



A Review on Inflammatory Myofibroblastic Tumour of the Kidney and Renal Pelvis: An Update

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Abstract

Inflammatory myofibroblastic tumours of the kidney and renal pelvis (IMTK& IMTRP) are rare and less than 100 cases have been reported. IMTKs/IMTKRPs have been diagnosed incidentally or following presentations of loin / abdominal pain, haematuria or palpable abdominal / loin mass. Radiological imaging features of the disease tend to show a cystic or solid or heterogeneous renal mass with slight contrast-enhancement. Diagnosis is made by pathological examination of biopsy or partial / radical nephrectomy specimens which tend to show spindle cells in myxoid background admixed with variable extra-cellular collagen, lymphocytes, plasma cells, and siderophages. IMTKs/IMTRPs stain positively for SMA, vimentin and HHH35 and CD34 but negatively with desmin, AIK-1, keratin and p53. Radiological imaging features of IMTKs/IMTRPs are non-specific. Most IMTKs/IMTRPs have been treated by renal sparing excision (partial nephrectomy / completed excision of the lesion) or radical surgery (nephrectomy / radical nephrectomy) without any subsequent recurrence. Conservative management of one case has resulted in resolution of the lesion. In one case radical surgical treatment of an invasive disease has been ensued by death due to complications of the invasive disease and treatment. One asymptomatic case following two-years of observation developed worsening pain requiring nephrectomy. There is no consensus on the treatment options. It is not clear whether or not there are certain pathological features of IMTKs/IMTRPs which could predict possible aggressive biological behaviour. Complete excision of IMTKs and IMTRPs tend to be associated with no recurrence but at times conservative management may result in resolution of the lesion. Perhaps if radiological-guided biopsies of slightly contrast-enhanced lesions of the kidney/renal pelvis are undertaken more IMTKs would be diagnosed pre-operatively to allow for conservative treatment and renal sparing surgery in cases of small non-invasive IMTK/RPs. A global multi-centre trial would be recommended to streamline lesions that should be managed: conservatively, by renal-sparing or radical surgery.

Key Words: Inflammatory myofibroblastic tumour, inflammatory pseudo-tumour; kidney; spindle cells; vimentin; smooth muscle actin; HHH 35; CD34; partial nephrectomy; radical nephrectomy

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Introduction

Inflammatory myofibroblastic tumour (IMT) which has also been called inflammatory pseudo-

tumour is a soft tissue lesion, the aetiology of which is not certainly known. [1] With regard to the urogenital tract IMT more commonly affects the urinary bladder and prostate gland but occasionally affects the kidney. [1] IMT has been considered a non-neoplastic reactive inflammatory lesion; however, these days IMT is regarded as a neoplasm in view of its recurrence and metastasis. [1] The ensuing paper contains a review of the literature on inflammatory fibroblastic tumour of the kidney (IMTK) and inflammatory myofibroblastic tumour of renal pelvis (IMTKRP).

Method

Various internet data bases were searched including Google, Google Scholar, Bing, PUB Med, and Educus. The search words used included inflammatory myofibroblastic tumour of the kidney

and inflammatory pseudo-tumour of the kidney. Forty two references related to case reports and literature reviews on inflammatory myofibroblastic tumours of the kidney were identified as suitable for the literature review.

Literature Review

(A) Overview

General Comments: Inflammatory myofibroblastic tumours of the kidney (IMTK) which are rare “spindle-cell” tumours associated with an inflammatory component that are found affecting the kidney [2]

Definition

Inflammatory Myofibroblastic Tumor has been defined under the Stanford Medicine Surgical Pathology Criteria as a tumour that is composed of cytologically bland spindled myofibroblasts with admixed inflammatory cells, predominantly occurring in infants and children. [3]

Alternative / Historical Names

Stanford Surgical Pathology Criteria has documented the ensuing alternative / historical names that had been used for inflammatory myofibroblastic tumour: [3]

- Inflammatory fibrosarcoma
- Inflammatory myofibrohistiocytic proliferation
- Inflammatory pseudo-tumour
- Omental-mesenteric myxoid hamartoma
- Plasma cell granuloma
- Plasma cell pseudo-tumour

Epidemiology

Inflammatory myofibroblastic tumours of the kidneys (IMTKs) have been reported in patients whose ages have ranged between 21 years and 76 years with a median age of occurrence at 57 years. [2]

IMTKs have been documented to be equally encountered in both sexes. [2]

Inflammatory myofibroblastic tumours have been reported in various organs of the genito-urinary tract including the urinary bladder, the kidney, the renal pelvis, and the ureter but the disease has on the whole been more commonly reported in the urinary bladder.

Presentation

Patients with inflammatory myofibroblastic tumours of the kidney and urinary tract tend to present with haematuria, loin or flank pain, and at times the diagnosis is established following further investigation of a radiological image finding of hydronephrosis

Clinical Examination Findings

Abdominal examination of a patient who has IMT may be normal but at times there may be evidence of a palpable mass in the loin and in cases of haematuria there may be visible blood in the external urethral orifice. When the patient is in pain there may be tenderness in the loin in the side of the affected kidney.

Investigations

Laboratory investigations

Urinalysis and Urine Culture

Routine urinalysis and urine culture is done as part of the initial assessment of the patient but not as an aid to the diagnosis of IMT

Haematological investigations

Full blood count and coagulation screen is done as part of the initial general assessment of the patient and usually this is normal unless the patient has a haematological problem not related to IMT

Blood biochemistry tests

Serum urea and electrolytes, liver function tests and serum glucose tests form part of the general assessment of a patient with IMT and this would be normal unless the patient has a non-related biochemical problem

Radiological investigations

Ultra-sound scan

Ultra-sound scan of the renal tract would reveal a lesion which could look cystic or solid and may show contrast enhancement but these features are not specific to IMT (see section B)

Computed tomography scan

Contrast CT scan of abdomen would show a lesion in the kidney which may show slight contrast enhancement but this is not specific to IMT (see section B)

Magnetic Resonance Imaging Scan

MRI scan of the abdomen would show a lesion in the kidney which may show slight contrast enhancement which is not specific to IMT (see section B)

Radiological image-guided biopsy of the renal lesion

Radiological image-guided biopsy of the renal lesion may be undertaken to obtain specimen of the lesion for pathological examination (see section B)

Treatment

IMTK has been treated on most occasions by means of nephrectomy [2], and also partial nephrectomy has been undertaken on other occasions. Conservative treatment has also been used.

Outcome

Kapusta et al. [4] stated that IMTKs tend not to recur following treatment by means of nephrectomy and that the lesion would recur or metastasize only in cases of inadequate excision of the lesion. However, a case of death related to recurrence of IMT has been reported.

Macroscopic features

It has been stated that macroscopic examination of Inflammatory myofibroblastic tumours of the kidney and renal pelvis, tend to show un-encapsulated tumours which have ranged in size of between 4 cm and 13 cm. [2] There tends to be a firm white tumour within the renal pelvis / adjacent soft tissue which has a gelatinous / myxoid feature. [2] There tends to be no evidence of haemorrhage or necrosis. [2]

Microscopic features

The microscopic features of inflammatory myofibroblastic tumours of the kidney / renal pelvis tends to be variable and these include: myxoid vascular (similar to nodular fasciitis) pattern, compact spindle cells associated with lymphoplasmacytic aggregates, and hyper-cellular keloid-like areas of fibrosis. [2]

Microscopic examination of inflammatory myofibroblastic tumour of the kidney / renal pelvis tend to show spindle cells that are bland and uniform [2]

Microscopic examination of inflammatory myofibroblastic tumour of the kidney / renal pelvis

may show occasional foam cells, osseous metaplasia or mild nuclear atypia [2]

Microscopic examination of inflammatory myofibroblastic tumours of the kidney / renal pelvis, tend to show no evidence of mitosis or rare mitoses. [2]

In summary, IMTK, Ns are composed of spindle cells that are admixed with variable components of extracellular collagen, lymphocytes, and plasma cells. [4]

Immunohistochemistry

Positive stains

Inflammatory myofibroblastic tumours of the kidney and renal pelvis tend to stain positively with the following:

Smooth muscle actin [2]

HHF35 [2]

Vimentin [2]

The tumours also show variable staining for CD34 [2]

Negative stains

Inflammatory myofibroblastic tumours of the kidney and renal pelvis on immunohistochemistry stain negatively with the following:

ALK1 [2]

Desmin [2]

Keratin [2]

P53 [2]

Diagnostic Criteria

The diagnostic criteria of Inflammatory Myofibroblastic Tumour, has been stratified under the Stanford Medicine Surgical Pathology Criteria as follows: [3]

- (a) Virtually all of the patients are under 30 years of age and most of them tend to be under 14 years of age.
- (b) The lesions (the tumours) tend to be grossly circumscribed: (I) microscopically they are usually infiltrative; (II) the lesions may be multi-

nodular; the lesions may have associated reactive lymphadenopathy

- (c) The lesions (the tumours) are composed of spindled myofibroblasts and inflammatory cells: (I) Microscopic examination of the lesion shows spindle or stellate cells that are bland to mildly atypical, (i) the cells tend to have large vesicular oval nuclei, (ii) there tends to be no hyperchromasia, (iii) the nucleoli tend to be small; (II) The cells tend to have variable amounts of pale eosinophilic cytoplasm; (III) Mitotic figures in the lesion tend to be variable and (i) these mitotic figures may be numerous but not atypical; (IV) Ganglion-like cells may be seen: (i) These cells tend to have abundant eosinophilic to amphophilic cytoplasm, (ii) the cells tend to contain prominent large nucleoli, (iii) these cells may be numerous; (V) The lesion (the tumour) tends to contain prominent inflammatory cells, which are predominantly lymphocytes and plasma cells; (i) they may include neutrophils and eosinophils, (ii) they may contain germinal centres, (iii) there may occasionally be foamy histiocytes present; (VI) Three patterns of cell mixtures had been described; (i) the patterns may vary within the same tumour, (ii) pattern 1, is composed of loose, or myxoid stroma with prominent vascularity, (iii) pattern 2 is composed of compact spindle cells, (iv) pattern 3 is composed of densely collagenous material with fewer spindle cells and inflammatory cells.
- (d) The ensuing have been proposed as predictors of malignant behaviour: (I) Aneuploidy by flow cytometry, (II) frequent ganglion-like cells, (iii) p53 positivity by immunohistochemistry studies, (iv) the utility of such grading system has not been confirmed.
- (e) There are rare reports of transformation to high-grade malignant pattern with features including: (i) increased cellularity, (ii) atypical mitotic features, and (iii) necrosis.
- (f) Calcifying fibrous pseudo-tumour has been proposed to represent a sclerosing stage of inflammatory myofibroblastic tumour.

