Renal transplantation for nephrogenic systemic fibrosis: a case report and review of the literature

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Abstract
Nephrogenic systemic fibrosis (NSF) is a rare fibrosing disorder described among patients with renal disease. Currently, no standard therapy exists, although therapeutic modalities have included plasmapheresis, extracorporeal photopheresis, sodium thiosulphate, imatinib and renal transplantation. We describe a patient with NSF who was physically debilitated and underwent renal transplantation. After transplantation, the patient's lesions improved clinically, and the patient was ambulatory. Despite developing worsening renal function, her lesions remained unchanged. We conclude that renal transplantation improves symptoms of NSF, and believe that in patients with NSF, careful consideration should be made for early renal transplantation.

Keywords: end-stage renal disease (ESRD); gadolinium; nephrogenic systemic fibrosis; renal transplantation

Background
Nephrogenic systemic fibrosis (NSF) was recognized as a unique entity in 1997 and was first reported in the literature in 2000 [1]. Individuals on dialysis manifested brawny hyperpigmentation and thickening of the skin on the extremities and trunk [1]. Although the disease was first termed ‘nephrogenic fibrosing dermopathy’, the name was later changed to NSF to reflect its recognition as a systemic disorder.

The pathophysiology of NSF is not known; however, there is a strong association with gadolinium-based contrast agent (GBCA) exposure in individuals with advanced kidney disease [2]. Although the cause of disease is not known, several lines of evidence suggest that circulating fibrocytes play a role in the disease process [3].

Individuals who develop NSF have limited options for treatment. These treatments have included extracorporeal photopheresis, plasmapheresis, sodium thiosulphate, imatinib mesylate and renal transplantation. We report the case of a patient who developed NSF and received a renal transplant with symptomatic improvement of her NSF. Although the patient's renal transplant function deteriorated—necessitating a return to haemodialysis—her dermatologic improvement has persisted.

Case report
A 58-year-old African American woman had normal renal function until 1992. At that time, she developed chronic kidney disease (CKD), thought to be due to prolonged non-steroidal anti-inflammatory agent use. A renal biopsy subsequently showed changes consistent with focal segmental glomerulosclerosis (FSGS). In 1998, the patient initiated peritoneal dialysis before being transferred to hemodialysis. In September of 2004, she was evaluated for mental status changes with a magnetic resonance imaging (MRI) of the brain with contrast. Consequently, the patient developed thickening of her skin in multiple areas on her body, especially over the arms, thighs and torso. A skin biopsy of the right thigh showed prominent fibrosis with increased numbers of fibroblasts and thickening of collagen bundles in the lower reticular dermis, consistent with NSF (Figure 1).

The patient received a living-donor kidney transplant in September 2006. The operative procedure was remarkable for difficult exposure of the right external iliac artery and vein. A conventional kidney transplant incision was performed; however, due to the extensive NSF involvement, medial retraction was limited at the level of the skin.

The post-operative course was largely unremarkable, and she was discharged on post-operative Day 6 with a creatinine of 124 μmol/L. Over the next 3 months, the patient continued to have excellent renal function and was noted to have dramatic improvement in the dermatologic manifestations of her NSF. The most remarkable improvement was in her ambulatory capacity. Prior to surgery, she had been largely wheelchair-bound due to extensive NSF. Following transplantation, she became fully ambulatory within 3 months.
FSGS recurrence was noted on an allograft biopsy 9 months following transplantation. Despite plasmapheresis and therapy directed to reduce proteinuria, her renal function continued to deteriorate. She restarted hemodialysis in May 2008. Concomitant with worsening renal function, the improved dermatologic symptoms remained stable, failing to improve further but did not worsen.

**Discussion**

The original cohort of NSF cases consisted of a series of 14 patients maintained on dialysis [1]. A recent review of the published literature noted that ~80% of reported NSF patients were on dialysis, while ~10% had acute kidney injury (AKI) or advanced CKD [4]. There is no identifiable relationship between ethnic background, gender, age and the development of NSF. The epidemiology of NSF, according to published studies, has demonstrated an equal incidence in males and females and a mean age of onset of 46.4 years [5].

GBCA administration has been linked to the onset of NSF in multiple reports in the literature [6,7]. In one study, all 13 cases of NSF received gadolinium prior to the development of symptoms [6]. In another study, by Deo et al. [7], the incidence of NSF was 4.3 cases per 1000 patient-years, with one GBCA exposure presenting a 2.4% risk for NSF in ESRD patients.

A number of treatment modalities have been reported in NSF patients; however, most therapies have been of limited benefit. Early physical therapy and pain management have been recommended to decrease the extent of contractures and limitations in mobility. Spontaneous improvement in kidney function or renal transplantation has resulted in improvement in NSF manifestations. As a result, several authors have advocated renal transplantation for those who are eligible [3,8–10].

