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Role of Surgery in Nephrotic Syndrome

Intezar Ahmed and Enono Yhoshu

Abstract

Nephrotic syndrome can occur at any age—adult or children—though the etiology and histopathology may be different in these groups. The management is mostly medical and supportive, but there is some role of surgery in certain complications of nephrotic syndrome, which are rarely discussed together. Here we would like to elaborate some of the areas that require the involvement of surgeons in patients with nephrotic syndrome, to list the complications, and to discuss in brief the surgeries involved. There is a need for randomized prospective studies of nephrotic syndrome patients needing surgical interventions to further project their precise relations and outcomes.

Keywords: surgery, nephrotic syndrome, proteinuria, obesity

1. Introduction

Nephrotic syndrome occurs as a result of pathological injury to the glomeruli of the kidneys. It can be a primary problem, with a disorder which is renal specific or secondary due to a systemic disorder like diabetes mellitus. Consultation of a nephrologist (ideally within 2 weeks) is necessary, and a renal biopsy may need to be performed. This helps in diagnosing what form of glomerular disease is present. More tests may be necessary to rule out secondary disorders, e.g., systemic lupus erythematosus, diabetes mellitus, amyloidosis (AL), etc.

Typically, around 80% of patients remit with oral corticosteroid therapy (steroid sensitive). About 75–85% of these children will have a relapse. Five percent fail to go into remission despite 8 weeks of high-dose steroid therapy and are called as steroid resistant. The primary aim of treatment is to achieve remission, improve symptoms, and prevent, if not at least treat, acute risks such as infection, thrombosis, hypovolemia, etc. On the long term the treating nephrologist's goal should be to prevent complications like high blood pressure, Cushing syndrome, bone disease, obesity, failure to thrive, striae, eye diseases, and a variety of psychological, social, and behavioral disturbances.

The role of surgery in nephrotic syndrome is not directed for patients with primary causes, but only as supportive or symptomatic care. Surgery has some role in nephrotic syndrome patients with secondary etiology, which will be mentioned below separately.

2. Primary causes of nephrotic syndrome requiring surgery

2.1 Infectious complications

An estimate of 17% of infection incidence is observed in nephrotic syndrome patients. Many complications are described in the literature pertaining to the nephrotic

syndrome such as skin infection, peritonitis, pneumonia, urinary tract infections, bacteremia, etc. Cellulitis is one of the troublesome complications of nephrotic syndrome. The major risk factor for cellulitis is hypoalbuminemia which occurs secondary to proteinuria in these patients [1, 2]. Edema, one of the pathognomonic features of nephrotic syndrome patients, is also credited to hypoalbuminemia as well. The lymphatic flow gets obstructed as a consequence of edema which causes the congregation of bacteria and leads to infection. Abscesses can occur as a consequence of untimely detection and management of cellulitis [3]. Abscesses in nephrotic syndrome have been reported, e.g., subphrenic, perinephric, submandibular, retroperitoneal, and subcutaneous tissues, the brain, and the lung [4]. The adequate drainage of these abscesses anywhere either by open drainage or with percutaneous drainage tubes in conjunction with the appropriate antibiotics is essential for a good outcome.

Out of many, one of the most common infections is bacterial peritonitis found in about 1.4–3.7% of the children and amounting to a mortality rate of 9%. The common bacterial causes of peritonitis have been Gram-positive bacteria, particularly *S. pneumoniae*, but of late Gram-negative bacteria, such as *E. coli*, have been seen to appear. The recommendation for antibiotics has been aminoglycosides and/or third-generation cephalosporins. The controversy regarding the management approaches with laparotomy and laparoscopy exists. Nevertheless, laparoscopic peritoneal washing is sometimes recommended, as it has been shown to decrease the bacterial load in these patients [5].

Studies from India regarding infections in nephrotic syndrome patients by Gulati et al. and Srivastava et al. reported infection rate to be around 32–38% [6, 7]. In spite of the frequent rate of infections in nephrotic syndrome patients as mentioned above, we could not find any literature about the frequency of surgical intervention required for each infective complication, rather, only case reports, probably suggesting the infrequent requirement of surgeries [3, 8]. This could be because of the response of the infections, be it cellulitis or peritonitis or other infections, to adequate and prompt medical supportive measure, including steroids. On the other hand, the fulminant nature of infections in nephrotic syndrome patients if not treated early has been reported.

