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CASE REPORT

Retroperitoneal Fibrosis Secondary to Different Etiologies (Hemilaminectomy and Hypothyroidism): Reports of Two Cases

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Retroperitoneal fibrosis (RF) is a clinical entity characterized by the progressive proliferation of connective tissue that rarely forms a mass involving the periaortic area of the abdomen, which may be idiopathic as well as a result of an inflammatory process after aneurysmal dilatation of the aorta.[1] This fibrotic tissue may cover both aorta and iliac arteries, reach the retroperitoneum and surrounding ureters, and cause serious obstructions and renal insufficiency in three-quarters of patients.[2] Most of the patients are known to have atherosclerosis and local inflammation against the antigens of the plaques.[3] A systemic autoimmune disease presenting with retroperitoneal fibrosis seems to be pronounced more frequently nowadays because of the elevated acute-phase reactant levels, positive autoantibodies, and concurrent autoimmune diseases affecting other organs in majority of the diagnosed patients.[4,5] Ultrasonography, computed tomography, magnetic resonance imaging, positron emission tomography, and retroperitoneal biopsy are useful in diagnosing and assessing the full extent of the disease.[6] Surgical interventions such as ureterolysis and aneurysm repair are frequently performed, but medical therapy including steroids and immunosuppressants is often needed because of the inflammatory and chronic-relapsing nature of the disease.[7]

In this paper, we described two cases diagnosed with RF secondary to hemilaminectomy and hypothyroidism, and we summarized the literature related to RF.

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CASE ONE

A 54-year-old male patient was referred to the nephrology clinic because of the suspicious diagnosis of RF according to his abdominal CT scan. He complained from a colicky pain in his flank and lower abdomen, reflecting the inguinal area, which has been resistant to analgesics for six months. He was known to be diabetic for six months and had irritable bowel disease diagnosed ten years ago. He was taking oral antidiabetics, prokinetic, and spasmolytic drugs. He was operated twice, five years and five months ago, because of disc herniation of lumbar vertebrae, and a hemilaminectomy was performed. He was not taking any alcohol, intravenous drugs, or ergots. He had no tuberculosis, arthralgia, or allergic diseases. His sister and mother were also diabetic, but there was no evidence of RF or any similar fibrotic or rheumatic diseases in his family. There were not any abnormalities except pallor in his physical examination. His vital signs were within normal ranges. The results of his complete blood count were: hemoglobin, 10.5 gr/dL; hematocrit, 32.2%; mean corpuscular volume, 80.2 fl; white blood cell count, 5900/mm^3 (52% granulocyte, 48% lymphocyte); and platelet count, 265.000/mm^3. Mild hypochromia and anisocytosis with no atypical cells were found in his peripheric blood smear. His erythrocyte sedimentation rate was 57 mm/hour. His renal and liver functions were within normal limits. Tests for antinuclear antibody and rheumatoid factor were negative. He had bilateral hydroureters without any mass or nephrolithiasis seen in his abdominal ultrasonography. His abdominal CT scan revealed a soft tissue mass, in 2 cm width, originating from and circulating

the middle part of the ureters, which is followed by abdominal aorta; yet his aortography was normal. The specimen taken from the mass by open biopsy was reported as fibrosis and inflammation, suggesting retroperitoneal fibrosis. He was started methyl prednisolone, 1 mg/kg, and followed up until quitting his periodic visits.

CASE TWO

A 51-year-old female was hospitalized because of acute renal failure (ARF). Her complaints were a decrease in urine output and abdominal pain. She was oliguric. Her abdominal ultrasonography revealed bilateral hydroureters; no mass or lithiasis existed. She underwent the process of ureteral catheterization bilaterally. After the catheterization, her elevated BUN and creatinine decreased and returned to normal values. When the catheters were taken out, renal functions regressed and BUN and creatinine levels rose again. The result was the same after the replacement of the catheters with the suspicion of extra ureteric compression. An abdominal CT scan was performed, the radiologic diagnosis was RF, and the patient underwent an operation. Ureterolysis could not be accomplished, so the periureteral mass was removed with left nephrectomy and splenectomy because of the strictures. The pathological examination showed chronic atrophic kidney and fibrotic periureteral mass, both of which were matched with RF. She was known to have hypothyroidism without any regular therapy for thirty years, and she had an internal cardiac pacemaker that was placed for complete A-V blocking in the past. She was started on thyroxine, and following the operation, her renal functions became normal again. On the fifteenth day of the operation, after being discharged, she was admitted, again complaining of nausea, vomiting, and yellowish skin colour. Acute hepatitis was diagnosed. Her tests revealed elevated liver enzymes and TSH. Renal functions were still normal. Ascites and hepatomegaly were shown by ultrasonography. She became confused and her serum ammonia levels elevated. The most likely diagnosis was toxic hepatitis because she was negative for viral markers. Despite supportive care, hepatic encephalopathy became obvious, and she died on the thirteenth day of this second hospitalization. Unfortunately, her family refused autopsy.

