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# Mixed connective tissue disease and idiopathic retroperitoneal fibrosis: A rare but important association

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ABSTRACT

Idiopathic Retroperitoneal fibrosis (RPF) is a fibro-inflammatory disease. In patients with known mixed connective tissue disease (MCTD) it has rarely been described. Our case illustrates a unique presentation of RPF in a patient with MCTD. We emphasise possible links between the two disease processes and the high level of clinical suspicion required to make a diagnosis.

## 1. Introduction

Idiopathic Retroperitoneal fibrosis (RPF) is a condition characterised by chronic inflammation and fibrosis of retroperitoneal structures. It may affect the inferior vena cava, aorta, mesenteric vessels and the ureters.[1]

Symptoms of ureteric involvement are due to the obstruction of urinary flow, hydronephrosis and obstructive uropathy.[1] Flank and lower abdominal pain are common.[1] Involvement of the retroperitoneal vasculature may lead to venous or arterial insufficiency with lower leg oedema and claudication.[1] CT with contrast is the diagnostic modality of choice and invasive biopsy of involved tissue is often required to exclude malignancy.[1]

Treatment typically involves steroid therapy with resolution of pain and constitutional symptoms within days.[1] Additional agents such as methotrexate, azathioprine and cyclophosphamide can be added.[1] However, if renal function is compromised urgent decompression by either percutaneous nephrostomy or ureteric stenting may be required.[1] Ureterolysis is occasionally indicated.[2]

Aetiology remains unknown. Most presentations are idiopathic where autoimmune vasculitic processes are suggested causes.[1] In these cases RPF is thought to be a manifestation of a systemic autoimmune disease, characterised by increased concentrations of acute phase reactants, autoantibodies, and known autoimmune disease.[1] Other possible causes included medications, malignancy and infection.[1] Here we present a rare case of idiopathic RPF in a patient with MCTD.

## 2. The case

A 43 year old male presented to the emergency department with a two week history of intermittent dull right flank pain with radiation to the right lower back and right lower quadrant. Associated symptoms included urinary frequency, fatigue and anorexia. No dysuria, haematuria or subjective fevers were reported.

Past medical history included MCTD diagnosed in 2016 inclusive of sjrogens syndrome (SS) and systemic lupus erythematous overlap (SLE). Previous rheumatological consults noted a high ANA (anti-nuclear antibody) titre of 1:1280 with speckled pattern while anti -double stranded DNA (anti-dsDNA) was positive when tested previously. The extractable nuclear antibodies including anti–sjögren's-syndrome-related antigen A autoantibodies (anti-SSA/Ro52), anti-smith antibodies (anti-Sm) and antibodies to ribonucleoprotein (anti-RNP) had all returned positive results. Prior symptoms included malar rash and alopecia for which hydroxychloroquine had been prescribed however was subsequently ceased due to gastrointestinal upset. Disease remained mostly asymptomatic without need for treatment. However, in 2017 the patient suffered superior mesenteric artery thrombosis (SMA) in the context of active vasculitis.

On physical examination the patient was afebrile with mild tenderness to palpation in the right flank. Examination was otherwise unremarkable. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were both elevated to 17mg/L and 109mm/hr respectively. Renal function was normal and urine was sterile with borderline microscopic haematuria noted. Voided urine cytology revealed no malignant cells.

General surgery were consulted first to exclude an acute surgical

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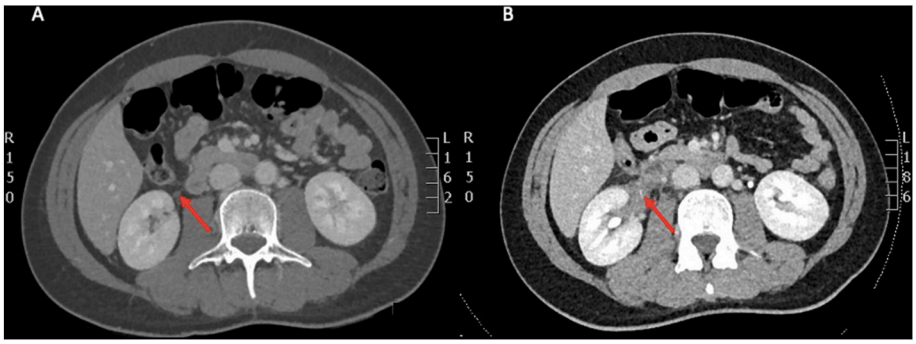


**Fig. 1.** A. The red arrow points to a normal right upper ureter. This CT was performed in 2019 as follow up for spontaneous SMA thrombosis from SLE. B. CT performed at presentation: the red arrow points to a thin right upper ureter surrounded by inflammatory tissue with mild hydronephrosis. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

