Ormond's disease accompanied by ankylosing spondylitis – a case report

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ABSTRACT

Idiopathic retroperitoneal fibrosis, or Ormond's disease, is a rare syndrome which is in essence the deposition of pathological fibrous tissue in the retroperitoneal space. In most cases, it is initially asymptomatic, but as the disease progresses, clinical symptoms develop. The main complaint are abdominal pain and symptoms resulting from the involvement of ureters, arterial and venous vessels. Diagnosis is based on computed tomography or magnetic resonance imaging, demonstrating a fibrotic tissue mass accumulated in the retroperitoneal space. Due to the typically late presentation of clinical symptoms, a diagnosis is difficult and is often made after complications occur. In our article, we present the case of a 71-year-old patient in whom coexisting ankylosing spondylitis and retroperitoneal fibrosis were diagnosed 15 years after non-specific abdominal pain occurred.
Keywords: retroperitoneal fibrosis; Ormond's disease; ankylosing spondylitis.

INTRODUCTION

Idiopathic retroperitoneal fibrosis, or Ormond's disease is a rare syndrome of unclear etiology. It is characterized by deposition of fibrous tissue in the retroperitoneal space with a tendency to involve aorta, vena cava and ureters and exertion of extraneous pressure on these structures, with 15% of cases involve the pelvis, mediastinum or duodenum [1].

According to a study conducted in Finland, the incidence of Ormond's disease was estimated at 1 case in 1 million people [2]. The 1st description of retroperitoneal fibrosis was made in 1905 by Joaquin Albarán, a Cuban urologist practicing in France. A detailed description of the disorder was made as late as 1948 by John Kelso Ormond.

About 90% of cases are asymptomatic in the early stages of the disease. In a clinical picture, abdominal and lumbar pain are dominant features. Pain is usually described as ceaseless, non-colic and irrespective of the position of the body, or urination and defecation. Symptoms of venous drainage deficiency like swelling of the lower limbs or deep vein thrombosis may also be found, as well as symptoms of the involvement of arteries, such as intermittent claudication, or symptoms of bowel ischemia. The most characteristic, however, are symptoms of the involvement of ureters, such as hydronephrosis, leading to renal insufficiency in advanced cases. Less characteristic symptoms include a loss of weight, exertion intolerance, chronic fatigue or mildly raised body temperature [3]. The first symptoms usually occur 50–60 years of age. Women are 2–3 times more frequently affected than men.

Clinical literature on the subject strongly points out a possible coincidence of retroperitoneal fibrosis with other diseases and clinical states such as:

- autoimmune diseases (IgG-4 dependent, thyroid gland dysfunctions – Hashimoto disease, primary biliary cholangitis, primary sclerosing cholangitis, vasculatis, rheumatoid arthritis, idiopathic juvenile arthritis, ankylosing spondylitis),
- hematological and oncological disorders (Hodgkin's lymphoma, non-Hodgkin's lymphomas, sarcomas, large bowel carcinomas, prostate cancer, breast cancer),
- after radiotherapy in rectal or testis cancer,
- after various operations like lymphadenectomy, colectomy or hysterectomy,
- during therapy with certain drugs (bromocryptine, ergotamine, methylodope or B-blockers) [4].

There is still an ongoing debate whether the aforementioned conditions are predisposing factors to retroperitoneal fibrosis or only accompanying conditions.

It is estimated that $2/3$ of cases are idiopathic and $1/3$ is related to other medical conditions. Recently there have been many reports on the coexistence of retroperitoneal fibrosis with IgG dependent diseases [5]. To date, there has been no clear clinical diagnostic criteria established for Ormond's disease.

The fundamental feature and cornerstone for eventual diagnosis is the presence of a pathological mass in the retroperitoneal space found by computed tomography (CT) or magnetic resonance imaging (MRI). Both methods permit identification of pathological tissue and assessment of systemic involvement.

Ultrasonography is less sensitive and accurate, but at the same time less invasive and cheaper, and is used in follow ups of the disease rather than in its final diagnosis [1].

If possible, treatment should be focused on possible causative conditions: inflammation or cancer. Glucocorticosteroids (GKS),

by inhibition of inflammatory responses, decrease synthesis of collagen and are the mainstay of general treatment. Unfortunately, in some cases, GKS are ineffective. In such situations immunosuppression with azathioprine or cyclophosphamide, cyclosporine, methotrexate or mycophenolate mofetil is incorporated into therapy.

