

## THE INTRIGUING CO-EXISTENCE OF A CHRONIC PERIAORTITIS, A PERICARDITIS AND A PANCREATITIS: CASE REPORT

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### Abstract

Chronic periaortitis (CP) refers to a spectrum of diseases whose common denominator is a fibro-inflammatory tissue developing in the periaortic space and frequently encasing surrounding structures like the kidney and ureters. There is no unified concept regarding the primary aetiology of CP, but recent studies have demonstrated that CP may present features of auto-immune diseases. CP involves three main entities, namely idiopathic retroperitoneal fibrosis (IRF), inflammatory aneurysms of the abdominal aorta (IAAAs) and perianeurysmal retroperitoneal fibrosis (PRF). These entities are usually diagnosed using computed tomography or magnetic resonance imaging, which typically show a retroperitoneal mass surrounding the aorta and that extends laterally without displacing it. Positron emission tomography is useful for the full assessment of the extent of the disease and its metabolic activity. The inflammatory and chronic relapsing nature of these diseases compels the use of medical therapy, which is based on high-dose steroids with a tapering scheme combined with immunosuppressive agents in refractory or relapsing disease. The authors report the clinical and radiological characteristics of a nonaneurysmatic form of chronic periaortitis in a woman presented with pericarditis, pericardial effusion and a pancreatitis. They also describe the investigation and management of this unusual condition

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### Introduction

Chronic periaortitis (CP) is an uncommon disease characterised by the presence of a fibro-inflammatory mass surrounding large-vessels like aorta and the iliac arteries and extending into the retroperitoneum, in which often entraps some of the surrounding structures, like the ureters and inferior vena cava<sup>1,2</sup>. CP includes a spectrum of idiopathic diseases: idiopathic retroperitoneal fibrosis (IRF), inflammatory aneurysms of the abdominal aorta and perianeurysmal retroperitoneal fibrosis<sup>2,3</sup>. However, the most accepted definition is the classification of CP in two forms: the *aneurysmal* form (dilated aorta) and the *non-aneurysmal* one.

Regarding the pathogenesis of CP, there is no unified concept. Initially, the leading theory was that CP was a localized inflammatory reaction against antigens in the atherosclerotic plaques of the aorta<sup>3,4</sup>. However, some recent studies have demonstrated a strong association between CP and HLA-DRB1\*03, which is a marker of auto-immunity, being linked to prototypical autoimmune conditions such as type 1 diabetes, myasthenia gravis and auto-immune thyroiditis<sup>5</sup>.

Some similarities can also be found in CP and a number of chronic inflammatory/autoimmune conditions that diffusely affect the aorta and its branches and are generically referred as aortitis<sup>6,7</sup>. Finally, the hypothesis that some cases of CP (particularly the non-aneurysmal forms) are part of a newly recognized clinic-pathological systemic disease, called IgG4-related systemic disease (IGG4-RSD), is sustained by recent works<sup>6,8</sup>. IgG4-RSD is characterized by increased serum IgG4 concentra-

tions and IgG4-expressing plasma cells diffusely infiltrating organs throughout the body<sup>8,9,10</sup>.

CP is characterized by non-specific signs and symptoms related to the mechanic and compressive effects of the retroperitoneal mass on the adjacent structures, such as back or abdominal pain, normally described as insidious, persistent and dull, constipation, deep vein thrombosis, leg edema, varicocele or hydrocele<sup>2,11,12-14</sup>.

Constitutional symptoms such as fever and weight loss may occur in the early stages. Laboratory investigation often shows increased acute-phase reactants, accompanied by normocytic anaemia, leukocytosis and hypoalbuminaemia<sup>2</sup>. Autoantibodies (particularly antinuclear antibodies) are positive in a varying proportion of the cases, but with no clinical correlation. The positivity of anti-neutrophil cytoplasmic antibodies, rheumatoid factor and antibodies against smooth muscle cells and thyroglobulin may indicate an associated auto-immune disorder<sup>2,15,16</sup>.

