Incidence of Acute Femoral Neuropathy Following Renal Transplantation

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Background: Case reports exist of femoral neuropathy following renal transplantation (RTSP) with possible pathophysiology, including direct compression and nerve ischemia. However, the occurrence of acute femoral neuropathy (AFN) following RTSP has not been studied prospectively.

Objective: To determine the occurrence of AFN following RTSP.

Methods: We prospectively studied the occurrence of AFN following RTSP from June 1, 1998, to October 31, 1999. A total of 184 RTSPs were performed during this period. All the patients had end-stage renal failure and had effective hemodialysis before RTSP. All patients with AFN underwent neurologic examination, nerve conduction and electromyographic studies (5 to 7 days after the onset of symptoms), and magnetic resonance imaging or computed tomography of pelvis and lumbosacral spine within 24 hours of onset of symptoms.

Results: Four (2.2%) of 184 patients developed AFN (ipsilateral to the RTSP surgery) postoperatively between 24 (3 patients) and 48 hours. All the patients achieved good renal function after RTSP. All the patients had excellent recovery of motor function in 4 to 9 months.

Conclusion: We believe that AFN following RTSP is an uncommon (2.2%) complication from which patients have an excellent chance of recovery.

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EMORAL NEUROPATHY has been described as a complication of compression due to hematoma from anticoagulation,1 hemophilia,2 leukemia,3 consumption coagulopathy,4 hysterectomy and pelvic surgery,5,6 lithotomy position,7,8 blunt trauma,9 iliac artery aneurysm,10 inguinal herniorrhaphy,11 malignancy and radiation therapy,12 Epstein-Barr virus infection,13 and diabetes mellitus (DM).14 Many case reports exist of femoral neuropathy following renal transplantation (RTSP)15-24 with possible pathophysiology, including direct compression and nerve ischemia. However, the occurrence of acute femoral neuropathy (AFN) following RTSP has not been studied prospectively.

RESULTS

CLINICAL FEATURES

Four (2.2%) of 184 patients developed AFN (ipsilateral to the RTSP surgery) postoperatively between 24 (3 patients) and 48 hours. All 4 patients received a cadaveric right iliac fossa renal transplant. In 3 patients the external iliac artery was anastomosed (end to end) to the renal artery, and in 1 patient the common iliac artery was anastomosed to the renal artery because of extensive atherosclerosis. All these patients experienced end-stage renal failure secondary to hypertension and underwent effective hemodialysis before RTSP. The primary renal disease in all these patients was chronic glomerulonephritis. One patient also had type 1 DM and another had thrombotic thrombocytopenic purpura. The clinical and electrophysiological data are summarized in the Table. In all patients, the neurologic examination findings, ipsilateral to RTSP, were remarkable for marked weakness of hip flexion, knee extension, an absent knee jerk, and impaired sensations over the anteromedial aspect of the thigh and medial aspect of the leg. All the patients achieved good renal function after RTSP.
PATIENTS AND METHODS

PATIENTS

We prospectively studied the occurrence of AFN following RTSP at the University of Miami, Jackson Memorial Medical Center, Miami, from June 1, 1998, to October 31, 1999. A total of 184 RTSPs (15 children: mean ± SD age, 1.5 ± 1.0 years; range, 6 months to 2 years; 169 adults: 107 women; mean ± SD age, 45.0 ± 7.4 years; range, 22-65 years) were performed during this period. All the patients signed informed consent forms. Three surgeons (including G.B.) performed all these RTSPs using standard techniques. The diagnosis of AFN was established by the following criteria: (1) the development of weakness of the quadriceps femoris and iliopsoas muscles with decreased or absent knee jerk ipsilateral to the renal transplant within 48 hours of RTSP, and (2) presence of acute (within 7 days of onset of symptoms) neurogenic changes (increased insertional activity or decreased motor unit recruitment with or without positive waves and fibrillation potentials) on needle electrode examination of the affected muscles (quadriceps and iliopsoas) and decreased compound muscle action potential (CMAP) amplitude of the quadriceps muscle obtained by near-nerve stimulation of the affected femoral nerve.