Differential diagnoses

Some of the differential diagnoses of inflammatory myofibroblastic tumour of the kidney / renal pelvis include:

Fibromatosis in which microscopic examination of the specimen tends to show culture-like fibroblasts with infiltrative border and usually no evidence of inflammatory infiltrate. [2]

Fibrous histiocytoma, in which, microscopic examination of the specimen, tends to show storiform pattern of fibro-histiocytic cells and possibly giant cells. [2]

Spindle cell sarcoma, in which, microscopic examination tends to show spindle cells that exhibit atypia. [2]

(B) Miscellaneous narrations and discussions from some reported cases and case series

Yoshida et al. [5] reported a 44-year-old man who presented with visible haematuria. He had computed tomography (CT) scan of abdomen and magnetic resonance imaging (MRI) scan which showed a tumour of the left renal pelvis. He underwent left nephroureterectomy based upon a provisional diagnosis of renal pelvis tumour. Histological examination of the specimen revealed proliferation of fascicular spindle cells in an oedematous myxoid background with an infiltrate of plasma cells. Immunohistochemistry studies of the tumour showed that the spindled cells were strongly positively stained for smooth muscle actin (SMA) and vimentin, and negatively stained for desmin and anaplastic lymphoma kinase (ALK). A diagnosis of IMT of the renal pelvis was made.

Kapusta et al. [4] reported their series of cases of IMTs which included 12 cases of inflammatory myofibroblastic tumour which had occurred in the renal pelvis (six cases), renal parenchyma, (four cases), and immediate peripheral soft tissue (two cases). Kapusta et al. [4] reported that two patients presented with flank pain, one patient presented with painless visible haematuria, one patient had uretero-pelvic junction stenosis with hydronephrosis, and the remaining eight patients were asymptomatic. All of the eight patients had undergone nephrectomy. The tumours were characterized by firm tissue that was white, or they had a myxoid “gelatinous” appearance. Kapusta et al. [4] identified three types of histological patterns in the tumours and these included: a myxoid vascular pattern, a compact spindle cell pattern, and a hypo-cellular fibrous pattern. Kapusta et al. [4] also reported that immunohistochemistry and electron microscopic studies of the lesions supported the diagnosis of myofibroblastic proliferation and that all

of the cases were negative for anaplastic lymphoma kinase. Kapusta et al. [4] additionally reported that follow-up data was available in eight cases and this had ranged from 1 year to 17 years without any evidence of recurrence. Kapusta et al. [4] concluded that based upon their case series, renal inflammatory myofibroblastic tumour is a proliferative lesion of myofibroblasts of uncertain pathogenesis without any identified potential for recurrence or metastasis.

Ho et al. [6] reported the case of a child who presented with prolonged fever and abdominal pain who ultrasound scan and CT scan of the abdomen which revealed a left renal pelvis mass. She was treated by means of conservative surgical treatment. Based upon the histopathological and immunohistochemistry features of the lesion, a diagnosis of IMT of the renal pelvis was made. Ho et al. [6] stated that distinguishing IMT from other malignant renal pelvis tumours in children is essential in order to prevent unnecessary nephrectomy.

Gwynn and Clark [7] reported a 46-year-old man who was referred for evaluation of a mass in his right kidney for which he underwent right radical nephrectomy. Pathological examination of the nephrectomy specimen showed inflammatory myofibroblastic tumour (IMT) and renal cell carcinoma. Gwynn and Clark [7] stated that to their knowledge, at the time of publication of their paper only 28 cases of IMT associated with the kidney had been reported in published series and that their case was the first reported case of IMT associated with malignancy in the urogenital tract. Gwynn and Clark [7] further stated that some investigators had suggested that biopsy-proven IMT can be managed conservatively; nevertheless, the findings in their report had illustrated the need for radical nephrectomy in this patient population to rule out associated malignancy.

Larbcharoensub et al. [8] reported a 51-year-old man who presented with bleeding from the gums due to thrombocytopenia and left flank pain. He underwent left nephrectomy for a left renal tumour mass and macroscopic examination of the left renal tumour showed a cortical mass. Histological examination of the specimen spindled-cells admixed with variable amounts of extra-cellular collagen, lymphocytes and plasma cells. Immunohistochemistry studies of the tumour showed positive staining for vimentin and focal positive staining for smooth muscle actin. A diagnosis of primary inflammatory myofibroblastic tumour of the

left kidney was made. Larbcharoensub et al. [8] reported that their case was the first reported description in the literature of primary inflammatory myofibroblastic tumour of the kidney associated with thrombocytopenia.

Boo et al. [9] in 2006, reported the case of a 9-year-old girl who had a left renal mass that mimicked malignancy on pre-operative diagnostic images. However, pathological examination of the excised lesion had revealed features that were consistent with a diagnosis of inflammatory myofibroblastic tumour of the kidney in the child. Boo et al. [9] stated that to their knowledge at the time of publication of their paper in 2006, only 22 cases of IMT of the kidney had been reported in the literature and that IMT of the kidney in children is difficult to differentiate from a malignancy such as Wilms' tumour.

Selvan et al. [10] reported a 56-year-old man who was diagnosed as having asymptomatic left sided hydronephrosis when he was undergoing investigation for rheumatoid arthritis. His investigations had included ultra-sound scan, intravenous urography, retrograde - ureteropyelogram, computed tomography (CT) scan, isotope renogram, and screening for tuberous sclerosis. The radiological imaging appearances were adjudged not to be typical of classical pelvi-ureteric junction obstruction with normal funnelling and ready drainage of contrast into the upper ureter. The isotope renogram had shown a differential renal function of 25% function on the left with a poor response to frusemide diuretic injection and the right kidney contributed 75% of the total renal function. The CT scan showed ill-defined fascial planes surrounding the kidney and thickening surrounding the hilum of the kidney which was suggestive of localized inflammatory change (see figure) In view of the fact that the patient was asymptomatic and the fact that he had significant ischaemic heart disease he was managed conservatively without surgical intervention. Two years later, he presented with worsening left loin pain and associated radiological imaging evidence of worsening hydronephrosis, significant thinning of his renal cortex as well as marked deterioration of his renal function. He underwent coronary artery bypass surgical operation after which he subsequently underwent left nephrectomy. He was well and free of pain at his one-year follow-up. Gross examination of the nephrectomy specimen revealed a hydronephrotic kidney associated with areas of fibrosis adjacent to

the renal pelvis and peri-renal fat. Microscopic examination of the specimen showed that within an area of fibrosis, hypo-cellular interweaving thick collagen bundles with extensive hyalinization that were intermingled with bland spindle cells were apparent. The microscopic examination also showed presence of inflammatory cells which included lymphocytes, eosinophils and plasma cells (see figures 2a –c). Some irregular projections of fibrous tissue into the adjacent fat, was also observed. Immunohistochemistry studies of the specimen showed positive staining for smooth muscle actin (see figure 2d) the paper], vimentin, and CD34 (see figures 3a and 3b) and it also showed negativity for ALK-1 which was adjudged to be consistent with a histological diagnosis of IMT. Selvan et al. [10] stated the following:

- (i) It had been stated that inflammatory pseudotumour of the kidney or IMT is a rare disease of unknown aetiology affecting young people which tend to affect females more than males. [11]
- (j) The differential diagnosis of IMT include malignant tumours including renal cell carcinoma, sarcomatoid renal cell carcinoma, inflammatory fibro-sarcoma, malignant fibrous histiocytoma, low-grade neurogenic tumour, myxoid leiomyosarcoma, [12] and non-malignant tumours including angiomyolipoma, xanthogranuloma pyelonephritis, and plasma cell granuloma. [13]

Heerwagen et al. [14] reported two cases as follows:

Case 1

A 40-year-old woman was referred for evaluation of a palpable mass in her right flank. Her laboratory investigations were normal. She had ultrasound scan of her abdomen which showed a 7 cm x 6 cm solid tumour in her right kidney. She had a contrast enhanced computed tomography (CT) scan which showed an exophytic, round, and solid tumour that had involved the right lower pole of the kidney. The tumour which was heterogeneous did contain multiple small calcifications. The renal vein and the regional lymph nodes were not involved by the tumour. The tumour was abutting the right lobe of the liver but it had not invaded the liver. The left kidney was normal. In view of the fact that differentiation from a malignant tumour was not possible with regard to the radiological imaging findings a right radical nephrectomy was undertaken. Macroscopic

examination of the specimen revealed a well demarcated tumour which had not involved the parenchyma, pelvis pelvis, or perirenal fat. The microscopic and immunohistochemistry characteristics of the tumour, was consistent with a diagnosis of IMT. There was no evidence of recurrence in her follow-up ultra-sound scans undertaken 12 months and 24 months pursuant to her nephrectomy operation.