CASE REPORT

A 71-year-old female patient was admitted to our Clinic of Rheumatology in March 2015. She had suffered for the last 15 years from constant abdominal pain, usually in the morning but also throughout the day. This had ben accompanied for the past few years by lower back pain. The patient also reported progressive exertion intolerance and fatigue. In 2014 she was diagnosed with myocardial infarction, and so had undergone angioplasty. She was also diagnosed with ankylosing spondylitis, based on New York criteria.

Previously, in 2012, the patient was diagnosed at the Clinic of Rheumatology and Internal Medicine UMW in Wrocław with lower-back pain which she had suffered for years. The pain tended to increase after physical exertion irrespective of the time of day. For years the patient's laboratory tests had shown increasing inflammation indicators and anemia. At the time of admittance, a reduction in lower spine mobility was observed, based on the Otto–Schobers test.

Detailed laboratory tests revealed microcytic anemia, increased serum levels of inflammatory markers: erythrocyte sedimentation rate (ESR) 129 mm, C-reactive protein (CRP) 112 mg/L, a decreased iron and increased serum ferritin: Fe 49 ug/dL, unsaturated iron binding capacity (UIBC) 217 ug/L, total iron binding capacity (TIBC) 266 ug/dL, ferritin 437 ug/L.

Serum levels of alkaline phosphatase and γ-glutamyl traspeptidase were increased, while aminotransferases and bilirubin, creatinine levels and glomerular filtration rate were normal. Serum protein electrophoresis showed hypoalbuminemia and hypergammaglobulinemia, but total serum protein level was normal.

Immunoelectrophoretic analysis revealed increased IgG levels 18.67 g/L and normal levels of IgA (4.15 g/L) and IgM 2.32 g/L. Immunofixation blood and urine testing did not detect mononucleal antibodies or globulins. Serum levels of electrolytes, parathormone, procalcitonin and tumor markers (CEA, CA 19-9, CA-15.3, CA 125) were normal. Indirect immunofluorescence testing detected antinuclear antibodies with a homogenic type of fluorescence and a 1:1000 titre. There were no other specific antibodies detected. A Quantiferon test was positive, but urine and speculum tests for tuberculosis proved negative. There were no pathologies observed on a plain chest x-ray. Human leucocyte antigens (HLA) B27 antigen was absent and a bone marrow myelogram did not show any significant abnormalities besides hypercellularity.

Abdominal ultrasound revealed retention in the pelvicalyceal systems of both kidneys. The retroperitoneal space was only partially visualized and in the inspected areas no enlarged lymph nodes were found.

Pelvis radiograph demonstrated partial ankylosis of the sacroiliac joints. A radiograph of the sacrolumbar spine showed intervertebral ankylosing spondylitis, massive calcifications in longitudinal ligaments, decreased bone radiodensity, and calcified syndesmophytes C5–C7.

Computed tomography of the sacrolumbar spine revealed advanced osteosclerotic changes in L2–S2 vertebrae, numerous foci of osteolysis and severe destruction of the bone structure. Additionally massive calcifications in anterior spinal ligaments and calcified syndesmophytes spanning intervertebral spaces were found. Differential diagnosis included atypical ankylosing spondylitis, atypical inflammatory changes of the spine of unknown etiology and osteolytic-osteosclerotic changes of metastatic nature.

Magnetic resonance images of the sacrolumbar spine exposed incomplete vertebral blocks, significantly diminished height of intervertebral discs and ossification of longitudinal ligaments. Vertebral bodies L3–L5 had a square-like appearance. Bone remodeling was observed with fatty deposits. Osteolytic foci which were previously depicted in CT scans within L3 and L4 vertebra were filled with fatty tissue. Magnetic resonance images confirmed partial ankylosis of both sacroiliac joints. A biopsy of the lumbar vertebra was performed but it did not demonstrate any atypical cells.

Computed tomography examination of the abdomen and pelvis demonstrated unclear margins of the aorta (Fig. 1) and common iliac arteries (Fig. 2) with increased radiodensity of fatty tissue in the retroperitoneal space, which probably corresponded with the inflammatory process. Dilation of both kidney renal collecting systems was confirmed. Ureters were also found to be widened and tortuous to the level of the iliac vessels, where they became rapidly narrow and eventually completely indistinguishable from inflammatory tissues on their way through the retroperitoneal space of the pelvis.