There is no data to date regarding the wound healing after surgery in nephrotic syndrome patients with cellulitis. Maroz et al. gave a description recently on the relation between the different types of renal impairments and their effects on wound healing [9]. This included acute kidney injury (AKI), chronic kidney disease (CKD), and end-stage renal disease (ESRD) patients and the various implications each has on poor wound healing, but there was no mention of nephrotic patients. Greff et al. in their writing on intra- and postoperative adverse effects of nephrotic syndrome patients needing surgery under general anesthesia reported that in their population of 24 patients, there were no infectious events observed up to 5 days postoperatively [10]. Their population of patients was on long-term antibiotic therapy and was added on specific antibiotics during and after surgeries.

2.2 Dialysis catheter insertion

In the long term, nephrotic syndrome can initiate irreversible kidney injury that further leads to kidney failure and makes treatment with dialysis or, ultimately, kidney transplant essential. Nephrotic syndrome constitutes up to 12% of the causes of end-stage renal disease in children. Dialysis can be of two types—hemodialysis (HD) and peritoneal dialysis [11]. The peritoneal dialysis catheter is usually inserted by a surgeon. For this procedure the abdominal wall is cleaned well in preparation for surgery, and a catheter is inserted surgically with one end in the abdominal cavity and the other outside the body. There are two methods for this procedure to complete

open surgery or minimally invasive surgery (laparoscopic). Nowadays, minimally invasive catheter placement technique is an acceptable method. The advantages of minimally invasive/laparoscopic technique are safety, less complications due to entire under vision procedure, less catheter malfunction, prolong catheter life-span, etc. There are well-known important catheter-related complications such as leakage due to tube blockage, infection at entry/exit site and/or tunnel, malposition of catheter tip, hernia, and peritonitis. Of late percutaneous catheter placement technique also emerged that can be performed by an interventional radiologist/nephrologist/surgeon to provide a fast, safe, and reliable peritoneal access.

2.3 Arteriovenous fistula creation

Appropriate and efficient vascular access is necessary for a successful HD. According to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guidelines, the ideal vascular access is described as one which can deliver an adequate flow rate along with durability and a low complication rate. An arteriovenous fistula (AVF) is usually considered to be the best access for HD in adults and, as commented on by an emerging body of evidence, that it is the same also in children [12].

It has been seen that children's vascular biology is not the same as that of adults; henceforth, the ideal size of the vein and artery, anastomosis maturation time, and volume flow rates for a functional fistula in children on HD are not known. Since its inception, advances in AVF creation, especially with improved surgical experience, primary failure rates have been gone down to as low as 5%. For an AVF creation, the preferred sites include, in order, the radial artery to cephalic vein (radiocephalic), brachial artery to cephalic vein (brachiocephalic), and brachial artery to basilic vein (brachiobasilic, with or without transposition). Alternatively, an ulnar artery to basilic vein AVF can be created. Though rarely utilized, an AVF between femoral artery to saphenous vein has also been described. Although there are no guidelines regarding ideal/minimum vessel size in the literature, the general consensus is a minimum venous diameter of 2.5 mm. The essential information before AVF creation includes adequate vessel size; venous stenosis/occlusion can be obtained by duplex ultrasound scanning or venography and is necessary to be carried out in children to decide on the best vessels for AVF creation [13]. Complications of AVF creation include stenosis/occlusion, thrombosis, steal syndrome, and possible discrepancy in limb length if the AVF is placed in the lower extremity. Time for anastomosis maturation may be prolonged, with reports of up to 6 months.

2.4 Renal transplantation

The ultimate treatment for pediatric patients with end-stage kidney disease, including that occurring as a consequence of nephrotic syndrome in the first year of life (NSFL), is renal transplantation. In the early years of renal transplantation era, the results were inferior in young children compared with older children or adults, but in the last few years, results have been improved tremendously mainly because its practice has substantially fine-tuned [14]. Chronic graft loss and opportunistic infectious complications can exist in spite of the improvement in immunosuppression demonstrating excellent results and leading to more 1-year graft survival rates. ESRD in children and adolescents is different from the adult population, in terms of the need to thrive well or have normal growth and have cognitive, psychological, social, and behavioral development. Therefore, the experience gained from adults cannot be extrapolated to pediatric population [15].

Preemptive transplantation (PET), which signifies transplantation prior to the initiation of dialysis, has recently been introduced in the pediatric population, as it is observed that children undergoing renal transplantation before the features of severe uremia sets in are helped by the avoidance of many of the associated long-term complications of ESRD and dialysis.

One of the common causes of ESRD is focal segmental glomerulosclerosis (FSGS). In idiopathic nephrotic syndrome, FSGS is a common pathologic diagnosis, especially in steroid-resistant cases. After kidney transplantation FSGS is known to recur and frequently followed by graft loss [16].