Retroperitoneal fibrosis was first reported by a French urologist named Albarran[8] in 1905. In 1948, an English practitioner named Ormond described and established it as a clinical entity, and it was named "Ormond's Disease."[9] The term *idiopatic retroperitoneal fibrosis* has been used until its course secondary to advanced atherosclerosis and its autoimmune pattern were also determined.[6] Since then, approximately 800 patients were reported with pathologic diagnoses of periureteritis fibrosa, periureteritis plastica, chronic periureteritis, sclerosing retroperitoneal granuloma, fibrous retroperitonitis, chronic periaortitis, and auto-allergic periaortitis. Mitchinson and Parums are the ones who first defined chronic periaortitis as a range of the diseases that includes idiopathic retroperitoneal fibrosis.[3] Nowadays, RF and associating pathologies are being pronounced as a synonym of a newly-named disease, "Hyper-IgG4 Disease," for containing IgG4-expressing plasma cells in the fibrotic tissue as well as elevated serum IgG levels of the same patients.[10,11]

There are no clear data established on the subject to determine epidemiological characteristics of the disease. Idiopathic retroperitoneal fibrosis is said to have an incidence of 0.1 per 100,000 person-years and a prevalence of 1.38 per 100,000 inhabitants according to a study reported from Finland.[12] It is most commonly seen in adults who are 40–60 years old, and men are affected twice or three times as often as women.[13] Children having the disease are also reported—23 cases in the English-language literature by 2003.[14] Atherosclerosis was considered to be the reason of the predominance of male sex. Genetic transition was reported, with cases diagnosed in twins and siblings. A family, two children with idiopathic retroperitoneal fibrosis and their father, showed evidence of systemic immunological diseases.[10,15] Two brothers, sons of a couple who were cousins, had different combinations of RF, mediastinal fibrosis, sclerosing cholangitis, Riedel thyroiditis, and orbital pseudotumor. Seronegative spondyloarthropathy together with mediastinal and retroperitoneal fibrosis in two sisters and RF in three siblings with sickle cell trait are other reports of concurrent involvements of the disease in family members.[10,16,17] No ethnic habit was determined.

The pathogenesis of the disease is still unknown. According to Mitchinson and Parums' hypothesis, serum antibodies to oxidized low-density lipoprotein (LDL) and ceroid (a lipoprotein polymer that results from LDL oxidation within plaque macrophages, which can also be artificially obtained by the oxidation of LDL) formed in the atheromatous plaque may cause the disease.[3] These lipids are normally sequestered spontaneously if media are intact and may cause an auto-allergic reaction when aortic media are thinned or breached. Plaque macrophages are supposed to present these oxidized lipids to T and B lymphocytes, which triggers an inflammatory response that causes an inflammation in the media and adventitia of the aortic wall. In doing so, aortic atherosclerosis transforms to fibrosis following medial thinning and adventitial and periaortic inflammation stages. Patients diagnosed as idiopathic retroperitoneal fibrosis often have raised concentrations of acute-phase reactants, positive autoantibodies, and autoimmune diseases of other organs.[4,5,7,18] The

inflammatory nature of the disease was supported by the presence of elevated ESR and CRP, reduced hemoglobin, and elevated gammaglobulin. ANA positivity in 10–20% of cases and good response to glucocorticoids support its autoimmune nature.[18] Idiopathic retroperitoneal fibrosis seems to be a manifestation of a systemic autoimmune disease in such situations rather than a local reaction to atherosclerosis. The vascular inflammatory process also involves the thoracic aorta and its branches in some patients with idiopathic retroperitoneal fibrosis, as noted in giant-cell arteritis and Takayasu's arteritis. Its similarity to systemic large-vessel vasculitides also supports the presence of a systemic disease.[19]

RF has been suggested as the most severe form of chronic periaortitis, because both inflammatory aneurysmal dilatation of the abdominal aorta and RF were almost the same pathology, except the diameter of the inflamed aorta.[10,19–21]