Because the presentation symptoms are often non-specific, in the presence of CP and retroperitoneal fibrosis, secondary causes such as drugs, infections and malignancies should be first excluded<sup>17-19</sup>.

The "gold-standard" imaging techniques used in the diagnosis and characterization of CP are: contrast-enhanced computed tomography (CT) scanning and magnetic resonance imaging (MRI)<sup>18-21</sup>. In the last years the <sup>18</sup>F-fluorodeoxyglucose positron emission tomography (FDG-PET) has been used for assessing the metabolic activity of the periaortic inflammatory tissue<sup>18</sup>.

The histology of the inflammatory periaortic tissue normally shows fibrosis with signs of active mononuclear cell inflammation<sup>6,17</sup>. This inflammatory infiltrate mainly consist of T and B lymphocytes, plasma cells and macrophages, although scattered eosinophils can also be found interspersed between collagen bundles and sclerosis.

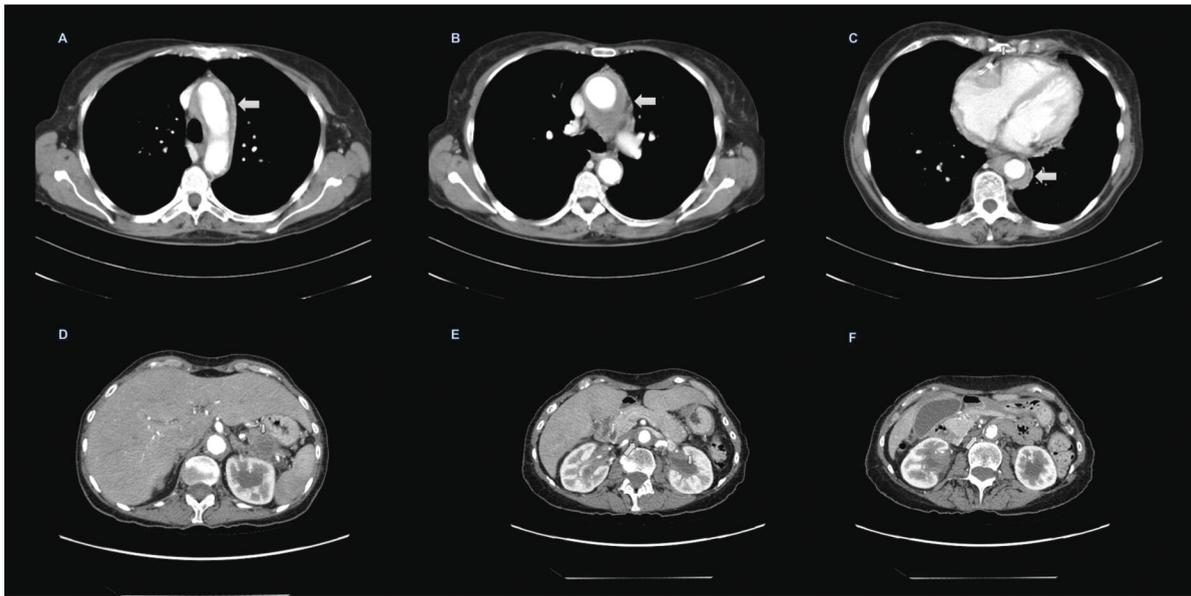
The initial clinical approach to these patients should rule out all the potential factors (i.e.: drugs, infections) that may exacerbate this disease. Steroids are considered the first choice option in medical treatment. The initial dose is 1mg/Kg/day and treatment decisions related to the degree of dose reduction must be individualized and based on clinical and radiological response. Besides steroids there are some immunosuppressive drugs, for instance methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil that

have been used as steroid sparing agents or in those cases not responding the initial steroid treatment<sup>9,19,22-24</sup>. Other drugs with different mechanisms of action, such as tamoxifen<sup>23</sup> and colchicine<sup>24</sup> have been used as adjuvant in steroid treatment cases.

