

FAMILIAL RENAL RETROPERITONEAL LYMPHANGIOMATOSIS: PERSONAL EXPERIENCE AND REVIEW OF LITERATURE

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Lymphangiomas of the kidneys and perirenal-retroperitoneal tissues is a rare disease of unknown etiology. We present two cases affecting members of the same family, supporting the familial nature of the disease. The natural history and related urological and systematic complications of the disease during a long-term follow-up are highlighted, while a comprehensive literature review is presented.

Key-words: Lymphangiomas – Kidney, diseases.

Lymphangiomas of the kidneys and perirenal-retroperitoneal tissues is an extremely rare disease of unknown etiology. Currently, only Meredith et al. (1) have supported the familial nature of the disease, having found exacerbation of renal lymphangiomas during pregnancy in two sisters. We present the cases of two siblings affected by the disease, supporting its familial predisposition, and we highlight the diagnosis, the natural history and the potential complications related to this rare entity. A comprehensive literature review also enlightens the reader's knowledge.

Material and methods

We present the cases of two siblings diagnosed with renal lymphangiomas. Following the diagnosis of the first case we have examined the whole family discovering one more affected patient. After establishing the diagnosis, we have followed the two patients to depict the natural history of the disease and its potential urological and systematic effects. Due to the rarity of the disease we have searched the Medline, Pubmed and EmBase databases to systematically review the literature published on this entity.

Results

In 1998, a 39 year-old woman (patient A), with a negative past-medical and past-surgical history, presented to the emergency department with a right lower quadrant abdominal pain radiating to the hypogastrium. There were no other concomitant symptoms. Physical examination revealed diffuse abdominal tenderness and a low

grade fever (37.3 °C). Routine blood tests and blood pressure measurement were normal. Urinalysis revealed microscopic haematuria (12-20 RBC / HPF), and leucocyturia (WBC 20-50/HPF) without proteinuria. Urine culture was positive for *Klebsiella* for which antibiotic therapy was given.

Abdominal ultrasonography (US) showed multiple parapelvic cystic lesions with bilateral low-grade dilatation of the renal pelvicalyceal systems. Abdominal computed tomography (CT) before and after the intravenous (IV) contrast material (CM) administration demonstrated multiple cystic lesions of low attenuation (0-10HU) in both renal pelvises. Similar lesions were also observed in the perirenal, pararenal and paraortic space. There was no contrast material uptake by the cysts. Some of the aforementioned cystic lesions demonstrated an irregular shape while others were tubular-shaped consistent with lymphangiectasias.

The lesions communicated with those on the contralateral side across the midline. The renal outline was not distorted and the renal parenchymal thickness was normal (Fig. 1). Based on the previously mentioned CT findings renal-retroperitoneal lymphangiomas (RRL) was the likely diagnosis. It was confirmed by fine needle aspiration (FNA) of the retroperitoneal lesions which confirmed the fluid to be lymph.

Following the establishment of diagnosis in patient A, her whole family (brother, sister and parents) was clinically examined and radiologically evaluated. A male sibling (patient B), aged 37, with a positive 17-year history of hypertension on ACE inhibitors, showed multiple bilateral parapelvic renal cystic lesions and a moderate dilatation of the pelvicalyceal system. Renal function was normal. Computed tomography revealed additional perirenal and paraortic lesions of various



Fig. 1. – Transverse contrast enhanced abdominal CT (CECT) demonstrates a tubular low attenuation lesion in the anterior pararenal and paraortic space. There is a communication between the pararenal lesions across the midline. Parapelvic cysts are demonstrated in both kidneys.