Case 2

A 75-year-old man had a standard staging computed tomography (CT) scan for lymphoma which revealed a large right renal tumour. His laboratory investigations on the whole were normal except for anaemia with haemoglobin of 6.5 mml per litre. He had ultrasound scan which showed a hypo-echoic, sparsely vascularized mass. He had two biopsies of the tumour and histological examination of the specimens showed fibrotic tissue mixed with chronic inflammatory cells. Her contrast enhanced CT scan, showed a solid homogeneous hypo-vascularized tumour that had involved the lower pole of the right kidney which measured 10 cm x 9 cm. The perirenal fat was oedematous. The renal vein and the regional lymph nodes were not involved by the tumour. The left kidney was normal. He underwent right radical nephrectomy with a suspicion of renal cell carcinoma. Macroscopic examination of the specimen revealed a grey white solid tumour, apparently encapsulated and demarcated from the encompassing tissues with the exception of the renal pelvis which was partially involved. The microscopic features and the immunohistochemical characteristics of the specimen were consistent with a diagnosis of IMT. At his 10-month follow-up he was well and his follow-up CT scan was normal.

Heerwagen et al. [14] stated the following:

- (1) A thorough review of the literature at the time of publication of their paper had revealed 24 reports of 37 cases of IMT of the kidney over the preceding 35 years and that Kapusta et al. [4] had summarized the clinical manifestations of 25 cases of IMT and the common symptoms had included flank pain in 5 patients, painless haematuria in 5 cases and as an incidental finding in 8 previously published cases as in their reported two cases.
- (2) The radiographic features of some neoplasms of the kidney for example angiomyolipoma can be diagnostic; nevertheless, with regard to many

cases of renal masses, the differentiation between benign and malignant neoplasms cannot be made based upon the radiological imaging features. IMTs of the kidney are no exception. Reports relating to the CT scan features of IMTs of the kidney had been minimal in the literature. Based upon contrast-enhanced CT scan, irrespective of the anatomical location, IMT had been reported as either being heterogeneous or homogeneous, and iso-, hypo-, or hyper-dense [15]. IMTs may contain cystic areas and / or calcifications. The various radiological appearances of IMTs of the kidney could be attributed to differences in the histological patterns of the disease, of which three features had been described including (a) a myxoid and vascular pattern, (b) a compact spindle-cell pattern, and (c) a hypo-cellular fibrous pattern. All of the three patterns have varying degrees of inflammatory cell infiltration. [16]. Kapusta et al. [4] had stated that one histological pattern tends to be predominant in IMTs of the kidney with some representation of one or both of the other patterns. Their two cases also showed different CT morphological features for example one was homogeneous and hypo-vascularized and the second one was heterogeneous and hyper-vascularized with calcifications. In comparison, the CT scan in cases of renal cell carcinoma tends to show a solid tumour that has significant and often strong enhancement upon intravenous contrast administration. However, this can also be seen in other neoplasms of the kidney. Areas of decreased attenuation which suggest necrosis tend to be present often in renal cell carcinoma. In renal cell carcinomas, calcifications if any tend to be internal, even though rim-like calcifications could be seen. On occasions renal cell carcinoma is predominantly a cystic mass with thick septations and nodularity of the wall of the cyst.

Petrescu et al. [17] reported a 57-year-old man who presented with haematuria, low-grade fever and right flank pain. He had ultra-sound scan and magnetic resonance imaging (MRI) scan which showed a tumour in the medial aspect of his right renal parenchyma that measured 2.5 cm in diameter. He underwent right nephroureterectomy. Gross examination of the excised specimen showed a 2 cm x 2 cm x 1.5 cm yellowish, gelatinous, well circumscribed mass in the medial aspect of the parenchyma of the kidney. Histological examination of the specimen showed a compact spindle cell proliferation, a hypo-cellular fibrous area in an

oedematous myxoid background which had been infiltrated by small lymphocytes, histiocytes, some plasma cells and a small bone area. The spindle cells on immunohistochemistry studies showed diffuse positive staining for vimentin (VIM), smooth muscle actin (ACT), CD68, and negative staining for desmin, MF116, SyN, S100, HMB 45, and CD 117. The final diagnosis was inflammatory pseudo-tumour of the kidney which highlighted the problem associated with establishing a pre-operative diagnosis. Petrescu et al. [17] stated the following:

- (i) Matsubara et al. [18] in 1998 identified infectious agents in inflammatory myofibroblastic tumour (IMT) which had included bacterial, rickettsial, fungal, or viral agents, but only in isolated cases.
- (ii) Presence of human herpes virus-8 DNA sequences, and an overexpression of human interleukin-6 as well as human cyclin D1 in myofibroblastic (inflammatory pseudo-tumours) had been reported. [19]
- (iii) The aforementioned cytokines perhaps have paracrine action and many sustain myofibroblastic growth. Inflammatory aetiology of IMT may perhaps not be applicable to all IMTs in view of the fact that some research had shown the presence of chromosomal abnormalities (2p23) and occasional reports of cases that had shown aggressive local behaviour and metastasis of the tumour which would support the postulate that at least some of these IMTs are true neoplasms [4] [16] [20] [21]
- (iv) Primary IMT of the kidney is an extremely rare neoplasm of uncertain biological potential
- (v) The pre-operative diagnosis of IMT has remained difficult despite developments in medical imaging and quite often requires surgical exploration.
- (vi) The diagnosis of IMT has been based upon a correlation of radiological and histological findings of the lesion.

Chen et al. [22] reported a 50-year-old man who was referred for evaluation of a kidney stone and a mass in the kidney. He underwent laparoscopic radical nephrectomy and pathological examination of the specimen showed features that were consistent with a diagnosis of inflammatory myofibroblastic tumour (IMT). Chen et al. [22] stated that at the time of the report of their case only 35 cases of IMT of the

kidney had been reported previously and that their reported case was the 36th case of IMT of the kidney to be reported and that their case was also the first case of IMT of the kidney to be reported which was associated with a renal calculus.

Ryu et al. [1] reported a 61-year-old woman who was incidentally found to have a left renal mass when she was being investigated for weight loss associated with gastrointestinal symptoms. Her full blood count, serum biochemistry and urinalysis tests were all normal. She had a contrast-enhanced computed tomography (CT) scan which showed a round, and solid mass that measured 3.0 cm x 2.0 cm which had originated from the lower pole of the left kidney. The mass lesion was slightly enhanced with contrast which was suggestive of a malignant tumour such as renal cell carcinoma. She also had magnetic resonance imaging (MRI) scan which showed a 3.0 cm x 2.5 cm x 2.0 cm heterogeneous mass with a portion of necrosis in the centre. T2-weighted MRI showed a mildly hyper-intense lesion, possibly renal cell carcinoma (see figure 4). There was no evidence of renal vein invasion or extension into the inferior vena cava. The contra-lateral kidney was normal. Based upon a provisional diagnosis of or suspicion of renal cell carcinoma, she underwent laparoscopic left radical nephrectomy and adrenalectomy. Macroscopic examination revealed that the tumours were well encapsulated with dense collagenous fibrous tissue (see figure 5). Microscopic examination of the tumour showed spindle cells with myxoid change that had been mixed with lymphocytes, and plasma cells (see figure 6 A, B). Immunohistochemistry studies did show that the spindle cells were diffusely positively stained for vimentin and focally positive actin and for epithelial membrane antigen (EMA). However, immunohistochemistry studies showed that the tumour did not show any staining for cytokeratin, HMB45, cyclin D1, S-100, C-kit, CD31, CD34, and desmin. Pathological examination revealed that the remaining renal parenchyma and adrenal gland were normal, the surgical margins were clear of the lesion, and there was no evidence of extension of the lesion into the renal vein, artery or ureter. A pathological diagnosis of inflammatory myofibroblastic tumour of the kidney was made. She was well without any evidence of recurrence at her 3-months follow-up.

Santos et al. [23] reported a 74-year-old woman who presented with right upper quadrant abdominal pain. She had computed tomography (CT) scan which showed a 4.5 cm mass in the upper pole

of the right kidney which was considered to be consistent with a renal cell carcinoma. She subsequently underwent a laparoscopic right radical nephrectomy. Pathological examination of the specimen showed spindle cells with prominent nucleoli and plasma cells as well as lymphocytes throughout the lesion. Immunohistochemistry studies of the tumour showed positive staining for anaplastic lymphoma kinase (ALK), vimentin, CK 18, CK-AE 1/3, and CAM 5.2 which was adjudged to be consistent with a diagnosis of IMT of the kidney. De Los Santos et al. [23] stated the following: IMT was first described by Davides et al. [24] in 1972, as a plasma cell granuloma of renal pelvis. Since then up to the time of report of their case, about 54 cases had been reported. Bell et al, [13] suggested that the kidney should be removed in the treatment for IMT. To the best of their knowledge, all cases of IMT of the kidney with the exception of 3 cases reported up to the time of publication of their paper had been treated by partial or total nephrectomy. There have been no reports of recurrence following surgical treatment. [25] [26]. They had found two recent cases of IMT of the kidney that had been treated conservatively. One of these patients had a history of recurrent systemic IMT which had involved the common bile duct, lymph nodes, tail of the pancreas, and both kidneys. The other patient had bilateral infiltrating renal tumours. In both of the cases, successful response to high dose corticosteroid therapy using prednisolone did allow the clinical confirmation of IMT. A biopsy of the renal lesion was performed in one of the two cases. Subsequent follow-up information was not available for both patients. Nevertheless, other authors did not have the same success with conservative treatment. [6] In their opinion, nephrectomy should still be the treatment of choice taking into consideration the fact that in majority of cases IMTs are indistinguishable from malignant tumours of the kidney. The age of manifestation of IMT has varied between 3 years and 89 years with a higher incidence reported in men. [27]

Lee et al. [28] reported a 48 year-old man who was referred as a result of incidental finding of a complex right renal mass. He had a past history of chronic Hepatitis B and Raynaud's disease. He had MRI scan which showed a 2.4 cm multi-septated cystic mass in the right kidney. He was placed on surveillance. At his 1-year-follow up, he had another MRI scan of abdomen which showed a 2.4 cm T2 hyper-intense, enhancing soft-tissue renal mass which was considered to be concerning for renal cell

carcinoma. With regard to the change in the radiological imaging appearance, he underwent a right laparoscopic partial nephrectomy. The specimen measured 6 cm x 5 cm x 4.5 cm. The well-defined nodule itself measured 3.5 cm x 1.8 cm x 1.5 cm and was noted to be grey / white colour with gelatinous consistency on macroscopic examination. Microscopic examination of the specimen showed bland looking spindle-shaped cells within a myxoid background and lymphoid aggregates. The surgical resection margins were free of the tumour and a diagnosis of inflammatory myofibroblastic tumour of the kidney was made. Lee et al. [28] stated that through a PUB Med search of Medline data bases between 1972 and 2010 they had found 38 reported cases of IMT of the kidney apart from theirs in the English language literature.