The pathogenesis of the disease seems to be multifactorial, and genetic transition is not a strongly advocated hypothesis. However, the high frequency of the existence of HLA-DRB1*03 allele in patients gives an idea about the genetic predisposition of the disease as it is also commonly seen in type 1 diabetes mellitus, myasthenia gravis, and systemic lupus erythematosus.[22,23] The similarities to systemic large-vessel vasculitides in some patients with idiopathic retroperitoneal fibrosis support the systemic disease idea.[24] The vascular inflammatory process involves abdominal aorta, common iliac arteries, and the thoracic aorta and its branches, as it is in giant-cell arteritis and Takayasu's arteritis.[24,25] Aortic adventitial inflammation seen in other large vessel vasculitis can be proved by histological examination. Vasculitis of the adventitial aortic vasa vasorum and periaortic small vessels is also a frequent finding in idiopathic retroperitoneal fibrosis that can initiate aneurysm formation by medial thinning of the aorta.[26] As is seen in chronic periaortitis, this fibrotic and inflammatory process seems to promote the formation of a mass in the retroperitoneum.

Another pathogenetic hypothesis is its being a primary B-cell disorder, as biopsies of the affected patients revealed the presence of IgG4-bearing plasma cells and clonal and oligoclonal immunoglobulin heavy chain rearrangement of these B-cells. In one UK study that started with an index case diagnosed as RF but first falsely as tuberculosis that benefited from steroid therapy, biopsy specimens of the patients diagnosed as RF in the last ten years were reevaluated for IgG4 presence.[10] It was seen that there was a significant increase in IgG4-positive plasma cells compared with control groups. The investigators had reviewed the literature to point out disease associations with idiopathic, systemic fibrosing conditions, and diagnoses of pseudotumor, myofibroblastic tumor, plasma cell granuloma, systemic fibrosis, xantofibrogranulomatosis, and multifocal fibrosis. They reached a long list of diseases that were named differently because they involved a wide spectrum of different organs and systems, and although pathology appeared confined to one organ, patients could have systemic symptoms and fever. They also found out that there was an acute phase response with a high serum concentration of IgG in the active period, and glucocorticoid steroid treatment results in a rapid clinical response during this phase. Again, these are the proof of its being a systemic disease.

The last possible cause is the environmental factors, such as exposure to asbestos, which increases both pleural and idiopathic retroperitoneal fibrosis.[12]

Two-thirds of the disease is idiopathic.[27] The secondary forms of retroperitoneal fibrosis due to different causes are well defined. Beta-blockers, hydralazine, ergot alkaloids, methysergide, ergotamine, analgesics, aspirin, phenacetin, dopamine agonists, pergolide, and methyldopa are the drugs most commonly blamed as a cause in the pathogenesis.[19,28–32] Methysergide and some other ergot derivatives can cause fibrotic reactions in the retroperitoneum, pericardium, pleura, and the lungs. In most cases, malignant diseases and their metastases are the initial pathology. Carcinomas of prostate, stomach, colon, or breast; primary tumors of the retroperitoneum; sarcomas; and Hodgkin's and non-Hodgkin lymphomas are commonly seen and cause the disease.[5,6,33] Serotonin and profibrogenic growth factors such as epidermal growth factor, insulin-like growth factors, and platelet-derived growth factor released from carcinoids may initiate the process.[34] Infections affecting retroperitoneum by spinal and paraspinal abscesses, as in tuberculosis, or histoplasmosis and actinomycosis may also cause this fibrotic tissue. In irradiated patients, focal fibrotic mass occurs in the radiation area because of the sclerose.[35,36] Trauma, amyloidosis, barium enema, and major abdominal surgery are the other uncommon causes of the disease.[19]

The disease is recognized with its typical macroscopic appearance: a white, hard mass in varying size, surrounding the abdominal aorta, the iliac vessels, the inferior vena cava, and the ureters.[19] It usually originates from the renal arteries and the pelvic brim. In some cases, it may extend to the spinal cord, mesenteric arteries, and presacral area.

The microscopic appearance is described as a sclerotic tissue infiltrated by mononuclear cells.[19] In the early stage of the disease, the tissue is vascular, oedematosus, and there is active chronic inflammation consisting of mononuclear cells within fibroblasts and collagen bundles.