Patients with preexisting diabetic amyotrophy or lumbosacral plexopathy and lumbosacral radiculopathy secondary to structural lesions in the lumbosacral spine were excluded. Similarly, patients with peripheral sensory motor neuropathy with significant motor deficit involving proximal and distal muscles with concomitant disease (paraproteinemia, preexisting endocrinopathies, connective tissue disorder, vitamin B12 or folic acid deficiency, heavy metal toxic effects, human immunodeficiency virus infection, hepatitis, Lyme disease, cancer, or chronic inflammatory demyelinating polyneuropathy25) were excluded. Patients with preexisting, predominantly distal sensory neuropathy related to DM or kidney dysfunction were not excluded. No patient had a family history of neuropathy.

NEUROLOGIC AND LABORATORY ASSESSMENTS

All 184 patients underwent preoperative and postoperative physical and neurologic examination. Four of these 184 patients who developed AFN following RTSP also underwent nerve conduction and electromyographic studies (5-7 days after the onset of symptoms), magnetic resonance imaging (3 patients), and computed tomography (1 patient) of pelvis and lumbosacral spine within 24 hours of onset of symptoms. The muscle strength was evaluated by using the Medical Research Council grading criteria (grade 0, no muscle contraction; grade 1, flicker; grade 2, partial movement with no gravity; grade 3, complete movement against gravity; grade 4, complete movement against variable resistance; and grade 5, normal power).26 Similarly, the recovery was also rated as follows: poor, no recovery; fair, 25% to 50%; good, 50% to 75%; and excellent, 75% to 100%. All patients underwent renal function tests before and after surgery. The status of immune function and levels of immunosuppressive drugs were assessed postoperatively.

ELECTROMYOGRAPHY AND NERVE CONDUCTION STUDIES

The nerve conduction studies were performed in both lower limbs using standard techniques. The studies included sural sensory nerve, saphenous nerve, superficial peroneal sensory nerve, tensor fascia lata, and corresponding F waves, peroneal motor and corresponding F waves, and femoral motor nerves.27 Needle electrode examination was performed to evaluate insertional activity, spontaneous activity, motor unit morphologic findings, and recruitment pattern in paraspinal muscles in the lumbosacral region, gluteal muscles, iliopsoas, sartorius, quadriceps, adductor longus, adductor magnus, hamstrings, tibialis anterior, and gastrocnemius muscles on the affected side.27

DATA ANALYSIS

The StatView II statistical software program (Abacus Concepts Inc, Berkeley, Calif) was used for data analysis. All of the data are expressed as mean ± SD. We determined the statistical significance (P<.05) of differences between categorical variables using a χ² test or Fisher exact test as appropriate.

Electroneurophysiology

The needle electrode examination showed occasional positive waves and fibrillation potentials and no voluntary motor unit action potentials in iliopsoas or quadriceps muscle in all patients. The near-nerve stimulation of the ipsilateral femoral nerve evoked decreased CMAP (reference, >4.3 mV) in all the patients with slightly prolonged distal latency in 2 patients (patients 3 and 4; reference, <6.0 milliseconds; Table). Saphenous nerve action potential amplitudes were diminished (reference, >4 μV) with slowed conduction velocity (reference, >42 m/s; Table) in all the patients on the affected side. Three patients (patients 2, 3, and 4) had underlying mild, distal, symmetrical, sensory, sensorimotor axonal peripheral neuropathy. Two of these patients (patients 3 and 4) had mild symptomatic polyneuropathy diagnosed preoperatively (decreased to absent ankle reflexes bilaterally in both patients and impaired primary sensory modalities distally in feet in patient 4), and 1 patient (patient 2) was asymptomatic (decreased ankle reflexes bilaterally) but had small sural sensory nerve action potential amplitude (<4 μV; reference, >7.0 μV) during postoperative electrodagnostic studies. The sural nerve–evoked sensory action potentials were absent bilaterally in patients 3 and 4. The tibial H reflex latency was prolonged in 3 patients (patients 2, 3, and 4: 34.2-36.6 milliseconds; reference, <32 milliseconds). The peroneal motor, tibial motor and corresponding F waves, and superficial peroneal sensory nerve conduction velocities were within the reference range, except in patient 4, in whom the peroneal CMAP was decreased (1.9 mV; reference, >2.5 mV) and superficial peroneal sensory nerve action potential amplitude on both sides were diminished (right side, 3.5 μV; left side, 3.1 μV; reference, >4 μV).
Three surgeons performed all the 184 RTSPs (G.B. [69 operations], Joshua Miller, MD [58 operations], and Gaetano Ciancio, MD [56 operations]), and there was no significant difference for the occurrence of AFN among these surgeons (for G.B., 2 AFNs of 69 RTSPs; for Dr Miller, 1 AFN of 58 RTSPs; and for Dr Ciancio, 1 AFN of 56 RTSPs; corrected $\chi^2=0.27$, $P=.87$).