Khallouk et al. [29] reported a 57-year-old man who presented with a two-month history of visible haematuria and left lumbar pain. He had been smoking 40 cigarettes per day for the preceding 35 years. He had ultra-sound scan of the abdomen and renal tract which showed a heterogeneous mass that measured 8 cm in the left kidney. He also had a contrast-enhanced CT scan which showed a huge cystic tumour in the left kidney that measured 9.0 cm x 6.5 cm x 5.0 cm. The mass was slightly enhanced with contrast which was suggestive of a malignant tumour for example renal cell carcinoma (figure 7)]. He underwent left radical nephrectomy based upon a provisional diagnosis of renal cell carcinoma. Microscopic examination of the specimen showed spindle cells that were admixed with variable amounts of extracellular collagen, lymphocytes, plasma cells and siderophages (see figure 8 and figure 9 in the paper). Immunohistochemistry staining of the specimen revealed positive staining for vimentin, and HHF-35, and focally positive staining for smooth muscle actin. A diagnosis of an inflammatory myofibroblastic tumour of the kidney was made. At his 14-month follow-up, the patient was free of disease. Khallouk et al. [29] stated that some authors [7] had reported malignancy associated with inflammatory pseudo-tumours and that it is difficult to establish a pre-operative diagnosis in view of the fact that the symptoms and imaging findings in inflammatory myofibroblastic tumour are not specific. Khallouk et al. [29] made the following concluding statements: In view of the fact that the pre-operative diagnosis of such a tumour is not possible, they would advise surgical operation because only pathological examination of nephrectomy specimen can establish the diagnosis

with certainty. Based upon their case report and review of the literature, they would suggest a diagnostic and therapeutic strategy for the management of this rare tumour.

Li et al. [30] reported a 48-year-old woman who presented asymptotically with an incidental radiological imaging (CT scan had shown a 1.6 cm x 2.9 cm x 2.0 cm lesion in the upper pole of the left kidney and contrast enhanced CT scans had shown marginal enhancement; Magnetic resonance imaging (MRI) scan had shown a heterogeneous mass which measured 2.6 cm with low intensity on T1-weighted images and high intensity, accompanied by hypointensity surrounding the centre lesion on T2-weighted images) finding of a mass in the left kidney. On the whole her haematological and serum biochemistry profile were normal. She underwent left radical nephrectomy. Pathological examination of the nephrectomy specimen revealed features consistent with the diagnosis of IMT in that microscopic examination of the specimen showed spindled fibroblast-like cells and collagen with infiltrating lymphocytes and plasma cells and immunohistochemical staining of the specimen was positive for vimentin and focally positive for smooth muscle actin, desmin, and Ki-67. The patient had a history of trauma of her left hypochondrium 13 years prior to her diagnosis of IMT. She also had a history of hepatitis B for 20 years. Li et al. [30] had iterated that the patient's subsequent development of cirrhosis of the liver, hypersplenism, and coagulation disorders after the diagnosis of hepatitis B might have played a significant role in her development of the IMT of the kidney and also that it might aid in the improvement of the understanding of the aetiology and pathogenesis of IMT of the kidney. At a follow-up of six months there was no evidence of recurrence.

Jenkins et al. [31] reported a 61-year-old man who presented with a 2-week history of back pain and haematuria. He had ultra-sound scan and computed tomography scan which revealed a 4.5 cm heterogeneous mass that had involved the lower pole of the left kidney as well as enlarged lymph nodes medial to the mass which was adjudged to be suggestive of renal cell carcinoma. He underwent left laparoscopic radical nephrectomy with regional lymphadenectomy. The pathological features of the mass, was consistent with a diagnosis of inflammatory myofibroblastic tumour of the kidney.

Navale et al. [32] reported a 32-year-old man who presented with pain in the lower abdomen and

urinary tract symptoms of one year's duration. He had a history of renal lithiasis 8 years preceding his presentation. His investigations including full blood count, serum biochemistry and urinalysis were normal. He had a CT scan which did show a heterogeneously enhancing mass lesion that measured 4.5 cm x 4.4 cm in the lower pole of the right kidney with an exophytic component. Calcific areas were also observed in the mass which was confined to the cortex of the kidney with no evidence of extension into the renal calyces. The right renal vein was patent with no evidence of thrombosis. The left kidney was normal. A renal cell carcinoma of the right kidney was the provisional suspected diagnosis for which he underwent right radical nephrectomy. Gross examination of the specimen showed a well-circumscribed hard grey white tumour in the lower pole of the nephrectomy specimen associated with an exophytic component. The tumour was noted to be hard and it had a gritty sensation on sectioning through. Microscopic examination showed a tumour which consisted of cellular and hypo-cellular hyalinised areas. The cellular areas consisted of spindle cells in short fascicles and prominent storiform pattern. The spindle cells exhibited mild atypia and mitotic activity which had ranged from 4 to 7 per 10 high-power, Field (HPF). There was evidence of lymphoid aggregates with germinal centre formation and plasma cells interspersed among the spindle cells. Extravasated red blood cells were also prominently apparent at many foci. The spindle cells in the hypo-cellular hyalinised areas were arranged in an unusual perivascular whorled pattern that mimicked meningeal whorls. Furthermore, heterotopic bone formation was observed which was encompassed by osteoblastic cells. The mitotic rate in the cellular areas was noted to range between 3 to 6 per 10 high-power Field, focally. Nevertheless, no atypical mitosis was observed. There was no evidence of conventional renal cell carcinoma after a thorough examination of the specimen. Immunohistochemistry studies of the tumour showed that the spindle cells were strongly positively stained for smooth muscle antibody but they were negatively stained for CD 34, ALK -1, CK7, CD 23, CD 21, and h-caldesmon. P53 was positive in few of the specimens. The surgical margins were clear of the lesion with no evidence of extension into the renal vein or renal pelvis. The patient was alive, asymptomatic at his 18 month follow-up.

Baspinar et al. [33] reported a 78-year-old woman who had IMT of the left kidney with local invasion to the peri-renal tissue and pancreas which

was initially misinterpreted as a renal cell carcinoma based upon radiological imaging findings. She underwent left radical nephrectomy, splenectomy and partial resection of the pancreas for the presumed renal cell carcinoma. The tumour cells were positive on immunohistochemistry studies for smooth muscle actin, anaplastic lymphoma kinase (ALT) and vimentin and these pathological features supported the diagnosis of IMT. She did not have adjuvant therapy. She presented 2 months later because of recurrent abdominal pain and pleural effusion. She had ultrasound guided thoracentesis and paracentesis and cytological examination of the fluid was reported as benign cytology. Seven months after her surgical operation, she died due to complications related her tumour invasion and treatment.

Galaway et al. [34] reported a case of an incidentally found renal mass in a 71-year-old woman which was diagnosed as inflammatory myofibroblastic tumour of the kidney following pathological examination of specimens of the lesion obtained from core needle biopsy of her renal lesion. The tumour was managed conservatively without surgical intervention and resolved spontaneously. They stated that IMT of the kidney is a rare and benign condition which is often confused with renal malignancy based upon clinical presentation and radiological evaluation that has commonly been treated by nephrectomy and that utilizing renal mass biopsy to help diagnose and guide therapeutic intervention is increasing but has not been universally globally-adopted to this point.

Taheri et al. [35] reported a 15-year-old girl who was referred because of a left renal mass. She had presented with weight loss of two months duration, haematuria and left flank pain. Her full blood count, serum biochemistry test results and urinalysis results were all normal. She had a contrast-enhanced CT scan which showed a solid mass with round borders in the upper pole of the left kidney. The mass was slightly contrast-enhanced which was suggestive of a malignant neoplasm. The right kidney was normal. The provisional suspected diagnosis was Wilms tumour. She underwent left radical nephrectomy and adrenalectomy. Macroscopic examination of the specimen revealed a yellowish well-defined mass that measured 13.5 cm in its greatest dimension in the upper pole of the left kidney with an intact renal capsule. Microscopic examination of the specimen showed proliferation of spindle cells which had elongated cytoplasmic processes in a loose oedematous and myxoid

background. The nucleoli showed occasional atypia and some of the nucleoli were prominent. There was also evidence of diffuse lymphoplasmacytic inflammation with occasional eosinophils and neutrophil infiltration. Immunohistochemistry studies of the tumour showed that the spindle cells were diffusely positive for vimentin, and focally positive for actin as well as for anaplastic lymphoma kinase (ALK) (see figure 1 and 2 in the paper). The immunohistochemistry study was negative for the following tumour markers: epithelial membrane antigen, cytokeratin 7, CD34, Bc12, and desmin. A final diagnosis of IMT was made. The remaining parenchyma of the kidney, and adrenal gland, as well as the surgical margin, was normal and the surgical margin was free of tumour. Taheri et al. [35] stated the following:

- i. Despite improvements in radiological imaging technology, the pre-operative diagnosis of IMT is still difficult and surgery is the only way for the diagnosis and treatment.
- ii. Taking into consideration the role of the pathological examination in the establishing the definite diagnosis of IMT, clinicians should be aware of the entity of IMT and IMT must be considered in the differential diagnoses of a renal mass.

Dogan et al. [36] reported a case of renal inflammatory myofibroblastic tumour (IMT) which was accompanied by multiple lung nodules that mimicked Wilms tumour with pulmonary metastasis in a 3-year-old boy. They stated that to their knowledge, their reported case was a unique case of IMT which had not been reported in the literature previously and that renal IMT is an extremely rare lesion especially in children.