Long-term follow-up is recommended in all patients and given to the array of therapeutic agents available it's possible a therapeutic approach capable of controlling the disease course that allows a sustained long-lasting remission.

## Case report

The authors report the case of a 71-year-old caucasian woman presented to the emergency department with a three-month-history of progressive shortness of breath, left side chest pain and left side flank pain. She also referred anorexia, 4 Kg weight loss and malaise in the previous months. The patient denied nausea, vomiting and diarrhoea. She had a past medical history of a strong cardiovascular disease with a myocardial infarction, in 2004, four coronary-stents and hypertension. Her usual medication was: bisoprolol 5mg/day; aspirin 100mg/day, pravastatine 40mg/day, telmisartan plus hydrochlorotiazide (40mg + 12.5 mg) and sertraline 50mg/day. On the initial clinical evaluation the patient was in distress, febrile (38.2°C), hypotensive (blood pressure was 91/51 mm Hg), the heart rate was 58 beats per min, the respiratory one was 18 cycles per min and saturation by pulse oximetry O<sub>2</sub> was 89% on room air. Chest auscultation revealed course breathe sounds bilaterally with no crackles. The cardiac auscultatory examination was unremarkable; specifically, there were no audible murmurs, gallops, or rubs. The electrocardiogram (ECG) showed a normal sinus rhythm (rate 60 beats per minute) with low-voltage QRS complexes not present in the previously ECG. Chest radiography presented marked cardiomegaly. Laboratory data revealed normocytic anaemia, hypoalbuminaemia, elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CPR) of 9 mg/dl (normal <0.5mg/dl), amylase was normal and myocardial enzymes were negative. The two-dimensional echocardiogram detected a large pericardial effusion, but with no diastolic collapse of the right heart chambers. The patient was admitted in the Coronary Care Unit (CCI), where she was submitted to a therapeutic pericar-