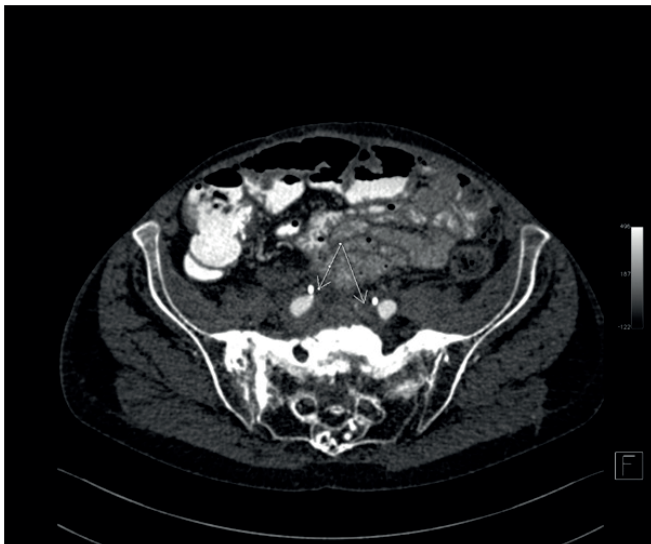**FIGURE 1.** Pathological tissue accumulated around the aorta

FIGURE 2. Pathological tissue accumulated around the common iliac arteries

Magnetic resonance imaging of the pelvis was also performed. It revealed as follows: "chronic, active inflammatory process of the right sacroiliac joint together with multiple erosions and bone marrow edema. Almost complete ankylosis of the left sacroiliac joint" and "soft-tissue infiltrates in the presacral space up to 1.3 cm thick. Higher up, around the aorta, and without a clear cut-off, these changes gradually become less distinctive". Collective systems of both kidneys and 1st parts of both ureters were significantly dilated.

Urography demonstrated enlargement of both kidneys. Bilateral significant dilation of the collective renal systems and ureters was confirmed: right ureter 1.9 cm in diameter, left 1 cm in diameter. Ureters were visible only to the level of the iliac crests. After 1 h only a trace of the contrasting agent was visible in the urinary bladder. The consulting urologist confirmed bilateral obstructive uropathy and suspicion of retroperitoneal fibrosis. The introduction of double J catheters was proposed, but was ineffective as a firm obstruction during propagation up the ureters was encountered about 10 cm from the bladder. The patient refused an attempt to relieve the renal collecting systems by probing the ureters during ureteroscopy. She also refused establishing a bilateral nephrostomy.

Densitometry of the proximal femur demonstrated a total T-score of 3.5 and a 54% reduction in bone density.

Additionally, the patient had been operated 2 times. First in 2000 when an exploratory laparotomy was undertaken. Extensive adhesions that were found were deemed to be the consequence of a previous acute appendicitis. This condition had been treated nonoperatively due to the lack of consent from the patient for operative intervention. Surgical management included release of the adhesions and appendectomy. In 2003 she was again operated on due to adhesive obstruction of the small bowel. During this intervention 80 cm of small bowel was removed.

In the UMW Clinic of Rheumatology and Internal Medicine, the patient was eventually diagnosed with axial

spondyloarthropaty, Ormond's disease and osteoporosis. Hitherto, the patient was treated with mesalazine, trimebutine, paracetamol, tramadol, pantoprazol, ibandronic acid and cholecalciferol. After introduction of metyloprednizolon at 24 mg/d and methotrexate at 15 mg/d together with folic acid, the general condition of the patient gradually improved and the lower back pain subsided. Continuous treatment with decreasing doses of GKS was planned for the next 12–24 months. Suppression of the immune response with methotrexate aimed at optimizing the GKS dosage and recurrence risk reduction. The patient failed to comply with the follow-up treatment and decided to stop taking the prescribed medication after a few months. In 2014, due to severe hydronephrosis introduction of double J catheters was necessary.

