Lymphocele After Kidney Transplantation
Where Are We Standing Now?

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INTRODUCTION

Lymphocele is a lymphatic collection around a transplanted kidney. Diagnosis is made when there is a pelvic collection with similar properties to the plasma. This can be confirmed with biochemical analysis of the fluid that shows similar electrolyte content compared with the plasma with low protein level. On microscopic evaluation, presence of lymphocytes can be a useful clue.[1]

Lymphocele occurs 2 weeks to 6 months after transplantation with its peak incidence being at 6 weeks. On the other hand, its development following trauma to the kidney and delayed formation 8 years after transplantation has been reported, too.[2] The incidence of clinically significant lymphocele is about 20%, but it may develop in 12% to 40% of transplant recipients.[3,4] Since the introduction of ultrasonography, in about half of transplanted kidneys, collections smaller than 50 cm^3 can be detected, most of which are less than 3 cm in diameter and resolve spontaneously. Indeed, most of the lymphatic collections are subclinical.[3]

ETIOLOGY

Radioisotope studies suggest that most lymphoceles originate from leakage of lymph from unligated iliac vessel lymphatics of the recipient. The drainage route of the lower limb lymphatic vessels is along the iliac vessels. As a consequence, when the iliac vessels are mobilized for anastomosis, some lymphatic vessels are unavoidably divided. Lymphocele can also originate from transplanted kidney lymphatic vessels.[1]

In a study by Sansalone and colleagues, cephalad implantation of the kidney in the ipsilateral iliac fossa to the common iliac vessels in comparison with standard operation (in the contralateral iliac fossa and anastomosis to the external iliac vessels) was accompanied by a significant lower rate of lymphocele formation (2.1% versus 8.5%), and it was assumed that this was due to less lymphatic manipulation in the former operative technique.[5] Hamza and colleagues demonstrated that there was no relationship between the extent of iliac vessel preparation and lymphocele occurrence[6]; however, they recommended that to prevent lymphocele formation, transplanted bed be restricted to the least possible and lymphatic vessels be ligated precisely at the hilum of the kidney allograft. Because the lymph does not have any clotting factor, all of lymphatic vessels must

be tied or clipped, but diathermy is not suggested.

It is unexplained why the lymph from the transplanted kidney has a small role in lymphocele formation. Probably, the inflammatory process associated with allograft presence increases the flow of lymph from lymphatic vessels around the iliac vessels.[1] Ligation of the lymphatic vessels during preparation of either the graft or the site of transplantation and appropriate external drainage thereafter can reduce the incidence of lymphocele.[7] It has been shown that limitation of vessel dissection does not increase the major vessel complications or pulmonary emboli after kidney transplantation.[8]

There is some evidence that incidence of lymphocele has decreased since introduction of low-steroid regimens for immunosuppression. However, there are controversies in literature about this matter.[9-11] In a study by Goel and colleagues, combination of sirolimus, mycophenolate mofetil, and prednisone was an independent factor for lymphocele occurrence by a mechanism of delayed healing of wound and injured lymphatic vessels.[9] Also, Langer and Kahan suggested the impact of sirolimus on the risk of lymphocele.[10] Tondolo and colleagues, however, questioned this mechanism and showed that the incidence of lymphocele is similar in multiple immunosuppressive regimens.[11]

There are also other factors associated with lymphocele in kidney transplant recipients. It has been reported that that obese patients have a longer operative time and more frequently suffer from wound infection, perinephric hematoma, and lymphocele.[12] Along with this finding, it should be noted that obesity (body mass index greater than 30 kg/m^2) is an independent risk factor for lymphocele formation.[9] There is evidence that although prophylaxis with high-molecular weight heparin can reduce graft losses secondary to thrombosis or vascular rejection, it can increase the incidence of lymphocele; Lundin and colleagues reported a higher frequency of lymphocele with heparin prophylaxis (43% versus 20%) in a group of 130 kidney allograft recipients. Such an increase was not associated with hemorrhagic events.[13] Finally, rejection episodes may have a role in lymphocele formation. In a study by Lipay and colleagues, high frequency of cellular rejection in patients with lymphocele was indicative of a possible cause-effect relationship.[14] In another study on 115 patients, multivariate analysis of possible lymphocele risk factors showed that only rejection was accompanied by high risk of lymphocele formation. The authors concluded that allograft rejection was most important contributing factor in lymphocele formation.[15]