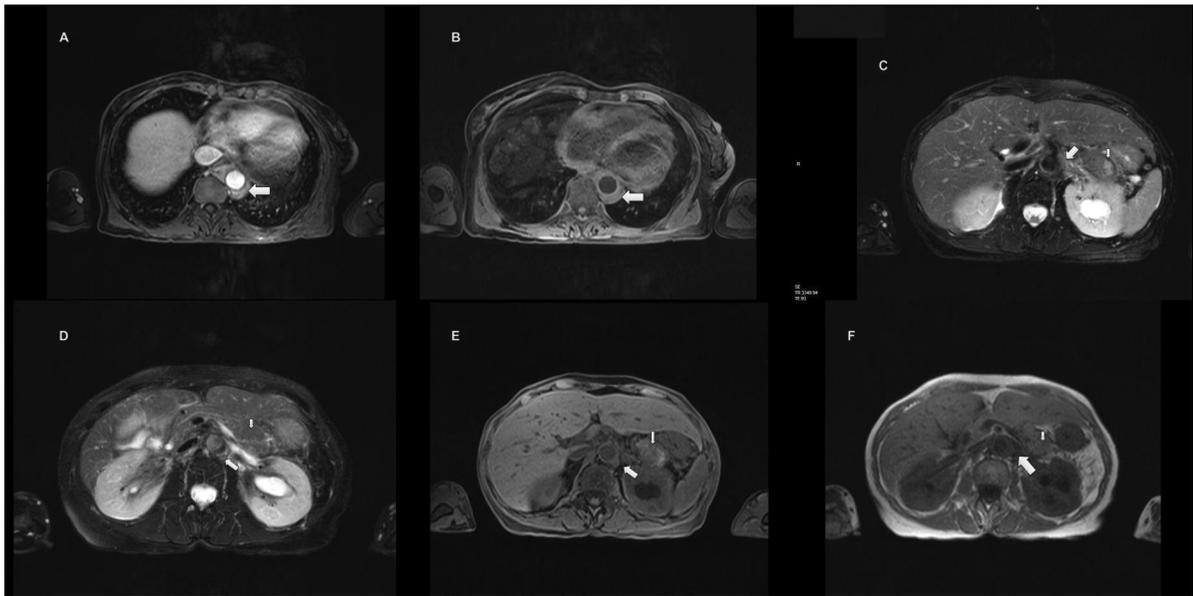


**Figure 1.** Computed tomography (CT) scan (axial views). **A, B** and **C** (thoracic CT) revealing a non aneurismal form of periaortitis involving the ascending and descending aorta (big arrows). **D, E** and **F** (abdominal CT) revealing a periaortitis of the aorta (big arrows). It also shows a hypodense and heterogeneous area in the tail of the pancreas (small arrow-image D) and calyceal dilatation (small arrow-image E).

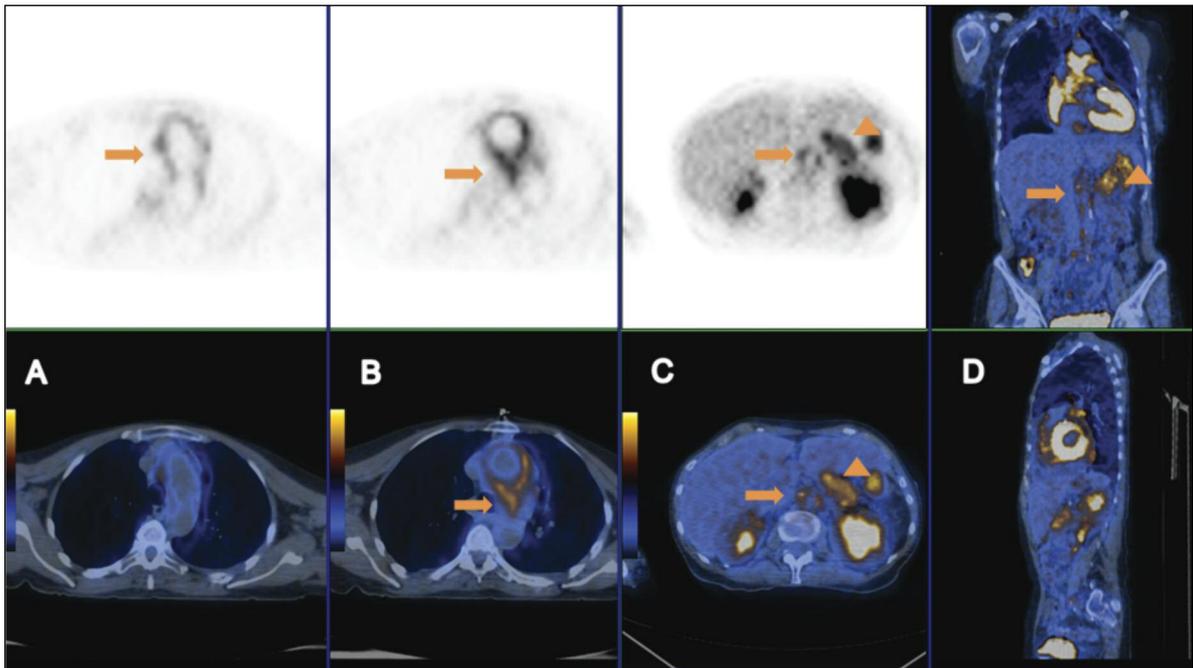
diocentesis. More than 800ml of pericardial fluid was taken. The laboratory workup of the pericardial exudate was negative for neoplastic cells, mycobacterium and other germens. After reaching cardiac stabilization the patient was transferred to the Internal Medicine Ward for a further study. There she was submitted to an abdominal ultrasound because of persistent left flank pain. The abdominal ultrasound showed dilated calyces and thickening of the urothelial wall suggesting an inflammatory process. Subsequently a scintigraphy was done, which excluded ureteric obstruction. Additional laboratory investigation including ANA, ANCA, and serological testing for Coxsackievirus B virus, EBV, CMV, Rubella virus, HSV, parvovirus B19, toxoplasmosis, HIV, hepatitis B and syphilis were negative. The serum proteinogram was normal with normal serum IgG4 concentration. A thoracic and abdominal CT scan (Figure 1) and MRI (Figure 2) were done. They revealed a soft tissue mass embracing the thoracic aorta and spreading down to the abdominal aorta without any abnormal aorta dilatation (Figures 1 and 2). Both exams confirmed the thickening of the ureteral wall and also revealed a hypodense and heterogeneous area in the tail of the pancreas. A positron emission tomography (PET) was undertaken to better characterize the soft tissue surrounding the aorta and the