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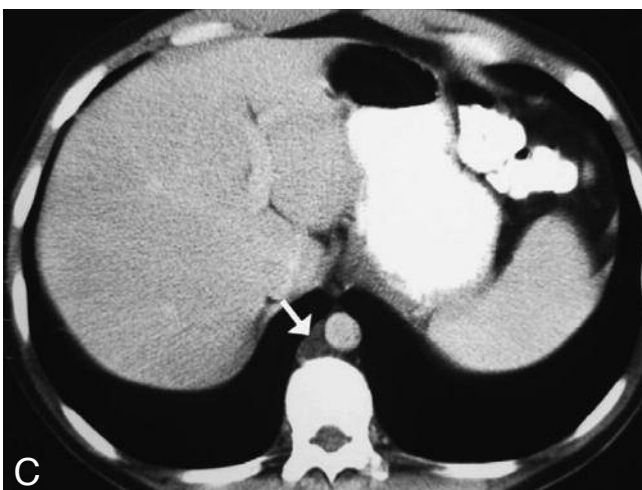


Fig. 2 A-C. — Abdominal CECT demonstrates dilated lymphatic vessels involving the right perirenal space and parapelvic cystic lesions in both kidneys. In comparison with previous CT examinations the parapelvic cysts increased in size. Perivascular lymphangiectasias surrounding the abdominal aorta and the inferior vena cava are also present. CECT demonstrated a moderate dilatation of the renal collecting system in both kidneys and a low attenuation lesion located in the right paravertebral space, extending to the thorax, representing dilated lymphatic vessels (white arrow).



Fig. 3. — CECT of patient A. In comparison to the previous CT (Fig 1) no changes were identified, apart from a slight increase in the size of the lymphangiectasias.

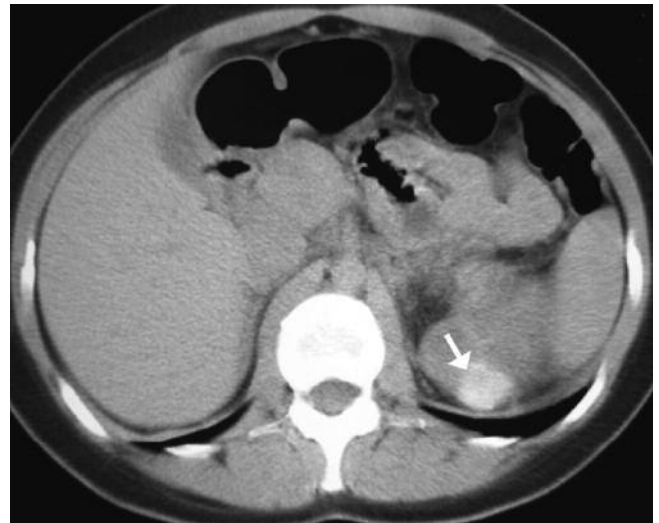


Fig. 4. — CECT section at the level of the upper pole of the left kidney shows dilatation and clubbing of the upper calyceal moiety (white arrow) with concomitant parenchymal thinning, findings consistent with focal chronic pyelonephritis. The patient suffered from frequent bouts of UTI.

shapes (lobulated, tubular-shaped) and of low attenuation (0-10HU), as well as a right paravertebral lesion with low attenuation which extended to the thorax. The pararenal lesions communicated with those on the contralateral side across the midline. Renal parenchymal thickness was normal (Fig. 2A-C). The aforementioned CT findings were diagnosed as lymphangiectasias and a diagnosis of familial renal-retroperitoneal lymphangiomas (FRRL) was made. Based on the lack of urinary tract complications on both patients at presentation and the long-lasting hypertension of the male patient, no further treatment was decided and