Liang [37] reported a 60-year-old woman who was found during health care examination to have “solitary cysts” in her left kidney. She did not have any pain or haematuria. Her abdominal examination did not reveal any tenderness or palpable mass. Her urinalysis was normal and her serum biochemistry examinations were normal. She had ultra-sound scan of abdomen which showed an 8.7 cm x 9.2 cm mixed echo-genic mass at the upper pole of the left kidney, most of the mass, was an anechoic mass which had slightly protruded from the capsule of the kidney and was associated with a well-circumscribed borders. The mass had rapid contrast-enhancement with fast fading upon a bolus injection of an ultrasound contrast agent. She had CT scan of

abdomen which showed about 9.4 cm x 10.1 cm round-like cystic- lesion in the upper pole of the left kidney and the edges were well-circumscribed. The upper inner wall of the cystic lesion was thick and associated with soft tissue. The solid component of the lesion did have gradual contrast-enhancement on the CT scans. Based upon the CT scan findings a provisional diagnosis of renal tumour was made. She underwent resection of the left renal cystic masses and during the operation the cystic wall was found to be thick locally and this was about 2 cm x 5 cm and it was hard in texture. Frozen section of the specimen was undertaken. Frozen section histological examination of the specimen confirmed a diagnosis of IMT with no obvious malignant cells, and in view of the pathology report the rest of the kidney was not removed. Immunohistochemistry studies of the resected cystic lesions showed strong positive staining for smooth muscle actin (SMA), positive staining for CD 68, positive staining for CD 10, interspersed positive staining for Ki67, negative staining for anaplastic lymphoma kinase (ALK), and negative staining for CD 34. At her 5 years and 3 months follow-up, she was well and asymptomatic and her follow-up ultrasound scan and CT scans had shown no evidence of recurrence. Liang [37] stated the following: CT scan images of the patient’s cystic lesions were categorized as Fuhrman grade IV. This was considered to indicate the presence of malignant lesions. Nevertheless, the gradual enhancement of the solid component in the case was different from the type of enhancement which tends to be associated with cystic renal cell carcinomas. The nature of the lesion was further identified by the use of intra-operative frozen sections, which did help in avoiding unnecessary nephrectomy.

Babu et al. [38] reported a 51-year-old man who presented with left flank pain of one month duration. He was asymptomatic otherwise. His examination was unremarkable and his urinalysis was normal. He had ultra-sound scan of abdomen which showed a contracted left kidney with cortical calcification and mild hydronephrosis. She also had contrast-enhanced computed tomography (CECT) scan of abdomen which showed a mass that measured 8.2 cm x 4.4 cm x 4.6 cm which had involved the upper pole and mid pole of the left kidney and this had extended medially and encased the left renal artery up to the left lateral wall of the aorta and extended along the left ureter with slight enhancement which was considered to be suggestive of tuberculosis or malignancy like renal cell carcinoma or transitional cell carcinoma. His

tuberculosis evaluation was normal. He had CT-guided biopsy of the mass and histological examination findings of the biopsy specimen revealed pyelonephritis. A laparoscopic radical nephrectomy was undertaken with a provisional diagnosis of renal cell carcinoma. Macroscopic examination showed that the left kidney had an irregular, invasive grey-white growth. Microscopic examination of the specimen showed a benign tumour which comprised of numerous interlacing fascicles of benign spindle cells which had been infiltrated by dense inflammatory cells that comprised of plasma cells, eosinophils and lymphocytes. Many collagen bundles were found within which was seen xanthogranulomatous change. Immunohistochemical staining of the tumour showed strong positive staining for vimentin, smooth muscle actin (SMA), and focal positive staining for anaplastic lymphoma kinase (ALK). Babu et al. [38] stated the following:

- I. Coffin et al. [16] had shared their experience with 84 cases of IMT occurring in the soft tissues and viscera and they had indicated that the patients tend to present with haematuria and abdominal pain but their patient presented with flank pain for which he was provisionally diagnosed as having calculus pyelonephritis.
- II. Cases of IMT had been reported in patients who had been aged between 3 years and 68 years with most of them being male, [39] their patient was aged 51 years.
- III. Although the literature had indicated that the clinical examination and radiological investigation findings are inconclusive and the diagnosis of IMT at the time of surgical operation, Park et al. [39] had described the radiological imaging features of IMT of the genitourinary tract and had observed that IMT of the kidney can be seen as hypo or heterogeneous echoic mass on sonography scan, well-defined hypo-echoic mass with intra-mural vascularity on enhanced power Doppler sonography, low-attenuation mass on CT scan, and hypo-vascular lesion on magnetic resonance imaging. It is very difficult to differentiate IMT from a malignant lesion, and definite differentiation on radiological imaging from malignancy is not possible. Nevertheless, familiarity with the radiological imaging features of IMT could avoid unnecessary surgery. In their case CECT findings had been suggestive of a malignant tumour of either renal

cell carcinoma or transitional cell carcinoma or tuberculosis.

Wu et al. [40] reported a 43-year-old man who presented with iterative visible haematuria and abdominal pain which did not respond to antibiotic treatment. He had computed tomography (CT) scan and magnetic resonance imaging (MRI) scan which showed a slightly enhanced mass in the left renal pelvis that measured 1.5 cm diameter. He underwent left nephrectomy under a provisional diagnosis of carcinoma of the renal pelvis. Nevertheless, during the operation, intra-operative fast-frozen section pathological examination of the mass was undertaken and the histopathological features of the tumour had exhibited proliferation of compact spindle cells which was adjudged to be consistent with a diagnosis IMT and based upon the frozen section diagnosis further ureterectomy which would have been performed at the same time if the tumour had been urothelial carcinoma was avoided.

Park et al. [39] illustrated the radiological imaging characteristics of IMTs of two patients as follows:

Case 1

A 67-year-old man had a CT scan with unenhanced, early excretory phase and images of dynamic CT which showed a solid mass in the lower pole of the left kidney. Subtle increased density was seen on unenhanced scan which was considered to possibly indicate calcification. On cortico-medullary and early excretory phases, the mass enhanced and washed out. Based upon the radiological features of the renal mass a radiological diagnosis of renal cell carcinoma was made. Left radical nephrectomy was performed and pathological examination of the specimen revealed features diagnostic of inflammatory myofibroblastic tumour (Inflammatory pseudo-tumour) of the kidney.

Case 2

A 46-year-old man had contrast-enhanced CT scans which showed bulbous enlargement of the pancreas and multi-focal low-attenuation lesions in both his left and right kidneys. Multiple enlarged lymph nodes were also seen in the porta hepatis and portocaval space. Based upon the CT scan findings a radiological diagnosis of lymphoma was made. Ultra-sound guided kidney biopsy was done and pathological examination of the renal tumour biopsy showed features diagnostic of inflammatory

myofibroblastic tumour (inflammatory pseudo-tumour).

Park et al. [39] stated that the radiological imaging features and locations of inflammatory myofibroblastic tumour (inflammatory pseudo-tumour) in the genitourinary tract varies a lot but this most commonly IMT tends to have a radiological of large masses that mimic malignant lesions. They also stated that IMT can also manifest as a multi-focal lesion for example lymphoma and local tumour recurrence or metastasis. Park et al. [39] further stated that, the role of the radiologist is to ensure that inflammatory myofibroblastic tumour (inflammatory pseudo-tumour) is a diagnosis that is suggested pre-operatively and differentiated from malignant lesions by either particular radiological imaging findings or by means of radiological imaging guided-biopsy. Park et al. [39] additionally stated that even though definite radiological differentiation between IMT and malignancy is not clearly possible, they would suggest that familiarity with the manifestations of inflammatory myofibroblastic tumour (inflammatory pseudo-tumour) can be helpful in avoiding unnecessary radical surgery before histological proof of malignancy is obtained.

There are postulates regarding the aetiology and pathogenesis of IMT which are multi-factorial; however, there is no consensus opinion. Ryu et al. [1] stated the following: initially IMT was considered to be an emanation of a reactive inflammatory process or “pseudo-tumour”. Thus IMT may ensue: surgery, trauma, or infection; No single aetiology or pathogenesis has been documented for IMT; a number of cases of IMT could be related to an infection or autoimmune process; a sub-group of IMTs would appear to be associated various types of infections including actinomyses, pseudomonas, mycoplasma; another aetiological agent which has been postulated is Epstein Barr virus; cases of IMT have been reported to be positive to Epstein Barr virus latent membrane protein especially in the liver and spleen. [41] [42]

Conclusions

Complete excision of IMTKs and IMTRPs tend to be associated with no recurrence but there is evidence that conservative management may result in resolution of the lesion at times. Perhaps if radiological-guided biopsies of slightly contrast-enhanced lesions are undertaken more IMTS of kidneys and renal pelvis would be diagnosed pre-

operatively to allow for conservative treatment and renal sparing surgery in cases of small non-invasive IMTS.

There is need for a consensus opinion meeting to decide upon the approach to the diagnosis of IMTs of the kidney and renal pelvis and indications for various treatment options including conservative treatment, kidney preserving surgery and radical nephrectomy as well as to review the pathological characteristics of the lesion that are likely to be associated with recurrence of the lesion.