hypodense area in the tail of the pancreas. This exam showed the hypermetabolic process embracing the thoracic and abdominal aorta, with the same metabolic pattern in the body and tail of the pancreas (Figure 3). This last finding in the pancreas was suggestive of an inflammatory process, which is characteristic in pancreatitis.

This case was discussed with the surgeons, because a tissue biopsy was needed not only to confirm the diagnosis of a CP, but also to exclude other diseases such as neoplasia or infections. Since the surgical approach of the pancreas was considered by the surgeons a complicated procedure, a percutaneous pericardial and periaortic soft tissue biopsy of the inflammatory mass, using a mediastinal window, was done. The histopathology revealed an inflammatory tissue with a lymphoplasmocytic infiltration, areas of fibrinoid necrosis and small-vessel vasculitis (Figure 4), which confirmed the diagnosis of chronic periaortitis confined to the thoracic and abdominal aorta and idiopathic retroperitoneal fibrosis. The patient began treatment with an initial dose of 60mg/day of methylprednisolone and 1mg/day of colchicine. The  $\beta$ -blocker was stopped. After the first month treatment a rapid clinical improvement was observed. The 3-month follow-up thoracic and abdominal CT scan showed mild regression in the in-



**Figure 2.** Magnetic Resonance imaging (MRI). **A** and **B** (thoracic axial view). The T1 (**A**) and T2 (**B**) weighted images reveal an intermediate intensity signal in the periaortic tissue. Image **C** (T2 weighted abdominal axial views) reveal hyperintense signal in the periaortic tissue (big arrow) and in the tail of the pancreas (small arrow). **D**, **E** and **F** (different sequences of T1 weighted images axial views) revealing an intermediate signal in the periaortic tissue (big arrow) and an intermediate and heterogeneous signal in the tail of the pancreas (small arrow).



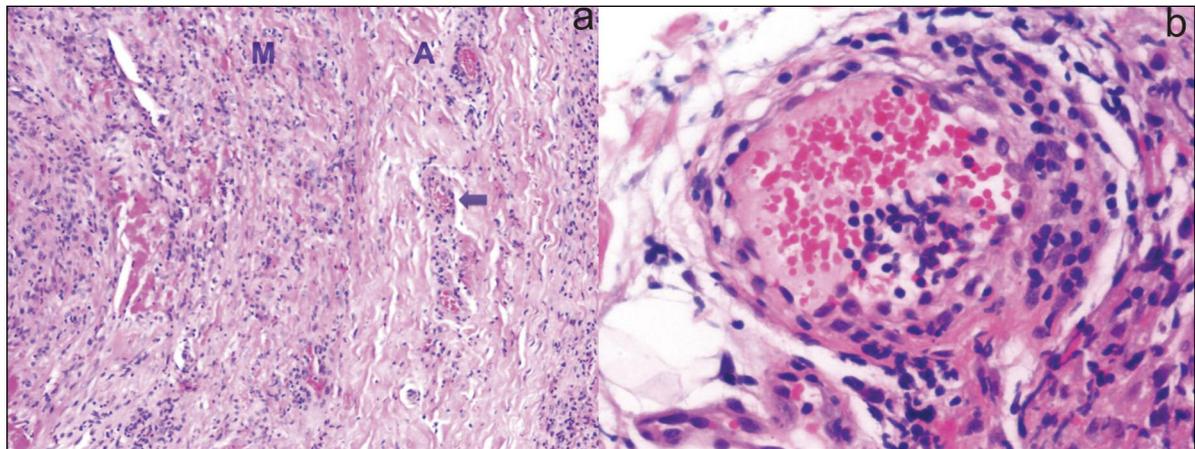
**Figure 3.** F18-Fluorodeoxyglucose (FDG) positive emission tomography. Images **A**, **B** and **C** (axial views) showing increased tracer uptake in the tissue surrounding the ascending aorta and the abdominal aorta (arrow). There is also an increased heterogeneous tracer uptake in the body and tail of the pancreas, suggestive of a pancreatitis (arrowhead). Image **D** (coronal and sagittal views) showing increased uptake in the ascending aorta and a segmented uptake in the abdominal aorta (big arrow) and in the body of the pancreas suggestive of a pancreatitis (arrowhead).