Later stages show sclerosis and calcifications. The inflammatory infiltrate consists of lymphocytes, macrophages, plasma cells, and eosinophils, but not neutrophils.[5,19]

The fibrous tissue often has a perivascular or perineural disposition. Granulomas are uncommon. Several spindle-shaped, fibroblast-like cells are present. Atherosclerotic degeneration of the intima, medial thinning, and adventitial inflammation are seen as the aortic wall changes. The inflammatory infiltrate is diffuse or nodular, and often centred on adventitial vasa vasorum, which can show necrotizing vasculitis. Aortic wall inflammation has been shown in the thoracic aorta, and this supports that aortitis can precede idiopathic retroperitoneal fibrosis.[37] When it is secondary to a malignant disease, retroperitoneal fibrosis is more irregularly shaped and localization is more atypic than it is in idiopathic one.[31] Neoplastic cells among the fibrous tissue and the invasion and disruption of neighboring structures are common. The inflammatory infiltrate can be monoclonal in lymphomas, granulomas can suggest an underlying infection such as tuberculosis, hemosiderin deposits indicate hemorrhage due to trauma, and sclerotic specimens with only small amounts of inflammatory cells can be seen in radiotherapy-induced retroperitoneal fibrosis.[19,36]

There is no specific clinic presentation of the disease. In the early stage, a dull pain, often occurring in the flank, loin, and/or abdomen in a girdle distribution, is the main complaint of the majority of the patients; in patients with ureteral involvement, pain is also colic-like.[6,37,38] Constitutional symptoms like fatigue, anorexia, weight loss, and fever may accompany pain.[6,39] Hydrocele, varicocele, or testicular pain; constipation; dysuria; polyuria; and, in cases with advanced bilateral ureteral stenosis, oligo-anuria are the complaints of the patients.[6,19] Pain could increase in time and be independent of postural changing.[6] Urinary symptoms are delayed until the obstruction of the ureter increases. With renal involvement, severe hypertension is a common finding. Other rare symptoms due to arterial and venous compress include edema of the lower extremity, thrombophlebitis, claudication, and intestinal ischemia. Deep vein thrombosis may also occur.[40–42]

Physical examination gives nothing specific: diffuse abdominal tenderness and a palpable mass can be found, and in the presence of aneurysm, a peri-umbilical bruit is usually heard.[19] Routine laboratory tests show high concentrations of acute-phase reactants, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP); anemia; and, in a high percentage of cases, azotemia.[5,6] The presence of several auto-antibodies, antinuclear antibodies (in up to 50–60% of the cases in low titre), anti-thyroid microsome, anti-thyroglobulin antibodies (in 25–30% of the cases), ANCA, rheumatoid factor, and antismooth muscle give an idea of associated systemic autoimmune diseases, such as rheumatoid arthritis and systemic vasculitis or accompanying autoimmune thyroiditis.[4,5,7,19,24]

There are no standardized diagnostic criteria for retroperitoneal fibrosis. In a patient with the symptoms told above, RF has to be in the probable diagnosis list, despite its low incidence. Usually, the patients are diagnosed while evaluating a urinary tract obstruction or venous or arterial insufficiency. Although there is no specific diagnostic test, the laboratory findings support the suspicion (i.e., anemia, elevated erythrocyte sedimentation rate and C-relative protein, mild or moderate renal disfunction, and oliguria because of urinary obstruction). An elevated ESR is seen in 80–90% of the patients.[6] Normocytic, normochromic anaemia and worsening renal function are common.[5–7,21] The diagnostic and sometimes therapeutic approach starts with imaging studies, ultrasonography, excretory urography, CT scanning, magnetic resonance imaging (MRI), and aortography. Ultrasonography is the first modality to perform, especially if an azotemic patient is being assessed. Usually a hypoechoic or isoechoic mass, which can involve the ureters and thus cause unilateral or bilateral hydronephrosis, is visualized. A mass surrounding the aorta and/or ureters may be visualized while nephrolithiasis can be excluded.[43] Ultrasonography is also useful for the follow-up of ureteral obstruction. Ultrasonography reveals hydroureters, while excretory urography shows the medial deviation of the ureters by extra ureteric compression, which typically begins at the level of the third or fourth lumbar vertebrae.[5,43] Intravenous urography revealing the triad of medial deviation, extrinsic compression of the ureters, and hydronephrosis can assess the extent of ureteral involvement, but cannot be used to diagnose because these aspects can be caused by ureteral tumors, inflammatory processes, and adenopathy, as well as retroperitoneal fibrosis.[5,43] Furthermore, up to 20% of healthy individuals may show medial ureteral placement.[19] By CT scan, of which reported sensitivity, specificity and accuracy for the diagnosis are 83.3%, 99.7%, 93.7%, respectively,[45] RF appears as a homogeneous plaque, isodense with muscle-circulating aorta and vena cava, around the anterior and lateral sides of the abdominal aorta and the iliac arteries, without causing their displacement, as well as lymphadenopathy and tumor.[44,46] In most retroperitoneal fibrosis secondary to malignant diseases, the mass tends to displace the aorta anteriorly and the ureters laterally. In the aneurysmal forms of the disease, CT helps to evaluate the extent of aneurysmal dilatation and its potential complications; aorto-enteric fistula, hydronephrosis, and infected iliac artery aneurysms.[6,47] If possible, contrast administration may show the periaortic mass better, as it significantly enhances during the active phases of the disease, compared with low enhancement in the chronic stages.[47] When compared to CT, MRI gives the chance to see the mass in multiple planes, avoids nephrotoxic contrast

