CASE REPORT

Late spontaneous decapsulation of the kidney graft in a patient with hepatitis C and treated with sirolimus: possible pathophysiological association in a rare complication

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SUMMARY

Late decapsulation with fluid collection is a rare complication of renal transplantation with deleterious effects on kidney function. Its pathophysiology is unclear but there might be an association with mammalian target of rapamycin (m-TOR) inhibitors, especially in patients with chronic hepatitis C. We report a case of late spontaneous decapsulation 12 years after kidney transplant in a patient infected with hepatitis C under treatment with sirolimus. He underwent marsupialisation of the collection, sirolimus was converted to cyclosporine and hepatitis C treatment was performed with success. This is the first successful case report of late spontaneous decapsulation of the kidney graft in a patient with hepatitis C.

BACKGROUND

Perirenal collections after kidney transplantation are common in the early postoperative period and the common aetiologies are urinomas, haematomas, abscesses and lymphoceles that can be easily identified. Despite, there is a rare entity, with only 11 cases described in literature that does not fit in the previous: fluid leakage from late spontaneous decapsulation of the kidney graft.^{1–7} These collections should be distinguished from usual lymphoceles for the different clinical features and also because treatment and prognosis are distinctive. Although more data are needed, there seems to be an interaction between mammalian target of rapamycin (m-TOR) inhibitors and hepatitis C virus (HCV) infection that increases the incidence of this lymphocele-like collection with spontaneous decapsulation.^{7–8} We present a second case of spontaneous kidney graft decapsulation with fluid collection in a patient with HCV under treatment with sirolimus, suggesting a possible pathophysiological association. He was successfully treated with marsupialisation, followed by HCV treatment and conversion from sirolimus to cyclosporine.

CASE PRESENTATION

A 54-year-old Caucasian man with HCV genotype 1b infection and end-stage renal disease of unknown cause underwent a deceased donor renal transplant in 2004. He was medicated with sirolimus (1 mg daily) and prednisone (5 mg daily) with sirolimus mean blood levels of 4.5 ng/mL in the

preceding 6 months. His baseline serum creatinine (sCr) was 1.2 mg/dL (0.72–1.18).

Twelve years after transplant he was admitted for progressive swelling and pain over his graft, without trauma, and slight decline of renal function (sCr=1.8 mg/dL). CT scan revealed a large fluid subcapsular collection encasing the renal graft, with 18×10×12 cm (figure 1). A subcapsular pigtail catheter was placed and over 2000 mL of a clear yellow-coloured fluid was drained that was compatible with a transudate with protein=0.4 g/dL, lactate dehydrogenase=34 µ/L, 27 cells/µL, creatinine=1.03 mg/dL, adenosine deaminase=2.6 µ/L (N<36 µ/L), triglycerides=4 mg/dL and negative cultures. The search for donor human leukocyte antigen (HLA) antibodies, cytomegalovirus and BK virus were negative. His HCV-RNA count was 627 117 µI/L but his liver function and enzymes were normal. For 20 days, fluid secretion through the pigtail catheter persisted with an output >2000 mL per day.

TREATMENT

He was converted from sirolimus to cyclosporine (50+25 mg, daily) plus prednisolone 5 mg daily. We instilled 30 mL of 5% povidine iodine through the catheter but the drainage did not decrease and the patient developed fever; *Pseudomonas aeruginosa* and *Enterococcus raffinosus* were isolated in the fluid. He was treated with meropenem and linezolid for 15 days. After the resolution of the infection, a laparoscopic exploration with fenestration of the kidney capsule to the peritoneal cavity was

Figure 1 Abdominal CT scan in the emergency room.

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Table 1 Main characteristics and outcome of the 11 cases of late decapsulation of kidney graft with fluid collection described in literature

Case report (authors)	Time post-transplant (years)	Collection volume (mL)	Immunosuppression treatment	Treatment	Follow-up
Koene 1979	5	4000–12 000	Azathioprine+prednisolone	Attempt to formation of new capsule	Nephrectomy
Koene 1979	3	>900	Azathioprine+prednisolone	Le Veen shunt	Nephrectomy
Nghiem 1982	7	2000	Azathioprine+prednisolone	Marsupialisation	Success
Tiggeler 1986	3	1500–3500	Azathioprine+prednisolone	New capsule with infrared coagulation	Success
Brown 1990	4	'Massive ascitis'	Azathioprine+prednisolone	Diuretics	Success
Mousson 1998	4	>1000	Azathioprine+prednisolone	Marsupialisation	Success
Mousson 1998	5	600–2000	Cyclosporine+prednisolone	Punctures	Success
Kulkarni 2004	1	'Massive ascitis'	Rapamycin+prednisolone	Retropertonealisation	Success
Yang 2008	12	>100 mL/day	Sirolimus+prednisolone	Marsupialisation	Nephrectomy
Myhre 2009	18	800	MMF+CsA+prednisolone	Marsupialisation	Success
Mestres 2012	4	'Profuse serous fluid'	MMF+everolimus+prednisolone	Marsupialisation	Success