CLINICAL MANIFESTATIONS

Most lymphoceles are clinically silent, but the most common manifestation is impaired graft function in the presence of perigraft collection and unilateral leg edema. Many other presentations have been recognized including: hypertension, pain, fever, frequency, ipsilateral thrombophlebitis, palpable mass, and lymphatic fistula.[1] even, a case of urinary retention due to compressive effect of lymphocele on the bladder neck has been reported.[16]

DIAGNOSIS

Ultrasonography is the key to diagnosis of lymphocele. Given its homogeneity and specific shape and position, lymphocele is distinct from blood clot. Most lymphoceles are inferior to the lower pole of the transplanted kidney, but are obviously separate from the bladder. Repeated ultrasonography after bladder drainage can differentiate the presence of lymphocele from a full bladder. Ultrasonography can show obstruction in the urinary tract that produces hydronephrosis. Furthermore, ultrasonography-guided aspiration allows biochemical and cytologic analysis. Infective lymphoceles are characterized by the presence of complex echo pattern inside the kidney.[1]

Most lymphoceles are routinely followed up with dynamic renal scintigraphy using technetium Tc 99m diethylenetriamine pentaacetic acid.[17] In a study on 14 patients by Kumar and colleagues, 3 patterns for lymphoceles were described: (1) an initial photopenic area that progressively fills with tracer activity with an equal level to the background activity in delayed films, (2) initial

photopenic areas with an activity more than the background activity in delayed films, (3) persistent photopenic areas in early and delayed films. In addition, they found that there is a rim of increased activity of tracer around the initial photopenic area in some patients.[17] The most common pattern of radiotracer activity in this study was an early photopenic area that is filled with tracer in delayed films. Presence of rim was in favor of lymphocele diagnosis.[17]

Additional radiological imagings such as intravenous urography and computed tomography are not necessary in typical cases, but they are required in complicated or equivocal ones.[1]

MANAGEMENT

Conservative Management. Small asymptomatic collections are common and usually resolve spontaneously. Therefore, conservative management can be satisfactory.

Simple Aspiration. Ultrasonography-guided aspiration is not only diagnostic, but also therapeutic in selected cases. It can be the initial treatment modality that allows relief of urinary obstruction, recovery of kidney function, and prevention of emergency situation. Although simple aspiration is sometimes therapeutic, it may be necessary to perform multiple sessions of aspiration and the rate of spontaneous recovery reduces after 3 recurrences. In addition, each aspiration brings about a low risk of infection.[1]

Sclerotherapy. Prolonged external drainage via percutaneous catheter and administration of a sclerosing agent (instillation) is also used. Recurrences have been reported in up to 20% of cases following sclerotherapy. Agents like ethanol, povidone iodine, and tetracycline have been used for this purpose.[1]

In a study by Tasar and colleagues, ethanol was used in 18 patients with symptomatic lymphoceles. The mean duration of therapy and mean alcohol volume in each session were 17 days and 30 cm^3, respectively. There was 1 case of recurrence, 1 graft loss, and 10 cases of minor complications including local discomfort and low grade fever. In their opinion, this method of sclerotherapy was safe and cost-effective.[18] In another study on 30 patients with lymphocele, alcohol injection was found to be safe and cost-effective, with a success rate of 94%. The authors reported 2 cases of recurrence. All complications were minor, including catheter-induced infection and catheter displacement.[19]

Povidone iodine, as a sclerotherapy agent, has a failure rate of less than 11%, but it lasts about 20 to 30 days to cease the leakage. Iodine-induced nephrotoxic acute kidney failure following the use of povidone iodine has also been reported.[20] Tetracycline seems not to be effective as a sclerosing agent.[1]