Conflict of interest: None

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Table 1: A List of some of the reported cases of inflammatory fibroblastic tumour of the kidney and renal pelvis

Authors Reference Year	Age & Presentation	Imaging & side	Treatment	Pathological findings	Outcome
Yoshida et al. [5] 2006	44 years Visible haematuria	CT & MRI Scan; Lesion left renal pelvis	Left nephroureterectomy	Spindled cells in myxoid background; + plasma cell infiltrate SMA +ve Vimentin +ve Desmin -ve ALK -ve	Details not available to author
Ho et al. [6] 2005	Child Fever & abdominal pain	Ultrasound & CT scans Left renal lesion	Conservative surgical kidney preserving resection of lesion	Features consistent with IMT	Details not available to author
Gwynn & Clark [7] 2005	46 years Male Incidental	Right Kidney	Right radical nephrectomy	Features of IMT as well as Renal cell carcinoma	Details not available to author
Larbcharoensub et al. [8] 2006	51 years male Bleeding gum, thrombocytopenia, left flank pain	Left kidney	Left nephrectomy	Spindled cells admixed with extracellular collagen, lymphocytes, plasma cells, vimentin +ve, SMA focally +ve	Details not available to author
Boo et al. [9] 2006	9 years, female Details not available to author	Left kidney		Histology consistent with IMT (no details)	Details not available to author
Selvan et al. [10] 2007	Asymptomatic, rheumatoid arthritis investigated for tuberosus sclerosis	Left Retrograde ureteropyelogram, CT & isotope renogram	Initially conservative treatment but 2 years later Left nephrectomy for worsening pain and hydronephrosis	Hydronephrosis fibrosis around perirenal fat, spindled-cells, intermingled with collagen bundles & hypo-cellular intercellular interweaving bundles of collagen. inflammatory cells including lymphocytes eosinophils, plasma cells; SMA + VE, Vimentin +VE, CD34+VE, ALK-1 - VE	Details of long term outcome not available or reported
Herwagen et al. [14] 2007	40 years, Female, Palpable mass right flank	Ultrasound & CT scans Right lower pole	Right radical nephrectomy	Microscopic & immunohistochemistry consistent with IMT	Alive after 2 ears & no recurrence
Herwagen et al. [14] 2007	75 years Male Asymptomatic, investigation for lymphoma & anaemia noted	Ultrasound scan showed Right renal mass & 2 biopsies showed fibrous tissue + chronic inflammatory cells only CT scan	Right radical nephrectomy	Histology & immunohistochemistry consistent with IMT	After 10 months CT showed no recurrence

Petrescu et al. [17]	57 years Male, Haematuria, low-grade fever; right flank pain	Ultra-sound scan & MRI scan; Right renal parenchyma tumour	Right nephroureterectomy	Compact spindle cells, hypo-cellular fibrous tissue, oedematous myxoid background; small lymphocytes, plasma cells, small bone area Vimentin +VE SMA +VE CD68 +VE Desmin -VE MF116 -VE SyN -VE S100 -VE HMB45-VE CD117 -VE	Details of long-term outcome not available to author
Chen et al. [22] 2008	50 years Male Incidental during investigation for stone disease	Details of imaging not available to author	Laparoscopic radical nephrectomy (site not stated in abstract)	Histology & imunohistochemistry consistent with IMT	Details of long-term outcome not available to author
Ryu et al. [1] 2010	61 years, Female Incidental finding during investigation for weight & gastrointestinal symptoms	Contrast-enhanced CT scan & MRI scan, Left kidney mass	Laparoscopic radical nephrectomy	Dense collagenous fibrous tissue; Spindle cells with myxoid change, lymphocytes & plasma cells, Vimentin +VE, Actin focally +VE EMA focally +VE Cytokeratin -VE, HMB45 -VE Cyclin D1 -VE, S-100 -VE, C-kit -VE, CD31 -VE, CD34 -VE, Desmin -VE	No recurrence at 3 months follow-up
Santos et al. [23] 2010	74 years, Female Right upper quadrant abdominal pain	CT scan Right renal mass	Laparoscopic right radical nephrectomy	Spindle cells with prominent nucleoli, plasma cells & lymphocytes; ALK +VE, Vimentin +VE CK18 +VE CK-AE 1/3 +VE CAM5.2 +VE	
Lee et al. [28] 2011	48 years, Male Incidental finding	MRI scan Septated cystic right renal mass	Laparoscopic right partial nephrectomy	Grey white lesion with gelatinous consistency, bland looking spindled shaped cells in myxoid background & lymphoid aggregates	Long-term outcome not available
Khallouk et al. [29] 2011	57 years Visible haematuria & left lumbar pain	Ultrasound scan & CT scan Cystic tumour in left kidney	Left radical nephrectomy	Spindle cells admixed with variable collagen, lymphocytes, plasma cells & siderophages. Vimentin +VE, HHHF +VE, SMA focally +VE	No recurrence at 14 month follow-up

Li et al. [30] 2013	48 years, Female Asymptomatic & incidental but history of trauma 13 years earlier, hepatitis B 20 years earlier & subsequently cirrhosis of liver, hypersplenism & coagulation disorder	CT Scan & MI Scan Upper pole left renal mass	Left radical nephrectomy	Spindle fibroblast-like cells, collagen, lymphocytes & plasma cells	At 6 months follow-up no recurrence
Jenkins et al. [31] 2013	61 years, Male Back pain & haematuria	Ultra-sound scan & CT scan, left lower pole kidney heterogeneous mass & enlarged nodes medial to mass	Left laparoscopic radical nephrectomy & lymphadenectomy	Histology & immunohistochemistry consistent with IMT	Long-term outcome not available
Navale et al. [32] 2013	32 years, Male Lower abdominal pain & lower urinary tract symptoms	CT scan Lower pole Right Kidney Heterogeneous mass & calcification in mass	Right radical nephrectomy	Hard gritty tumour with cellular and hypocellular hyalinised areas; spindle cells in short fascicles and storiform pattern with atypia & prominent mitotic activity 4-7 per HPF, lymphoid aggregates germinal centre formation & plasma cells, extravasated red blood cells in some areas, heterotopic bone formation & osteoblastic cells; mitotic state 3 to 6 per HPF, SMA strongly +VE P53 +VE in few CD34 -VE ALK-1 -VE CK7 -VE, CD23 -VE, CD21-VE, H-Caldesmon --VE	He was alive & well with no recurrence at his 18-month follow-up
Baspinar et al. [33] 2013	78 years, Female	Imaging not stated but had ultrasound guided thoracentesis and paracentesis for pleural effusion and ascites 7 months after operation left renal mass with local invasion	Left radical nephrectomy & splenectomy plus partial resection of pancreas	Histology consistent with IMT SMA +VE ALK +VE Vimentin +VE	She subsequently developed pleural effusion & ascites and underwent ultrasound guided thoracentesis and paracentesis and its

					cytology was benign but died 7 months postoperatively due to complications of tumour invasion and treatment 7 months post-operatively
Galaway et al. [34] 2014	71 years, Female Incidental	Imaging technique was not available to author but had core biopsy of kidney and site not available to author	Conservative treatment after biopsy with no surgical operation	Histology consistent with IMT	The renal tumour resolved spontaneously and this was confirmed by radiological scanning
Taheri et al. [35] 2014	15 years Female Weight loss, haematuria, Left flank pain	CT scan Upper pole left kidney solid mass	Left radical nephrectomy & adrenalectomy	Yellowish well-defined mass with intact capsule Spindle cells with elongated processes in myxoid background & occasional atypia in nucleoli, at times prominent nucleoli, lymphoplasmatic infiltration, occasional eosinophils & neutrophil infiltration; SMA +VE Vimentin +VE Actin focally +VE EMA -VE Cytokeratin 7 -VE CD34 -VE Bcl2 -VE Desmin -VE	Long-term outcome not available
Dogan et al. [36] 2015	3 years Male	Details of radiological imaging not available to author	Kidney with multiple nodules	Details of treatment not available to author	Details of outcome not available to author
Liang et al. [37] 2015	60 years Female Health care screening	Ultrasound scan & CT scan “Solitary cyst” in upper pole of left kidney mixed echo-genic mass	Resection of renal cystic mass with frozen section histological examination	Histology consistent with IMT; SMA strongly +VE CD68 +VE CD10 +VE Interspersed Ki67 +VE ALK -VE CD34 -VE	Case not reported with details of long term outcome
Babu et al. [38] 2015	51 years Male Left flank pain	Ultrasound scan showed contracted left kidney & hydronephrosis + cortical calcification Contrast enhanced	CT guided left renal biopsy showed features of pyelonephritis Laparoscopic left radical nephrectomy	Interlacing fascicles of spindle cells, plasma cells, eosinophils, collagen bundles with xanthogranulomatous change Vimentin strongly	Details of long term outcome not available to author

		CT showed mass in upper pole of left kidney		+VE; SMA strongly +VE ALK focally +VE	
Wu et al. [40] 2015	43 years Male Iterative visible haematuria	CT Scan & MRI Scan Slightly enhanced mass in left renal pelvis	Left nephrectomy	Spindle cells with features consistent with IMT	Details of long-term outcome not available to author
Park et al. [39] 2008	67 years Male Presentation not stated	CT scan Solid lesion lower of left kidney	Left radical nephrectomy	Pathological results indicated IMT	Details not in paper
Park et al. [39] 2008	46 years Male Presentation not stated	CT scan Bulbous enlargement of pancreas & multifocal low-attenuation lesions in both kidneys	Ultra-sound guided renal biopsy led to the pathological diagnosis of IMT Details of treatment was not documented in paper	Pathological examination of renal biopsy revealed features diagnostic of IMT	Details of treatment and outcome were not reported in paper