medium, and may also provide a better definition. T1-weighted images are hypointense, whereas T2-weighted images may be hyperintense in the early stages or active phases because of hypercellularity and edema.[19,47] Fluorodeoxyglucose-positron emission tomography (FDG PET), despite its being nonspecific for the diagnosis, can be a reliable tool in assessing the metabolic activity of the mass.[48] It detects other sites of inflammation and discloses infections or neoplastic lesions as the cause of or aligning with RF.[48,49] And also, FDG PET can help to detect the presence of the metabolic activity of the residual tissue and, therefore, point out if further treatment is needed, as residual retroperitoneal mass usually persists after medical therapy.[5] It is still controversial whether patients diagnosed with RF on the basis of CT/MRI require retroperitoneal biopsy. CT-guided biopsy is usually adequate to exclude malignancy in RF, though open, multiple, deep biopsies may occasionally be required. Of course, biopsy should be performed if the retroperitoneal mass has atypical localizations, such as pelvic, peri-pancreatic, or peri-ureteral.[19]

The treatment of retroperitoneal fibrosis is to stop the pain, treat its progression, relieve the obstruction of the ureters, control the acute-phase reaction and its systemic effects, and prevent recurrence or relapse, but not to cease the disease.

There are two aspects of treatment of the disease: surgical and medical. The glucocorticoids and immunosuppressive drugs such as azathioprine and cyclophosphamide are the basis of the medical therapy.[7] Although the role of steroids in chronic periaortitis is controversial, they have been used along with surgery with good results.[50] The use of steroids is supported by the presence of inflammatory cells in the fibrous tissue. In most patients, they induce the remission of the clinical symptoms; normalization of the acute-phase reactant levels, such as a decrease in the sedimentation rate; reduction of ureteral re-stenosis complete resolution of back/abdominal pain; and reduction in size of the retroperitoneal mass.[5–7,19,50] A long duration of treatment and follow-up is suggested, because failure to respond and recurrence after stopping steroids as late as 9 years after treatment have been reported.[51] Prednisone 1.0–1.5 mg/kg per day for three weeks, then tapered to zero within six months,[7] or an initial daily dose of prednisone 40–60 mg is usually administered. To prevent relapses, treatment courses of up to two years[52] are recommended regimens, although there is no accepted standard for the dose, administration route, and duration of steroid treatment.[6] Corticosteroids alone may be preferred in RF for uncomplicated disease without ureteric obstruction and in addition to surgery for those with persistent symptoms and inflammation following surgery. Serious comorbid conditions contraindicating surgery may be other indications for steroids.[6]

Azathioprine, cyclophosphamide, and methotrexate have been used effectively as steroid-sparing agents and in patients unresponsive to steroids alone.[53] These can induce stable disease remissions and regression of the mass, although they can be very toxic.[19] There are no randomized studies held to compare the effectiveness and toxicity of immunosuppressive drugs with steroids.[19] Cyclophosphamide may be useful in severe cases, especially if vasculitis is present in the fibrotic mass.[6] Prednisone may be given in combination with azathioprine, 2.5 mg/kg per day for six months and 1.5 mg/kg per day for another six months, or with oral cyclophosphamide, 2.0 mg/kg per day for three months and tapered to zero within six months or intravenously 1000 mg/m^2.[7] Mycophenolate mofetil and tamoxifen are also used in numerous clinical trials.[54] Tamoxifen, a selective oestrogen receptor modulator, is useful in pelvic desmoid tumors. However, unlike pelvic tumors, retroperitoneal tissue does not contain oestrogen receptors. Tamoxifen has been found to be effective as a single agent and in combination with steroids. Tamoxifen inhibits protein kinase C, an obligatory mediator of cell proliferation, increases apoptosis with the production of transforming growth factor. There are still small series demonstrating resolution in fibrosis with tamoxifen, except one on a relatively large cohort of chronic periaortic patients showed its effectiveness in up to 75% of the cases with very low toxicity.[55] Therefore, it is suggested to use immunosuppressants and tamoxifen as second-line therapy in steroid-refractory patients in clinical practice.[19,56]

