Thus, treatment should be adjusted to the patient very carefully and both overall risk and patient’s quality of life have to be considered.

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