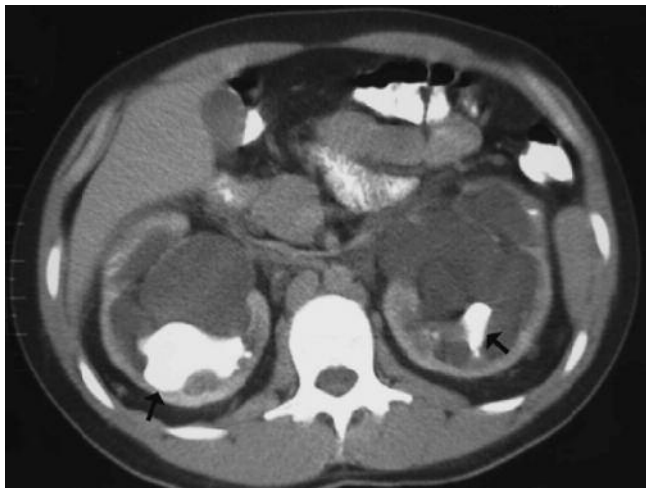


Fig. 5. — CECT of patient B at the level of the kidneys shows bilateral large parapelvic cystic lesions, compression of the contrast enhanced renal cortex and dilatation of the renal collecting systems (black arrows). In comparison with previous CT examinations the parapelvic cysts increased in size.

the patients were advised for regular follow-up.

During the first two years of follow-up, patient A remained asymptomatic and no further changes in comparison to the previous CT were identified, apart from a slight increase in the size of the lymphangiectasias (Fig. 3). On occasion of recurrent urinary tract infections started in 2005 (2-3 bouts per year), an ultrasound confirmed the slight increase in the pelvicalyceal system dilatation, more prominent in the left kidney. In 2007, during a new UTI episode, CT scan findings were indicative of chronic pyelonephritis with clubbing of the upper calyceal moiety of the left kidney and concomitant parenchymal thinning (Fig. 4). A lesser pelvis fluid collection was also seen. The urine culture was positive for *Escherichia Coli* at that time for which the patient received the appropriate antibiotic therapy. A follow-up US performed one month later showed a marked decrease of the pelvic fluid collection.

Patient's B compliance to follow-up was not strict and he underwent a repeat CT scan in 2004, which showed thinning of the renal parenchyma, a greater bilateral pelvicalyceal dilatation as well as a slight increase in the size of the perirenal, paraortic and paravertebral lymphangiectasias in comparison to the previous CT examination performed six years ago (Fig. 5). Despite the worsened CT findings the patient's renal function remained

stable. The patient declined a renogram and no further treatment was initiated, while he denied further radiological follow-up.

Discussion

RRL is a rare disease of unknown origin (1, 2). Although the familial nature of the disease has been previously inferred (3), the affection of siblings has been presented only once in the literature previously (1). Our report adds to the presumption of RRL's familial nature, strengthens the anatomical findings and the extension of the disease, adds to the understanding of the natural history, and finally recognizes factors that may exacerbate the disease.

Disease pathogenesis indicates that a failure of the developing lymphatic tissue to establish normal communication with the rest of the lymphatic system results in an abnormal lymphatic drainage with subsequent cyst formation (1, 4-9). These cysts are lined by endothelium (2), indicative of their vascular origin, and contain lymph and proteinaceous material (2).

The anatomical distribution of renal lymphatics, its drainage to the retroperitoneal lymphatic system and the connections to the contralateral site explain the findings in RRL. Involvement of the intrarenal medullary and cortical lymphatics, of the big renal lymph node system and the paraortic lymph nodes lead to lymphatic vessel obstruction and finally to the formation of parapelvic,

perirenal, pararenal, retroperitoneal and paravertebral cysts (8). Autopsy studies showed that kidney's lymphatics also reach distant lymph nodes (10). This may explain the lack of anatomical consistency of findings in all patients as well as a cyst location distally to kidneys. The findings in our cases are relevant to the anatomical distribution and drainage of renal and retroperitoneal lymphatics, support the bilateral nature of RRL, while for the second time in literature show a midline connection between the pararenal lymphangiectatic lesions. The later can be explained by autopsy studies showing a connection across the midline between the anterior pararenal spaces in contrast to the perirenal spaces (11, 12).

While RRL can be asymptomatic and incidentally diagnosed by imaging modalities (6, 13), clinical manifestations include abdominal pain and distention, a palpable abdominal mass (8, 13), and haematuria and/or proteinuria (2, 6). Early at diagnosis renal function tests are within normal limits (8). CT findings in combination with clinical and laboratory tests are considered sufficient to establish the diagnosis of RRL (2, 7, 14). FNA of the lesions may also be helpful, but it is not always diagnostic for the disease (9, 15). RRL's differential diagnosis includes polycystic kidney disease (6, 8); tumors such as multilocular cystic nephroma; cystic renal cell carcinoma; lymphoma; sarcomas (5, 6); renal abscess; urinoma (6) and renal pelvis lipomatosis (2).