Surgical treatment can relieve ureteral obstruction but does not prevent disease progression and recurrence or help systemic manifestations to resolve.[2,52] Surgery can be preceded or followed by steroid treatment. Of course, ureteral stenting and/or percutaneous nephrostomy is also required. The surgical management of the disease depends on a large surgical exploration with ureterolysis[2,57] with lateral transposition, and wrapping ureters with omentum is the procedure of choice for patients with hydronephrosis in RF.[19,39,47] In small case series, laparoscopic ureterolysis was also successful.[58] Surgery also allows multiple retroperitoneal biopsies to be done. It is advised to use steroids concomitantly.[2,4,6] Before this process, in anuric patients, percutaneous nephrostomy tubes and indwelling double-J catheters help to stabilize the critically ill patient with renal failure until surgical manipulations. Of course, the operative repair of aortic aneurysm is the definitive treatment.[25] Surgery is recommended when the aneurysm is greater than 5 cm in maximal transverse diameter by surgical aneurysmectomy or endovascular aneurysm, but in some cases, the tissue may persist or even progress.[59,60]

When there are no indications for aneurysm repair but the patient is symptomatic or suffers from obstructive complications, steroid therapy may be indicated.[19] As in many inflammatory and autoimmune diseases, RF also has a chronic-relapsing course. The frequency of relapse may depend on the treatment approach—occur in 10–50% of patients treated with surgery alone and in about 10% when combined with immunosuppressives.[61]

Patients with retroperitoneal fibrosis are usually monitored by subjective symptoms and regular assessment of ESR and CRP concentrations. Ultrasonography as mentioned previously is a non-invasive modality useful in the follow-up of ureteral obstruction. To follow-up the changes in the size of the retroperitoneal tissue, CT and MRI are the most reliable techniques.

Because most of the published studies do not have an adequate follow-up, the relapse rate of the disease is unclear. However, ureteral obstruction is estimated to recur in up to half of patients if surgery is performed alone and in about 10% of those also treated with steroids.[2,61] RF will recur despite medical and surgical therapy usually in the first five years of diagnosis.[2] There are cases of recurrence reported even 10 years after diagnosis in the literature.[2,61]

The treatment of the secondary forms of retroperitoneal fibrosis is based on the cause. In drug-induced retroperitoneal fibrosis, drug withdrawal (i.e., beta blockers and methysergide should be discontinued if being prescribed before) generally results in the resolution of the disease.[19] Steroids are usually contraindicated. In retroperitoneal fibrosis secondary to infections, antimicrobial therapy is instead recommended where chemotherapy and/or radiotherapy might be indicated, according to the type of underlying neoplasm[3,19] in a secondary disease or other proliferative disorder, such as histiocytosis. Retroperitoneal fibrosis secondary to untreatable cancer, trauma, major surgery, and radiotherapy have no proven indications for systemic medical treatment, and only palliative surgical approaches will be beneficial.

In summary, we described two cases with RF secondary to hemilaminectomy and longstanding hypothyroidism. Clinical findings of our patients were renal failure, abdominal pain, anemia, and elevated ESR. RF was diagnosed with abdominal tomography and histopathologically (in one case). A second patient was treated successfully with surgical repair, but an uneventful condition, toxic hepatitis, caused her death. In the first case, glucocorticoids helped in the improvement of the clinical condition, but we could not follow this patient a long time. RF may be a systemic and immunologic condition, and, in the very near future, hyperimmunoglobulin G4 syndrome can be used to name some of the cases. Immunological diseases, trauma, surgery, a wide spectrum of drugs, hypothyroidism, and some infections may cause RF. Clinical presentation of the disease is not specific, nor are laboratory findings. Radiologic imaging, especially computed tomography, is useful for diagnosis. Glucocorticoids, azathioprine, cyclophosphamide, cyclosporine, and mycophenolate mofetil can be used as immunosuppressive therapy, and tamoxifen, surgical intervention, or a discontinuation of drugs causing this disorder can be effective for treatment.

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