flammatory tissue in the aorta wall, and the evolution into a pseudocyst of the hypodense and heterogeneous area in the pancreas (Figure 5). A 3-month follow-up echocardiogram was also done and showed no residual pericardial effusion. The patient has had regular follow-ups and after an 8-month-treatment she is now on a maintenance dose of 8mg/day of methylprednisolone and 1mg/day colchicine.

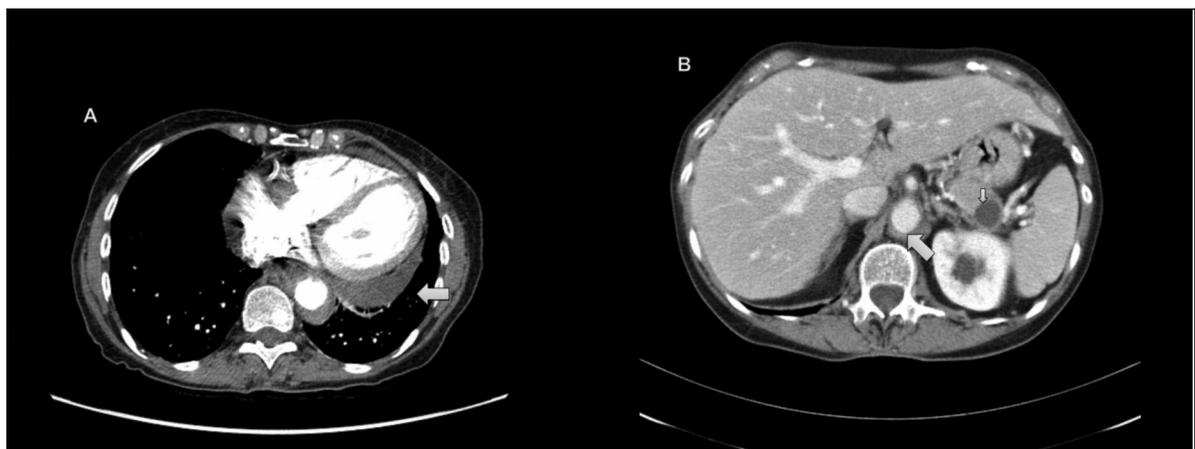
## Discussion

Chronic periaortitis is an uncommon fibro-in-

flammatory disorder of the aorta characterized by a perivascular fibrotic tissue that may spread into the retroperitoneum encasing the ureters and other structures. This patient had a nonaneurysmal form of a chronic periaortitis that extended caudally from the thoracic to the abdominal aorta and retroperitoneum. The chronicity of this inflammatory process was based not only on the radiologic findings, but also on the constitutional symptoms, the elevated acute-phase reactant levels and negative serologic tests presented in this patient for months. The diagnosis of CP and retroperitoneal fibrosis was initially suggested based on the CT, RMN and FDG-PET findings, which were