In renal transplantation, patient size and age matching are generally not essential. In fact, it was seen that there is very high rate of graft loss if one matches very young donors to very young recipients, as a consequence of thrombosis. Hence, now pediatric programs are considering the transplant of adult kidneys into small children, once the recipient attains a sufficient size, typically 6.5–10.0 kg of body weight. It has been seen that the peritoneal cavity of an infant has enough space to accommodate an adult kidney without fear of the compression of graft. It has been observed that if body weight of a child is more than 30 kg, the surgical procedure for a kidney transplantation will be similar to that in an adult. However, if the body weight is less than 10 kg, a midline longitudinal abdominal incision is required, and blood vessels from the donor are connected to the recipient's aorta and inferior vena cava. But a tailored approach is needed in children with a body weight of 10–30 kg, in terms of incision site/size, anastomoses of vessels, and allograft sites on the basis of the child's anatomy [17].

3. Secondary causes of nephrotic syndrome requiring surgery

Increasing evidences are available regarding an emerging causal relationship between renal artery stenosis (RAS)/ischemia and the development of nephrotic syndrome. It is well established now that patients with accelerated hypertension used to have proteinuria of nephrotic range. However, it is rarely seen in patients with essential hypertension. Varying degrees of proteinuria are in unilateral RAS patients but normally in around 0.5 g/day. Reduction in this proteinuria is possible with surgical correction of this hemodynamic problem. Various kinds of surgical corrections are reported like nephrectomy, arterial stenosis correction, percutaneous transluminal angioplasty, and stenting. The use of angiotensin-converting enzyme inhibitors (ACE-I) also has shown benefit in minimizing the proteinuria and degrees of hypertension [18].

3.1 Immunoglobulin light chain amyloidosis (AL)

Up to half of all patients presents with renal involvement at the time of diagnosis. About 40% of patients will land up into end-stage renal disease and ultimately will require renal replacement therapy. Management of nephrotic syndrome is difficult and challenging for patients not yet on dialysis. Ablation of natural filtration through medical and/or surgical means has been used to achieve remission from massive proteinuria associated with the nephrotic syndrome. Conservative treatments consist of mercury salt (sodium mercaptomerin), angiotensin II and cyclosporine, and inhibitors of prostaglandin synthesis. Bilateral renal infarction has been used as a substitute to nephrectomy in patients with chronic kidney disease and massive proteinuria. This is carried out by percutaneous route and renal artery embolized using ethanol and irritant coils. Removal of the kidney surgically offers complete relief from proteinuria but carries the risks of complications of an open surgery in severely debilitated patients. Nephrectomy through minimally invasive techniques is a less invasive procedure, even though this procedure also has been

used frequently due to the hazards of complications of hypoalbuminemia, hypotension, deranged coagulation profile, and impaired renal function. A novel approach to renal ablation is laparoscopic ligation of both ureters which has been considered by some surgeons for these patients with proteinuria as a disabling refractory complication [19]. The patient will need a long-term hemodialysis after this.

3.2 Bariatric surgery in nephrotic syndrome due to obesity

About 30 years ago, the initial descriptions of nephropathy associated with obesity were published, which were followed by lots of reports of kidney disease in obese subjects without diabetes. Obesity-associated nephrotic syndrome has been described as a glomerulopathy that presents with a variable kind of proteinuria. The mechanisms of renal injury are attributed to the body adapting adversely to the rise in the excretory load, salt retention, and the direct or indirect effects of hyperinsulinemia/insulin resistance and renal lipotoxicity. The most commonly used treatment for nephropathy associated with obesity stresses on the use of antiproteinuric agents, with ACE inhibitors and angiotensin II receptor blockers, which in turn improve sensitivity to insulin and protect the kidneys and cardiovascular system. Bariatric surgery has been accepted as one of the essential procedures for achieving these goals but involves a reasonable risk [20].

Ramirez et al. in their report of two cases of nondiabetic obese patients with FSGS stated that there was an effective reduction of body weight by bariatric surgery and this was successfully accompanied by sustained remission of proteinuria allowing significant reduction or total removal of blockers of the renin-angiotensin system. Huan et al. also reported a case of obesity-related nephropathy and FSGS on renal biopsy. The patient underwent bariatric surgery and attained successful weight reduction with significant decrease in proteinuria and stabilization of renal function [21].

4. Conclusion

The literature on the role of surgery in nephrotic syndrome is scanty, though the association of nephrologists with surgeons has been ongoing. We have tried to enumerate some of the role of surgeons in nephrotic syndrome patients, with some review of the available literature. In order to bring out more specific outcomes of complications of nephrotic syndrome patients being managed surgically, more randomized controlled studies with better documentation of interventions being done is essential and much needed.

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