CsA, cyclosporine; MMF, mycophenolate mofetil.^{1–7}

made. Immediately after the marsupialisation, the daily drainage decreased and finally disappeared.

OUTCOME AND FOLLOW-UP

Serial abdominal ultrasound scan showed no ascites or collection recurrence and sCr was stable at 1.2 mg/dL.

Immunosuppression with cyclosporine (with target blood levels of 150 ng/mL) and prednisolone 5 mg was maintained and norfloxacin 400 mg daily was started to prevent spontaneous bacterial peritonitis. Two weeks after discharge HCV therapy was started with ledipasvir 90 mg+sofosbuvir 400 mg daily for 12 weeks, and cured. Eight months after the procedure, there is no sign of recurrence, no ascites and his sCr is 1.1 mg/dL.

DISCUSSION

Perirenal collections after kidney transplantation are common in the early postoperative period and the common aetiologies are urinomas, haematomas, abscesses and lymphoceles that can be easily identified.

Despite, there is a rare entity, with only 11 cases described in literature that does not fit in the previous: fluid leakage from late spontaneous decapsulation of the kidney graft (table 1).^{1–7}

This condition is a lymphocele-like fluid collection with some unusual characteristics: late occurrence, subcapsular location, and large amount of fluid and rapid recurrence after puncture. These collections should be distinguished from usual lymphoceles for the different clinical features and also because treatment and prognosis are distinctive: they are usually symptomatic, cause renal function decline and frequently require surgical treatment.

The physiopathology of these collections remains unclear. The fluid composition, suggests transudation from the kidney cortex after decapsulation or a rupture of the subcapsular lymphatics of the graft leading to the capsule detachment.^{2 4}

In our case as well as three other reported cases,^{1 6 7} there is a possible pathophysiological mechanism similar to lymphoceles, the higher incidence in patients under m-TOR inhibitors. There is evidence that m-TOR inhibitors interfere with the activation of lymphatic endothelial cells by vascular endothelial growth factors (VEGF)-C and antilymphangiogenic activity is a general phenomenon of m-TOR inhibition.^{9 10}

Another interesting issue regarding our clinical case, and also present in the report by Yang *et al*⁷ is the occurrence of spontaneous decapsulation in patients with HCV infection. There is a retrospective study that evaluated 85 consecutive patients with

renal transplant for the development of lymphoceles that found that five out of the seven patients with HCV and under treatment with sirolimus developed a lymphocele.⁸ In patients with chronic inflammation such as with HCV, there is a release of inflammatory cytokines that may interfere with the release of VEGF.¹¹

Although more data are needed, there might be an interaction between m-TOR inhibitors and HCV infection, through a mechanism related with the regulation of VEGF that increases the incidence of this lymphocele-like collection with spontaneous decapsulation.

Regarding therapy, there is no consensus on the best approach, and we based our actions on the cases previously described in the literature (table 1).

First, we tried instillation of sclerosing agents to avoid a surgical procedure, but without success. Afterwards, we performed marsupialisation of the kidney capsule to the peritoneal cavity with immediate resolution of the collection and no recurrence so far.

In conclusion, we present the second case of spontaneous kidney graft decapsulation with fluid collection in a patient with HCV under treatment with sirolimus, suggesting a possible pathophysiological association. He was successfully treated with marsupialisation, followed by HCV treatment and conversion from sirolimus to cyclosporine.

Learning points

- ▶ Late decapsulation with fluid collection is a rare complication of renal transplantation with deleterious effects on kidney function.
- ▶ These collections should be distinguished from usual lymphoceles because treatment and prognosis are distinctive.
- ▶ There might be an interaction between m-TOR inhibitors and hepatitis C infection that increases the risk of lymphoceles and lymphocele-like collections.
- ▶ Marsupialisation of the kidney capsule to the peritoneal cavity was the most effective treatment in our case and other cases described in the literature.

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Competing interests None declared.

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