**Figure 4. A.** Periaortitis – lymphoid cells and plasma cells invade adventitia (A) and dissociate medial layer (M). Vasa vasorum are involved with vasculitis phenomena (arrow). HE X 100. **B.** Small vessel vasculitis revealed by lymphocytes, plasma cells and eosinophils in the endothelium. HE X 400



**Figure 5. A.** Three months follow-up CT scan of the chronic periaortitis. **A.** (Thoracic axial view) regression of the periaortic thoracic mass and of the pericardial effusion (arrow). **B.** (Abdominal axial view) regression of the inflammatory periaortic tissue (big arrow) and the evolution into a cyst of the initial hypodense area in the body and tail of the pancreas (pancreatitis)(small arrow).

done when searching for a neoplasm because of the initial presentation of a pericarditis with pericardial effusion. The histological analysis of the periaortic and pericardial tissue confirmed the diagnosis of a CP. The FDG-PET revealed the same metabolic pattern in the periaortic tissue and in the body and tail of pancreas, which was suggestive of an inflammatory process, such as pancreatitis. The 3-month follow-up thoracic and abdominal CT scan revealed a mild regression of the inflammatory tissue embracing the aorta, reduction of the ureteric wall thickening, resolution of the pericardial effusion and the evolution into a pseudocyst of the hypodense area in the pancreas. These last findings supported the hypothesis that the pericarditis and the pancreatitis were in relation with an abnormal extension of the inflammatory periaortic process. The hypothesis that these findings could be related to the newly recognized IgG4-related systemic disease was also considered, since this disorder may manifest as thoracic aortitis or retroperitoneal fibrosis<sup>8</sup>. This disorder was first recognized to involve the pancreas as autoimmune pancreatitis and is now known to involve other organs<sup>8,15</sup>. Therefore, IgG4 related systemic disease should always be considered in any patient found to have periaortitis or retroperitoneal fibrosis. Since our patient had normal serum IgG4 concentration and no histological features characterized by the presence of IgG4-expressing plasma cells, the diagnosis of an IgG4-related periaortitis and pancreatitis was ruled out. As a biopsy of pancreatic hypodense area was not performed, because of the difficult technical approach, there is no histological result that could document the diagnosis of a pancreatitis of possible autoimmune origin, only the evidence of radiological improvement. The successful medical treatment spared the patient an unnecessary surgical approach of the initial hypodense area in the pancreas.

In this case we didn't use MRI for the radiological follow up, instead we preferred CT, since the risk (even though the patient didn't have chronic renal disease) of developing Gadolinium related Nephrogenic Systemic Fibrosis might exist in this patient with an already inflammatory-fibrosing disease. The strong cardiovascular background of this patient sustains the original theory that CP and IRF are a result of a local reaction to advanced Atherosclerosis. Though the patient didn't have any history suggestive of an underlying autoimmune disease, the histological findings, such as lympho-

plasmocytic infiltration, suggestive of small-vessel vasculitis support the hypothesis that CP is related to an inflammatory/autoimmune systemic disease. Currently, there is no standardized treatment for CP and IRF. Therapeutic options vary from steroids to other immunosuppressive drugs. The promising results of some studies<sup>25</sup> prompted the initiation of methylprednisolone and colchicine in this patient. Other effective treatments options were available, such as tamoxifen with less long-term hazardous side-effects<sup>23</sup>. However, because of the clear clinical and radiological improvement, the patient is being maintained on the same treatment with steroids (with slower reduction in the dose) and colchicine.

This case report illustrates the importance of the awareness and recognition of imaging findings that are crucial for an early diagnosis and institution of adequate therapy. It is also an example of an atypical presentation of a CP and IRF and calls attention for the rare association with a pericarditis and a pancreatitis.

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