Although renal transplant for NSF has been described in the pediatric literature, the benefits have not been universally documented. Renal transplantation for NSF may have different outcomes as demonstrated in Table 1 and may be dependent on the time of transplantation and the underlying disease process. Our case report reiterates the theory that restoration of renal function with renal transplantation can improve lesions of NSF and is consistent with the findings of Panesar et al. [8]. The improvement of our patient's dermatologic lesions remained stable, despite a recurrence of FSGS in her renal allograft requiring dialysis. One important technical intra-operative lesson in performing kidney transplantation in patients with extensive abdominal NSF is to modify the kidney transplant incision to a more medial position. Due to poor tissue compliance, medial rotation may provide better exposure of the iliac vessels and bladder for anastomosis at time of transplantation.

**Table 1. Different outcomes of renal transplantation for NSF**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age/gender</th>
<th>Cause of end-stage renal disease</th>
<th>Mode of dialysis</th>
<th>Location of lesions</th>
<th>Type of transplant</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan et al. [9]</td>
<td>16/Female</td>
<td>Brachio-oto-renal failure</td>
<td>HD (changed to PD)</td>
<td>Thick, linear plaques on inner thighs, lower extremities, arms, Abdomen, upper arms, posterior neck and sacrum</td>
<td>Cadaveric kidney transplant</td>
<td>Oedema/pruritus slightly improved</td>
</tr>
<tr>
<td>Jan et al. [9]</td>
<td>8/Male</td>
<td>Membranoproliferative glomerulonephritis type II</td>
<td>PD</td>
<td>Hypertrophy; hypopigmentation and thinning over anterior tibial regions</td>
<td>Kidney transplant</td>
<td>Skin lesions improved; after kidney transplant failed, no worsening of lesion</td>
</tr>
<tr>
<td>Auron et al. [10]</td>
<td>13/Male</td>
<td>Membranoproliferative glomerulonephritis type II</td>
<td>PD</td>
<td>Contractures/stiffness/skin tightening; thick brawny induration of hands, forearms, upper thighs</td>
<td>Kidney transplant x2</td>
<td>Worsening of dermatological condition</td>
</tr>
<tr>
<td>Panesar et al. [8]</td>
<td>42</td>
<td>Diabetes mellitus</td>
<td>PD for 14 months, HD for 12 months</td>
<td>Fibrosed left arm with limited range of motion. Right fingers with fusiform appearance</td>
<td>Kidney transplant</td>
<td>Softening of the skin and increased mobility of the joints</td>
</tr>
<tr>
<td>Panesar et al. [8]</td>
<td>34</td>
<td>Diabetes mellitus, Hypertension</td>
<td>HD for 2 years</td>
<td>Right arm thick skin and stiffness</td>
<td>Kidney transplant</td>
<td>Softening of the skin and increased mobility of the joints</td>
</tr>
<tr>
<td>Panesar et al. [8]</td>
<td>53</td>
<td>Diabetes mellitus</td>
<td>HD for 2 years</td>
<td></td>
<td>Kidney transplant</td>
<td>Softening of the skin</td>
</tr>
</tbody>
</table>

PD, peritoneal dialysis; HD, haemodialysis.
This case report contributes to the literature describing renal transplantation and improvement of NSF lesions. For patients who are eligible for transplantation, we advocate that an early renal allograft be considered to help improve or halt the progression of NSF.

Conflict of interest statement. None declared.

References


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Cryoglobulinaemia and rapidly deteriorating renal function in chronic lymphocytic leukaemia

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Abstract

Cryoglobulinaemia is a rare condition characterized by serum immunoglobulins or immunocomplexes which precipitate at temperatures below 37°C and redissolve on warming. Cryoglobulinaemic vasculitis develops in ~15% of patients positive for cryoglobulin serology and is often associated with an underlying infectious, autoimmune or lymphoproliferative disease. We describe a case of cryoglobulinaemic vasculitis, which manifested as purpura and rapidly deteriorating renal function in a patient with chronic lymphocytic leukaemia and coexistent parvovirus infection. This case illustrates the complex pathophysiology of cryoglobulinaemic renal injury, and suggests that infection may serve as a trigger in the presence of other pathophysiological factors.

Keywords: chronic lymphocytic leukaemia; cryoglobulinaemia; parvovirus; renal failure

Background

The symptoms of cryoglobulinaemic vasculitis include characteristic purpura, Raynaud’s syndrome, acrocyanosis, livedo reticularis, ecchymosis, skin ulcerations, and even ischaemic necrosis or gangrene. Arthralgias, weakness, peripheral neuropathy, and renal, cardiac and liver manifestations are frequently encountered [1]. Cryoglobulinaemias are classified into three types according to the immunoglobulin composition. Type I cryo-