DM as Risk Factor

Among the 184 patients who underwent RTSPs during June 1, 1998, to October 31, 1999, 14 patients (7.6%) also had DM (types 1 and 2). In addition, AFN occurred in 1 (7.1%) of the 14 patients with DM and in 3 patients (1.8%) of the remaining 170 patients without DM (corrected $\chi^2=0.14$, $P=.70$), suggesting that DM was not a significant risk factor for the development of AFN as postulated earlier.24 However, there are some limitations to this conclusion because of the small number of patients with DM in our study cohort.

FOLLOW-UP

All the patients underwent physical therapy and follow-up neurologic examination. Within 4 to 8 weeks of onset of symptoms, all of them had significant improvement in motor deficit (Table) and were able to stand on their affected leg and walk with a walker. One patient (patient 4) achieved complete motor recovery after 4 months, 2 others (patients 1 and 3) after 6 months, and 1 patient (patient 2) after 9 months. This excellent recovery observed in our patients with AFN following RTSP was similar to that noted in previous studies.18,19,21-24 Similarly, the renal function in these patients remained satisfactory until the last follow-up as observed in most previous studies.18,20,22-24

ANATOMY

The femoral nerve is the largest branch of the lumbar plexus (L2, 3, and 4). The femoral nerve derives from the posterior divisions of the anterior primary rami of the second, third, and fourth lumbar spinal nerves. Formed within the psoas muscle, it emerges from the lateral border of that muscle to lie between it and the iliacus deep

<table>
<thead>
<tr>
<th>Patient No./ Sex/Age, y</th>
<th>Renal Disease</th>
<th>Associated Disease</th>
<th>Postoperative Onset, h</th>
<th>Findings</th>
<th>EMG/NCS Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Quadriceps/ Iliopsoas, IA/SA†</td>
</tr>
<tr>
<td>1/F/58</td>
<td>CGN</td>
<td>HTN</td>
<td>24</td>
<td>Right hip flexor 3/5, quadriceps 2/5, absent knee jerk, decreased anterior thigh sensation</td>
<td>1+ Positive wave</td>
</tr>
<tr>
<td>2/F/63</td>
<td>CGN</td>
<td>HTN</td>
<td>48</td>
<td>Right hip flexor 3/5, quadriceps 1/5, absent knee jerk, decreased anterior thigh sensation</td>
<td>1+ Fibrillation</td>
</tr>
<tr>
<td>3/F/32</td>
<td>CGN, DM</td>
<td>HTN</td>
<td>24</td>
<td>Right hip flexor 3/5, quadriceps 3/5, absent knee jerk, decreased bilateral ankle jerk</td>
<td>Increased IA</td>
</tr>
<tr>
<td>4/M/41</td>
<td>HTN, TTP</td>
<td></td>
<td>24</td>
<td>Right hip flexor 3/5, quadriceps 2/5, decreased sensation in stocking pattern, absent knee jerk, absent bilateral ankle jerk</td>
<td>Increased IA</td>
</tr>
</tbody>
</table>

*All patients had an excellent outcome and satisfactory transplant function. EMG/NCS indicates electromyography/nerve conduction study; IA, insertional activity; SA, spontaneous activity; CMAP, compound muscle action potential; CV, conduction velocity; CGN, chronic glomerulonephritis; HTN, hypertension; DM, diabetes mellitus; and TTP, thrombocytopenic purpura.