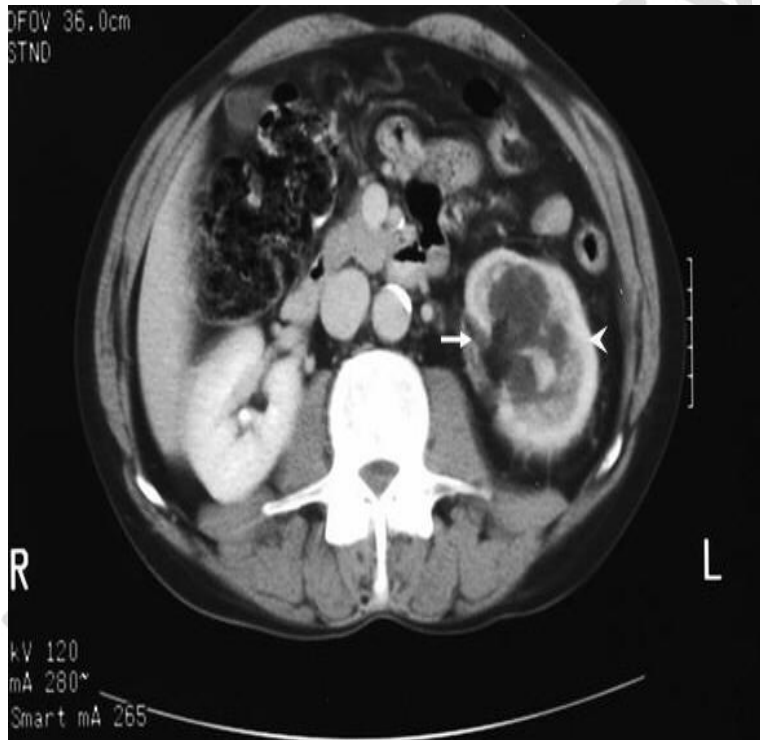


Figure 1: CT scan showing PUJ obstruction (arrow) with ill-defined fascial planes around the left kidney (arrow head) that is consistent with inflammation. Reproduced from [10] Selvan D R, Philip J, Manikandan R, Helliwell T R, Lamb G H R, Desmond A D. Inflammatory pseudotumor of the kidney World Journal of Surgical Oncology 2007 Sep 24; 5: 106 DOI: 10.1186/1477-7819-5-106 under the Creative Commons Attribution License This article is published under license to Bio Med Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Figure 2: Photomicrograph showing: [a] vaguely nodular areas of collagenous tissue with scattered spindle cells and darker inflammatory cells at the edges of the collagenous nodules. (H & E, x 60) [b] More cellular area where there is a pale, eosinophilic collagenous background with pale spindle cells and darker inflammatory cells scattered without any particular pattern. (H & E, x 150) [c] Pale nuclei of the spindle cells with scattered darker lymphocytes and plasma cells in a pale, eosinophilic background. (H & E, x 250) [d] Immunocytochemical labelling for smooth muscle actin, shown as brown strands of filamentous material in the cytoplasm of the myofibroblasts. (Immunocytochemical labelling, smooth muscle actin, x 250) Reproduced from: [10] Selvan D R, Philip J,

Manikandan R, Helliwell T R, Lamb G H R, Desmond A D. Inflammatory pseudotumor of the kidney World Journal of Surgical Oncology 2007 Sep 24; 5: 106 DOI: 10.1186/1477-7819-5-106 under the Creative Commons Attribution License This article is published under license to Bio Med Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

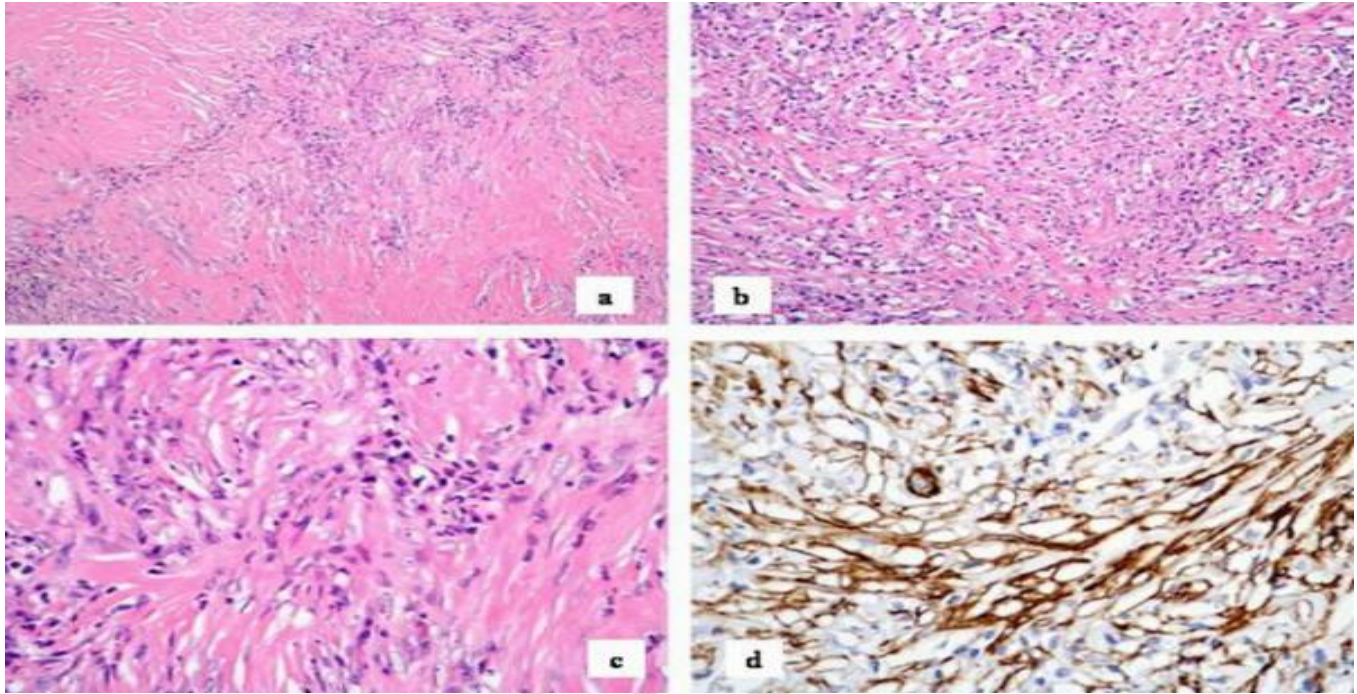


Figure 3: Immunocytochemical labeling for vimentin (3a) and CD34 (3b) showing spindle cells within the tumour positive for vimentin and CD34 (x 250) Reproduced from: [10] Selvan D R, Philip J, Manikandan R, Helliwell T R, Lamb G H R, Desmond A D. Inflammatory pseudotumor of the kidney World Journal of Surgical Oncology 2007 Sep 24; 5: 106 DOI: 10.1186/1477-7819-5-106 under the Creative Commons Attribution License This article is published under license to Bio Med Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License(<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

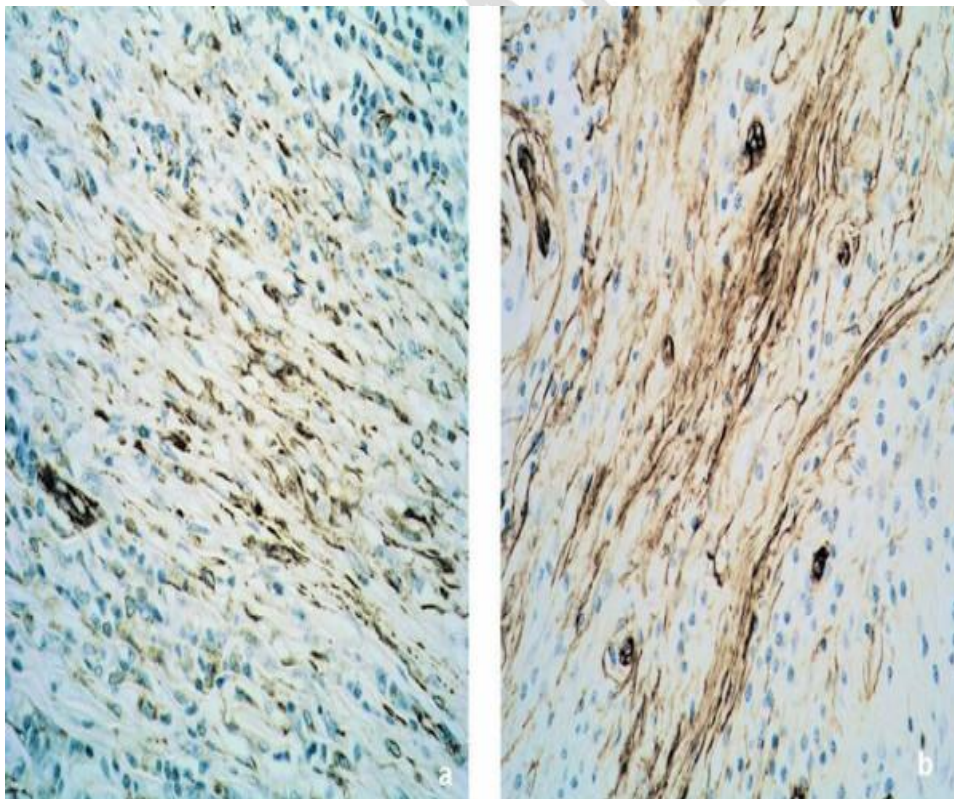




Figure 4: Magnetic Resonance image demonstrates a 3.0 x 2.5 cm size solid mass with mildly enhancement on left with a central necrotic portion. Reproduced from: [1] Ryu K H, Im C M, Kim M K, Kwon D, Park K, Ryu S B, Choi C. Inflammatory Myofibroblastic Tumor of the kidney Misdiagnosed as Renal Cell Carcinoma. J Korean Med Sci 2010 Feb; 25(2): 330 – 332 published online 2009 Jan 26. DOI: 10.3346/jkms.2010.25.2.330 under the Creative Commons Attribution License Copyright © 2010 The Korean Academy of Medical Sciences This is an Open Access article distributed under the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.