During hospitalization in the Clinic of Rheumatology of Pomeranian Medical University in Szczecin, normocytic normochromic anemia (Hgb 10.5 g/dL; Hct 33%), moderate leukocytosis with elevated levels of neutrophils (WBC 10.84; NEU 6.8) and an elevated concentration of inflammatory markers (CRP 17.03; ESR 69) were found. Moreover, urinalysis demonstrated the presence of fresh blood (10–20 erytrocytes per field of view) and dysmorphic erythrocytes (20–30 per field of view). Proteinuria at 0.77 g/24 h was discovered. Plasma levels of both creatinine and urea were slightly elevated (1.14 mg/dL; 55 mg/dL). Glomerular filtrate rate (GFR) was estimated at 50.16 mL/min/1.73 m^2. Serology analysis confirmed the presence of antinuclear antibodies with a homogenic type of fluorescence at 1:1 280 titre. There were no changes observed in the antinuclear antibodies profile.

Another CT examination of the abdomen and pelvis described the presence of the double J catheters (Fig. 3). The right kidney was slightly enlarged to 142 mm in the long axis. The left kidney had normal diameters (116 mm in long axis). There were small, up to 5 mm in diameter, hypodense foci in both kidney cortices. Severe hydronephrosis was confirmed in both kidneys. The renal pelvises looked bulbous and were up to 35 mm in diameter in the left kidney, and up to 41 mm in diameter in the right kidney. Calices were symmetrically widened up to 26 mm. Renal function was severely impaired in the left kidney – only traces of contrast shadowing were visible in delayed phase of enhancement. Still, output of the right kidney seemed adequate. Ureters were bilaterally distended up to 19 mm proximally for 6.5 cm and gradually becoming narrow as they travelled down. In the retroperitoneal space pathological fibrous tissue was visualized from the level of vertebra L4 down to the common iliac arteries. It completely surrounded the aorta, inferior vena cava and ureters. This pathological tissue of 30 Hounsfield Units in non-enhanced phase, gradually enhanced up to the level of 70–80 Hounsfield Units in the late phase.

The CT scans of the tissue suggested a fibrous character. Pathological tissue impinged on and distorted the inferior vena cava. The right iliac artery was constricted within pathological fibrotic tissue. The left iliac artery could be traced from the periphery in the cephalad direction up to level vL5,
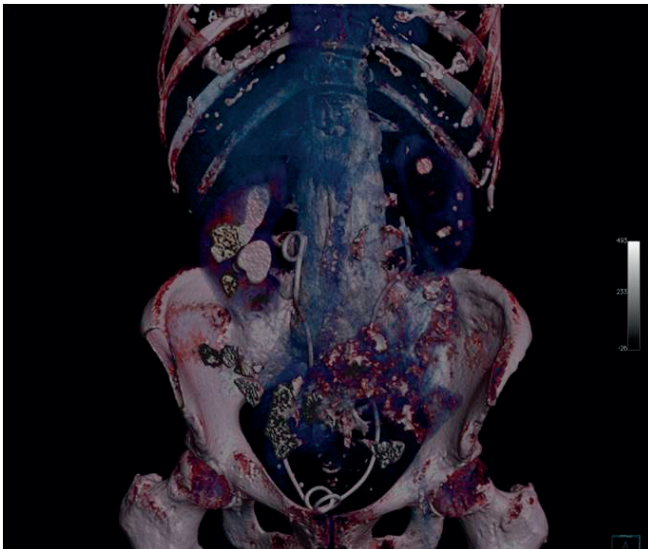
FIGURE 3. Location of D–J catheters

where it disappeared within fibrous infiltration. Veins of the lesser pelvis were tortuous and distended up to 10 mm. Ovarian veins were bilaterally distended up to 21 mm along their whole lengths. Parietal atherosclerotic changes in the abdominal aorta were found. Intervertebral osseous blocks involving intervertebral spaces, joints and spinous processes from level vL2 down to vS2 were present. Both sacroiliac joints were narrowed with incomplete ankylosis on the left side.

Bone structure of the sacrolumbar spine demonstrated irregular hyperdense foci (sclerotization) with the presence of numerous irregular foci of destroyed bone structure. Similar changes were observed around the sacroiliac joints. Radiological findings strongly suggested ankylosing spondylitis. Additionally osteophytes of vertebral bodies and occasional Schmorl's nodules were noticed.

Based on the clinical picture, laboratory tests and radiological findings, idiopathic retroperitoneal fibrosis and ankylosing spondylitis were diagnosed, although only after severe hydronephrosis developed requiring introduction of the double J catheters.

The patient was qualified for repetitive treatment with intravenous boluses of methylpredisolone and prednisone given daily in 15 mg doses. Unfortunately, at present the condition of the patient remains unknown as she failed to comply with the follow-up treatment and assessment at our ambulatory.