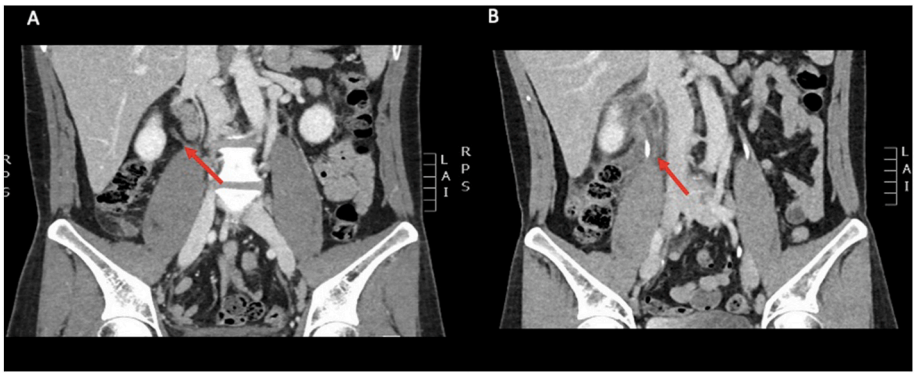


**Fig. 2.** A. CT from 2019: The red arrow points to normal right ureter with normal retroperitoneal tissue medial to the lower pole of the right kidney. B. CT at presentation: The red arrow highlights soft tissue inflammatory change surrounding the right upper ureter. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

pathology. Examination findings were not consistent with an acute abdomen and a computed tomography abdomen and pelvis with intravenous contrast was ordered. The CT showed mild right hydronephrosis (Fig. 1) secondary an ureteric stricture beginning in the upper right ureter. There was periureteric inflammation and stranding (Fig. 2).

Urology review indicated that the findings were consistent with RPF. IgG4 (immunoglobulin G) RPF was considered a possible diagnosis. Serum IgG assays were performed with total IgG and IgG 1 both above normal limits. However IgG 4 was within the normal range. As renal function was normal and the right hydronephrosis was mild, ureteric stenting was not performed.

In the context of known connective tissue disease, autoimmune RPF resulting in severe ureteric stenosis was considered the most likely diagnosis by rheumatology. This was in keeping with urological opinion. Prednisolone was commenced at 50mg daily with a plan to wean. Further imaging with FDG PET was also recommended. Urology follow up with US KUB and renal function tests had also been organised for six weeks time.

Following one week of steroid treatment the diagnosis of RPF was supported by significant improvement in abdominal pain. Methotrexate 10 mg once weekly was commenced for two weeks with a plan to increase to 20 mg. A prednisolone weaning plan was also initiated.

At follow up three months later urine cytology was negative for high grade urothelial carcinoma. US KUB displayed resolution of the right sided hydronephrosis and renal function remained normal.

## 3. Discussion

This case reports a rare presentation of RPF in a patient with mixed connective tissue disease. To date only one other presentation has been described.[3]

Interestingly, no cases of RPF in patients with MCTD and a history of prior SMA have been recorded. Whether these entities are linked is unknown. However the vasculitic processes underlying connective tissue disease may well cause the fibrotic inflammation of the retroperitoneum seen in RPF.

The signs and symptoms of RPF can be vague and a high level of diagnostic suspicion is required. Given the pathophysiological similarities between RPF and systemic connective tissue autoimmune disease, recognition of such presentations leads to the early and effective initiation of immunosuppressive therapy. This case illustrates that prompt commencement of steroid therapy and addition of methotrexate can prevent a deterioration in patients symptoms and renal function.

Additionally this case emphasises the importance of a multidisciplinary approach involving radiological, rheumatological and urological specialities.

## 4. Conclusion

The case presented describes a rare presentation of RPF in a patient with MCTD. The exact autoimmune links between these two entities is currently unknown and requires further exploration. A high level suspicion must be exercised in patient with known MCTD presenting with symptoms of RPF which are often vague in order to avoid delays in starting treatment.

## Consent for publication

Written informed consent was obtained from the patient for publication of this case report and the accompanying images. A copy has been

provided to the editor of this journal and can be obtained for review on request.

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## Author's contributions

Not applicable.

## Availability of data and materials

Not applicable.

## Declaration of competing interest

None.

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## Abbreviations

| | |
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| RPF | Retroperitoneal fibrosis |
| MCTD | Mixed connective tissue disease |
| CT | Computed tomography |
| SS | Sjrogens syndrome |
| SLE | Systemic lupus erythematous overlap |
| ANA | anti-nuclear antibody |
| Anti-dsDNA | anti -double stranded DNA |
| Anti-SSA/Ro52 | anti–sjögren's-syndrome-related antigen A autoantibodies |
| Anti-Sm | Anti-smith antibodies |
| Anti-RNP | Antibodies to ribonucleoprotein |
| SMA thrombus | Superior mesenteric artery thrombosis |
| CRP | C-reactive protein |
| IgG | Immunoglobulin G |
| US KUB | Ultrasound kidney ureters bladder |

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