Magnetic Resonance Imaging (MRI) is also considered a useful diagnostic tool for RRL and several imaging findings have been described (13, 16-18).

Cystic lesions in RRL are demonstrated with the typical fluid signal intensity, that is low on T1-weighted and high on T2-weighted images (16). However, varying signal intensities of cysts have also been described, probably due to different internal ratios of fat, fluid or chyle (17).

MRI is also helpful in demonstrating thin retroperitoneal perivascular fluid-filled lymphatic channels (18).

Furthermore, rare but possible complications of RRL may be depicted with MRI, such as haemorrhage inside the cysts, demonstrated as hyperintense foci on T1-weighted images, or cystic rupture with ascites representing an indirect finding (13, 16, 18).

Advantages of MRI over CT include primarily the lack of patient

irradiation and also administration of iodinated intravenous contrast agent. Considering repeatability of imaging during follow up of patients with RRL as well as the possible contraindication of contrast enhanced CT due to potential renal impairment, MRI is probably considered safer than CT.

Multiplanar MRI is also helpful in revealing the exact extent of renal and retroperitoneal disease as well as the non-parenchymal origin of the cysts (18).

Additionally, MRI with MR urography (MRU) images obtained, with or without iv contrast administration, may evaluate both urinary tract morphology and renal function, while MR angiography (MRA) may yield information about renal vessels (18). The latter, is of great importance in patients with RRL complicated with arterial hypertension.

The natural history of the disease has not been well documented due to its rarity. In our cases the follow-up was 11 years for the first patient and 6 years for the second patient, which constitutes the larger follow-up ever documented in literature. During the course of the disease increase in cyst size, infection of the cystic fluid (14), obstructive uropathy and abnormal renal function due to renal parenchymal compression from the cystic lesions (19), bilateral renal vein thrombosis (15), and perirenal fluid collections and ascites may develop (1, 14). Radiological findings of development of chronic pyelonephritis were also shown as a complication of the disease in our series.

Although we were unable to unfold the etiology of longstanding hypertension in one of our cases, the latter may be secondary to the activation of rennin-angiotensin system due to ischemia caused by renal parenchyma compression from the cystic lesions (Page kidney) (20). The latter explains the successful treatment of hypertension with ACE inhibitors in our case.

Disease exacerbating factors are also not well known. Pregnancy was correlated with increase in perirenal fluid collection, superinfection of the fluid collections and the development of ascites (14). Our study shows for the first time in literature that urinary tract infection is another significant triggering factor of increase of parapelvic lymphatic vessels' size, deterioration of the pelvicaliceal dilatation and increase in fluid collection.

Asymptomatic RRL does not require treatment (13, 18). On the

other hand, percutaneous drainage (1, 14), laparoscopic cauterization (21) and surgical excision (2, 19) of the cystic lesions should be the treatment options in symptomatic patients. Surgery should be considered an option only in severe cases due to its high risk of nephrectomy and haemorrhage (2). Nephrectomy is no longer considered a choice, since in case of asymmetrical bilateral involvement, the cysts in the contralateral kidney may increase in size (2, 20). Antibiotic treatment is reserved for the case of superinfection of the lesions (14) and may lead to significant decrease of cystic and perirenal fluid accumulation in the case of a concomitant urinary tract infection, as shown in our case.

Conclusions

Renal lymphangiomas may be a disease of familiar origin. Most characteristic CT findings are parapelvic cystic lesions and perirenal and pararenal, hypodense lesions of various shapes, often tubular, corresponding to lymphangiectasias. During the course of the disease the dilated lymphatic vessels may increase in size, obstruct the urinary collecting system and in time result in chronic pyelonephritis and hypertension. Concomitant urinary tract infections may exacerbate the disease and necessitate appropriate treatment.

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