DISCUSSION

The diagnosis of idiopathic retroperitoneal fibrosis may be difficult as the initial symptoms are non-specific. Laboratory tests may also present a variety of abnormalities. Most commonly, elevation of inflammatory markers are noted. Both prolonged inflammation and renal insufficiency may result with normocytic anemia which is also frequently observed.

Impaired renal function parameters like lowered GFR, elevated plasma concentrations of urea and creatinine may also be present. At times erythrocyturia and proteinuria are seen. Roughly 60% of cases demonstrate the presence of anti-nuclear antibodies. Anti-smooth muscle antibodies, anti-thyroperoxidase antibodies, anti-thyroglobulin antibodies and anti-neutrophil cytoplasmic antibodies may also be detected [4].

The diagnosis is mainly based on CT or MRI scans, exposing a pathological fibrous mass in the retroperitoneal space. These diagnostic modalities provide a detailed description of the pathological tissue and involvement of the surrounding organs. Ultrasonography is less sensitive and accurate, but at the same time less invasive and cheaper, and is used in follow ups of the disease rather than in its final diagnosis. In dubious cases, PET or sampling of the abnormal tissue for histopathological verification may be useful [1, 4].

Treatment of Ormond's disease is focused on ceasing the deposition of fibrotic tissue, relieving compressed structures, decreasing systemic inflammatory response, and preventing recurrence. Most commonly GKS are used to impede cytokine production, diminish inflammatory response, and slow down the synthesis and maturation of collagen.

In most cases, prednisone at 0.5–1 mg/kg/day for 4 weeks with a gradual reduction to 10–15 mg within the following 3–4 months effectively reduces the pathological fibrous mass and symptoms. In recalcitrant cases cytostatic drugs are included in the treatment plan. Most commonly utilized are azathioprine, cyclophosphamide, methotrexate, cyclosporine and mycophenolate mofetil. Unfortunately, we still lack prospective randomized trials that would compare the effectiveness of these drugs in the treatment of idiopathic retroperitoneal fibrosis. Also, there are no clear guidelines on how long the treatment should be continued. Most authors state that treatment should be continued for at least several months up to 3 years.

Although in most cases remission is obtained, recurrence is frequent and observed in 50–70% of patients. There are incidental reports on successful treatment with TNF-α inhibitors, rituximab and tocilizumab [6].

Hydronephrosis is the most common of the severe consequences of retroperitoneal fibrosis. It is estimated that 75% of patients demonstrate impaired renal function at the time of diagnosis. Interventional treatment of the urinary obstruction is a very important aspect of treatment. Typically, double J catheters are introduced into the ureters to facilitate urine flow into the bladder. In extreme cases ureterolisis (freeing the ureters from constricting fibrotic tissue) or nephrostomy may be indicated.

There are only sporadic reports of Ormond's disease coexisting with ankylosing spondylitis [7, 8, 9, 10, 11]. Mostly these are focused on males with axial spondyloarthropathy. Because lower-back pain is a common symptom of Ormond's disease, retroperitoneal fibrosis must be included in the differential diagnosis. A possible causative relation between Ormond's disease and ankylosing spondylitis remains unclear. Spondyloarthropathy usually precedes the symptoms of retroperitoneal fibrosis, suggesting its propitious role in the development of

Ormond's disease. There is still no proven correlation between antigen HLA-B27 and a predisposition to retroperitoneal fibrosis. There is also insufficient data on the involvement of the sacroiliac joints in the course of Ormond's disease. Due to the scarcity of case reports on the coexistence of spondyloarthropathy and retroperitoneal fibrosis, it is only possible to conclude that this is a coincidence, and no predisposition for the development of retroperitoneal fibrosis can be proven in patients with spondyloarthropathies. If the inflammation predisposed retroperitoneal fibrosis it would be prudent to assume that more of reports should exist on the coincidence of rheumatoid arthritis and Ormond's disease. It is also possible that the extremely low incidence of retroperitoneal fibrosis results from the high frequency of administering GKS and disease-modifying drugs.

CONCLUSIONS

In diagnostics and treatment the possibility of a coexistence of various disorders should always be taken into consideration. Strict follow up and adjustment of the treatment to the disease activity are of paramount importance both in dealing with spondyloarthropathy and retroperitoneal fibrosis.

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