Figure 5: Left kidney coronal opening specimen shows a well-circumscribed encapsulated mass measuring 2.7 x 2.8 cm size, involving the lower pole. The mass revealed areas of myxoid change necrosis, and cystic change. Reproduced from: [1] Ryu K H, Im C M, Kim M K, Kwon D, Park K, Ryu S B, Choi C. Inflammatory Myofibroblastic Tumor of the kidney Misdiagnosed as Renal Cell Carcinoma. J Korean Med Sci 2010 Feb; 25(2): 330 – 332 published online 2009 Jan 26. DOI: 10.3346/jkms.2010.25.2.330 under the Creative Commons Attribution License Copyright © 2010 The Korean Academy of Medical Sciences This is an Open Access article distributed under the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Figure 6: Microscopic findings (A): The lower power appearance demonstrating a capsule of dense collagenous fibrous tissue and myxoid zone and inflammation with cellular zone consisting of spindle cells arranged in fascicles. B: The area of myofibroblastic proliferation showing densely cellular fascicles. The tumor cells were positive for smooth muscle actin (C) and vimentin (D). Reproduced from: [1] Ryu K H, Im C M, Kim M K, Kwon D, Park K, Ryu S B, Choi C. Inflammatory Myofibroblastic Tumor of the kidney Misdiagnosed as Renal Cell Carcinoma. J Korean Med Sci 2010 Feb; 25(2): 330 – 332 published online 2009 Jan 26. DOI: 10.3346/jkms.2010.25.2.330 under the Creative Commons Attribution License Copyright © 2010 The Korean Academy of Medical Sciences This is an Open Access article distributed under the Creative Commons Attribution

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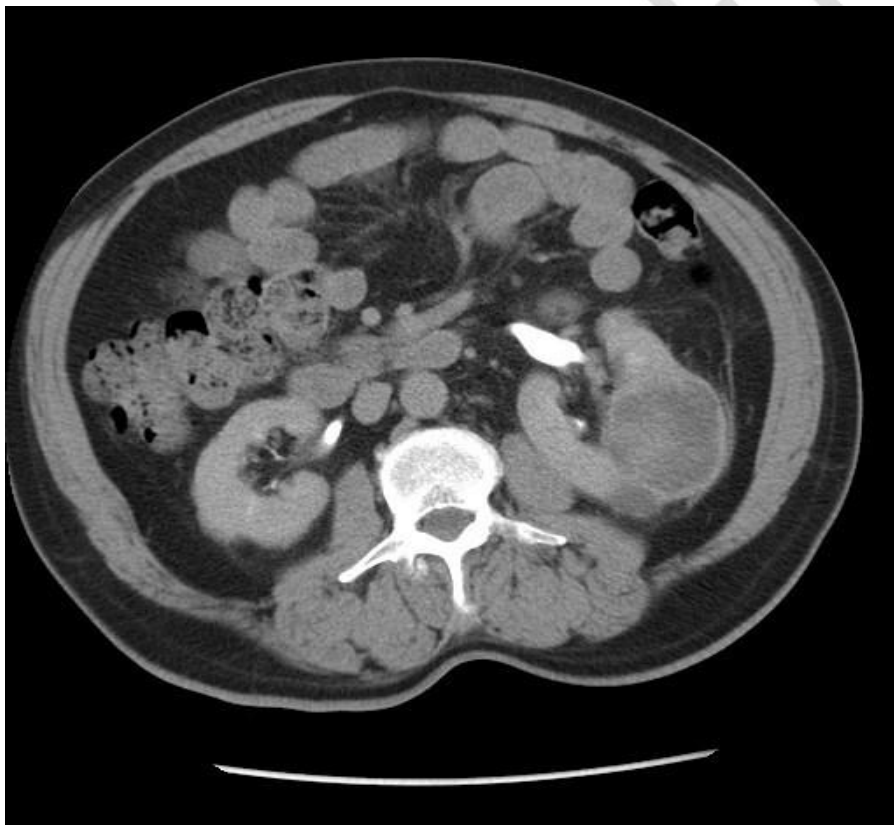
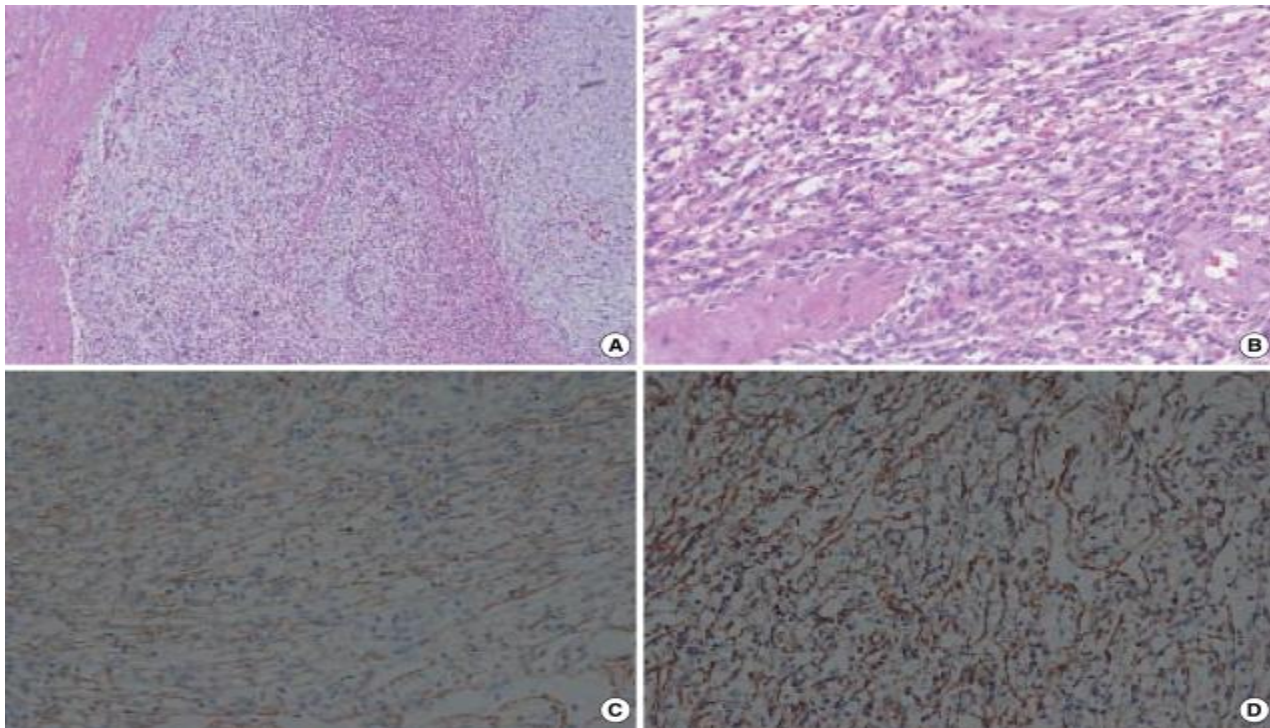


Figure 7: CT scan showing a huge cystic tumour of the left kidney
Reproduced from: [29] Khallouk A, Ahallal Y, Tazi M F, Elfatemi H, Tazi E, Elammari J, Elfassi M J, Farih M H. Inflammatory pseudotumor of the kidney: a case report. Journal of Medical Case Reports 2011 Aug 24; 5: 411. DOI: 10.1186/1752-1947-5-411 under the Creative Commons Attribution Licence © 2011 Khallouk et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Figure 8: Photomicrograph showing dense collagen fibrous tissue and inflammation with cellular zone consisting of spindle cells (HES x 5) Reproduced from: [29] Khallouk A, Ahallal Y, Tazi M F, Elfatemi H, Tazi E, Elammari J, Elfassi M J, Farih M H. Inflammatory pseudotumor of the kidney: a case report. Journal of Medical Case Reports 2011 Aug 24; 5: 411. DOI: 10.1186/1752-1947-5-411 under the Creative Commons Attribution Licence © 2011 Khallouk et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

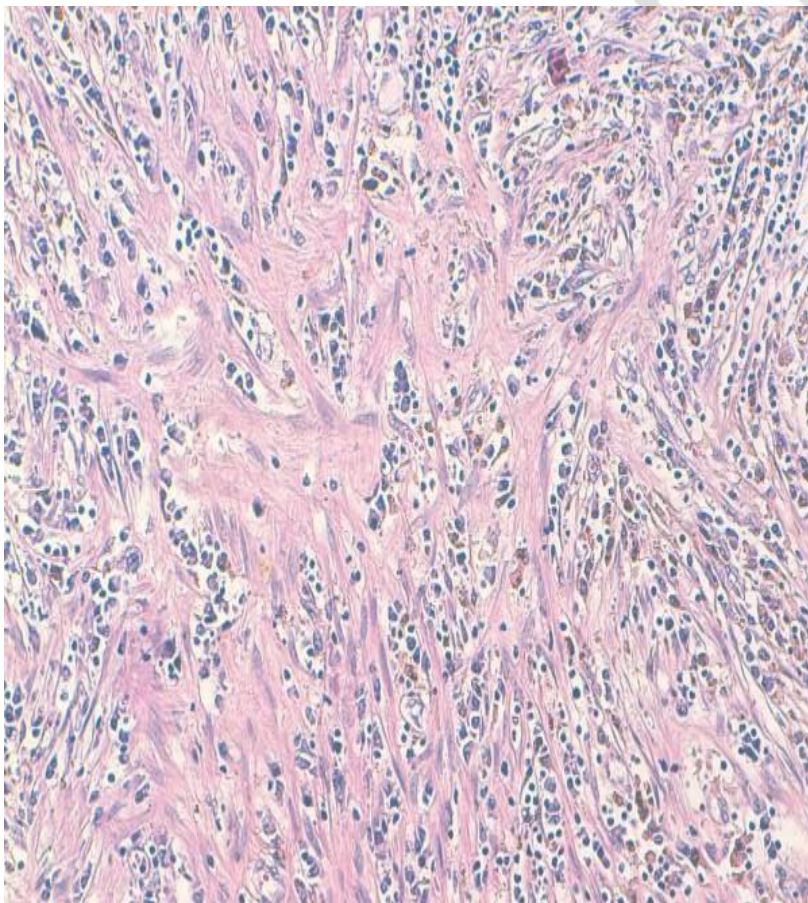


Figure 9: Photomicrograph showing area of myofibroblastic proliferation with plasma cells and siderophages (HES x 20) Reproduced from: [29] Khallouk A, Ahallal Y, Tazi M F, Elfatemi H, Tazi E, Elammari J, Elfassi M J, Farih M H. Inflammatory pseudotumor of the kidney: a case report. Journal of Medical Case Reports 2011 Aug 24; 5: 411. DOI: 10.1186/1752-1947-5-411 under the Creative Commons Attribution Licence © 2011 Khallouk et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.