†All patients exhibited no voluntary motor unit action potentials.
to the iliac fascia for the last third of its intrapelvic course. The branch to the psoas muscle may originate here, where the femoral nerve is still a part of the lumbar plexus, or after the nerve is fully constituted, although some controversy exists. It enters the thigh lateral to the femoral sheath and femoral artery, behind the inguinal ligament, dividing approximately 4 cm below the inguinal ligament into anterior and posterior divisions. The anterior division gives rise to the medial and intermediate cutaneous nerves of the thigh and muscular branches to the sartorius and pectineus muscles. The posterior division supplies the quadriceps femoris muscle and then continues along the medial border of the calf as the saphe nous nerve, a sensory branch.

MECHANISMS OF AFN

There are several possible mechanisms that could be involved in the pathogenesis of AFN following RTSP. The most common mechanism postulated is one of instrument-induced injury during operative procedure. The surgical site is above the psoas and distant from the path of the femoral nerve. Therefore, the possibility of direct trauma from diathermy or stretching is unlikely. Also, hematoma, as noted following RTSP in one study and also after pelvic surgical procedures and hysterectomies, was unlikely in our subjects because the imaging of the pelvis was negative as noted in most other studies. The compression from prolonged use of self-retaining retractors is a possible explanation. The inferior and medial blades of the retractors are in close proximity to the middle portion of femoral nerve, which gets its blood supply from the iliac ramus of the iliolumbar artery. It is more vulnerable to ischemia because it lies in the intraoperative region just proximal to the inguinal ligament compared with the proximal and distal portions of the femoral nerve, which receives blood supply from the local branches. The lumbar plexus has a rich anatomic vascular supply from inferior mesenteric and vesical arteries, whereas the middle and distal portions of the femoral nerve depend primarily on the integrity of the internal or external iliac artery for their blood supply. With the anastomosis of the renal artery to the graft to the internal, external, or common iliac artery, the possibility of significant localized “steal” exists. Proximal end-end anastomosis of the renal artery to the internal iliac artery can shunt blood away from the vasa nervosum. The existence of local atherosclerosis and presence of additional factors, such as DM, makes the femoral nerve more susceptible to ischemic injury.

Mild injury to the femoral nerve from retraction and ischemia could give rise to neuroparic injury, which would recover rapidly as observed in this study and by other investigators. On the other hand, more severe and prolonged ischemia from disruption of blood supply to the femoral nerve may give rise to axonal loss and a slow, incomplete recovery as observed in some previous studies. Yazbeck et al attributed the underlying severe advanced atherosclerosis of vessels as a compounding factor for the ischemic cause of post-RTSP AFN, which was similar to one of our patients (patient 3).

Diabetes is the most common metabolic cause of spontaneous, isolated femoral neuropathy with good recovery in months. Data from our study do not support the earlier postulated hypotheses that DM might be a risk factor in the development of post-RTSP AFN. In that retrospective study from 1972 to 1992, 5 of the 654 patients who underwent RTSP had AFN, and 2 of these 5 patients with AFN had DM in addition to hypertension as the cause of chronic renal failure. However, these studies did not provide the total number of patients with DM among the entire group of 654 patients who underwent RTSP during the 20-year period of the study.

CONCLUSIONS

We believe that AFN following RTSP is an uncommon (2.2%) complication from which patients have an excellent chance of recovery. The possible pathophysiology includes combination of stretch injury to the nerve from the use of the self-retaining retractors or nerve ischemia caused by a steal phenomenon, occurring after the anastomosis of the graft renal artery to the internal or external iliac artery.

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