Surgery. Surgery for lymphocele is needed in the presence of local symptoms, graft dysfunction, or both. Surgical treatment is named incorrectly as *marsupialization*, but *unroofing* or *fenestration* is more precise.[1] This therapy is an intraperitoneal drainage of lymphocele. Because of its effectiveness and safety, surgery should be the first line of the treatment.[21]

Laparoscopy is the procedure of choice for surgical management of lymphocele. The most susceptible organ to injury during laparoscopy is the transplanted ureter. In addition, bulging induced by extraperitoneal kidney might be sometimes mistaken by lymphocele.[1] Organ injury during laparoscopy can be avoided by the use of intra-operative ultrasonography. In a study by Schips and colleagues, a method of laparoscopic fenestration of lymphocele with diaphanoscopic guidance was described. In their method, after puncture and ultrasonography-guided dilation, it was possible to determine the exact site of incision by detecting the light of cystoscope.[22] Tie and colleagues introduced a method of replacement of a guide wire or drainage catheter under ultrasonography or computed tomography guidance. They used this marker as a guide for laparoscopic marsupialization of lymphocele.[23]

In different series, the rate of recurrence following laparoscopic marsupialization has been reported between 5% to 13%, and it has been noted that there is a risk of injury to other organs such as the bladder.[21,24] In a study on laparoscopic

treatment of lymphocele, the mean operative time was 123 minutes and the mean blood loss was 43 mL. The authors reported an average duration of hospitalization of 1.5 days. Only minor complications were seen. They concluded that laparoscopy is an effective minimally invasive treatment and an excellent alternative for open surgery.[25]

Open surgery may be required in patients with a previous abdominal surgery, for lymphoceles with inappropriate characteristics or location, or when other simultaneous procedures should be done. For deep lymphoceles around the lower pole of the kidney, it seems that open surgery is safer. In other unusual cases, including thick wall of lymphocele or bladder rupture during laparoscopy, open surgery may be necessary.[1] In a study by Fuller and colleagues, the most common indication for open drainage was uninfected wound complication and high probability of injury to the ureter or the vessels because of proximity to the hillar structures.[26]

Open surgery can be done by re-opening of the transplant incision, or preferably through a lower midline abdominal incision and transperitoneal approach. Intraoperatively, lymphocele can be seen in the form of a bulge into the peritoneal cavity, and it is possible to make a 5-cm opening between these two cavities. It must be noted that according to the variable anatomy of the transplanted structures, several vital organs may be present between these two cavities that makes avoidance of injury to these organs a crucial point. When a simple incision is made in the wall between the lymphocele and the peritoneum, a low but significant rate of recurrence is anticipated. For prevention of recurrence, it is recommended to perform techniques such as oversewing of the edges and mobilization of the peritoneum with omentopexy.[1] In children, prophylactic fenestration between the two cavities at the end of the operation is recommended by some authors.[27] Nghiem and colleagues introduced a new method named *intraperitoneal catheter drainage of lymphocele* as an outpatient procedure in 14 patients with local anesthesia and Seledinger method. Under ultrasonography guidance, a 13-F Hickman catheter was introduced to the lymphocele, and it was connected to a small window of the peritoneum via subcutaneous tissue.[24] In a period of 8 years, this procedure has been done with success. One case of wound infection led to catheter removal and 1 case of lymphocele recurrence due to retraction of the catheter beneath the peritoneum was reported in this study. It was mentioned by the authors that this was an effective outpatient procedure that obviated the need for anesthesia. However, they emphasized that further conclusions require a multicenter study.[24]

COMPLICATIONS

Most lymphoceles are managed without complication, but infections, especially with organisms like yeasts, in an immunocompromised recipient may be a problem. In addition to impaired graft function, lymphoceles that put pressure on the renal vein or iliac veins may predispose the patient to venous thrombosis.[1]

CONFLICT OF INTEREST

None declared.

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