Shunt nephritis

Case report

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The incidence of shunt nephritis has decreased over the past several years due to the increased use of ventriculoperitoneal (VP) shunts rather than the ventriculovascular systems for which this complication was originally reported in 1965. Despite this trend, the syndrome has been reported in cases of VP shunting and, for this reason, merit a renewed look. Shunt nephritis is thought to be secondary to immune complex formation and deposition in the kidney in response to Staphylococcus epidermidis. The diagnostic workup and management of this disease is discussed.

Key Words: nephritis • glomerulonephritis • shunt infection • shunt complication

Because many children with ventricular shunts placed for hydrocephalus also have myelomingocele with subsequent neurogenic bladder, urinary stasis and reflux are considered to be the primary mechanism by which these patients develop renal infection. However, an uncommon though serious complication of infected ventricular shunts is glomerulonephritis which, if untreated, can be fatal.11,12,18 Shunt nephritis is usually associated with ventricular-atrial (VA) or ventriculovascular shunts, but two cases stemming from ventriculoperitoneal (VP) systems have been reported.12,14 The purpose of this paper is to review the syndrome of shunt-associated glomerulonephritis and its treatment, which is effective in preventing irreversible renal damage if the disease is recognized early in its course.

Case Report

This 20-year-old man was referred to the Neurosurgery Department at the University of Puerto Rico. He had had a right VA shunt placed in infancy for congenital noncommunicating hydrocephalus. His medical history was significant for moderate psychomotor retardation, documented membranoproliferative glomerulonephritis, arterial hypertension, and multiple shunt revisions. He was admitted by the pediatrics department at the age of 20 years for evaluation of an episode of active nephritis associated with a febrile course and staphylococcal bacteremia. Laboratory studies documented hypochromic microcytic anemia. Urinalysis was significant for proteinuria and gross hematuria. The blood urea nitrogen (BUN) and serum creatinine levels were both grossly abnormal. Serum immunoglobulin revealed elevated immunoglobulin (Ig) G and IgA levels with depressed complement component C3. Blood and ventricular cerebrospinal fluid (CSF) cultures both grew Staphylococcus epidermidis. Prior renal biopsies reportedly had confirmed the diagnosis of membranoproliferative glomerulonephritis.

The patient’s VA shunt was converted to a VP shunt with concomitant institution of high-dosage systemic antibiotic therapy. Continuous headaches and frequent vomiting, both suggestive of sustained intracranial hypertension, as well as abdominal swelling prompted complete shunt removal with the simultaneous insertion of a ventriculostomy. The patient was started on a 21-day course of vancomycin, which he tolerated well. His symptoms improved rapidly. With documentation of sterile CSF and blood cultures, the patient underwent final VP shunting in October, 1988. His postoperative course was uneventful. The patient is being actively
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followed by the nephrology and neurosurgery departments. To date, he has had no further episodes of nephritis or evidence of shunt malfunction or infection.

Discussion

Incidence of Shunt Nephritis

The overall incidence of ventricular shunt infection varies between 3% and 11%.2,22 It is a significant cause of death in these patients, who may present in one of four ways: 1) with sepsis; 2) with signs of increased intracranial pressure; 3) as an asymptomatic state with positive shunt CSF cultures associated with leukocytosis and hypoglycorrhachia; or 4) with renal disease.1,6-8

This last syndrome, shunt nephritis, was first described in 1965.3 Since then, it has been found to occur in 0.7% to 2.25% of patients with an infected shunt and, in total, less than 86 cases have been reported in the literature.22 It appears to occur with equal frequency in both sexes, more frequently in patients under the age of 16 years, but the same clinical picture has been noted in several adults.2,14 including a 72-year-old patient.2

Symptomatology

Symptoms appear in a well-defined pattern.4,36 Review of the 86 published cases gave the following presentation and incidences: hematuria (89%), fever (88%), anemia (86%), proteinuria (70%), hepatosplenomegaly (35%), nephrotic syndrome (30%), nonthrombocytopenic purpura (19%), and hypertension (15%).22 Patients present with a low-grade fever, occasionally occurring only at night, and with malaise, lethargy, or anorexia. Some cases start with only nausea and vomiting, requiring that shunt malfunction be ruled out; others present with hepatosplenomegaly alone. A few patients later develop high fever and chills, low-back pain, costovertebral angle tenderness, palpebral or pedal edema, or generalized convulsions. Other symptoms associated with VA shunting include urticaria vasculitis,14 necrotizing cutaneous vasculitis,1 and arthritis.1

An outstanding characteristic of the disease is the long interval from shunt placement to recognition of symptoms. Although the time elapsed between insertion of the shunt, the beginning of the illness, and diagnosis has varied, diagnosis has been made from 1 month to 8 years later, averaging about 3 years.

Laboratory Findings

Laboratory findings are characteristic.2,13,22,26,32,34 Urinalysis reveals proteinuria and microscopic or occult hematuria. Renal casts of many different types, including coarse or fine granular casts and white and red cell casts, may be present. An iron-deficiency anemia or a moderate normochromic normocytic anemia is usually present, probably due to decreased erythropoietin production. Renal function may vary from mild azotemia to temporary oliguria and even to anuria. Although normal BUN values appear to dominate the picture during the early course of the disease, some decrease in glomerular filtration rate invariably occurs. Coagulase-negative S. epidermis has been reported in over 70% of these patients.2,26 Other organisms such as S. aureus, Streptococcus, Propionibacterium acneus, Listeria monocytogenes, Corynebacterium bovis, diphtheroids, Micrococcus, Pseudomonas aeruginosa, Cryptococcus neoformans, and filamentous Histoplasma capsulatum also have been described in cases of infected VA, VP, and ventriculoujugular shunts.1,6,10,13,19,21,24,26,27,33-35 However, since some of these organisms, frequently considered skin contaminants, were found in blood cultures examined as part of the patient's initial workup, specific therapy for infected shunt was delayed. Cultures of CSF were thought by some to be too unreliable as diagnostic aids, although shunt reservoir sites tapped later yielded positive results in almost 90% of the cases.34

Immunological Studies

Immunological studies have suggested that shunt nephritis is analogous to other known immune complex diseases of the kidney, including those associated with subacute bacterial endocarditis, syphilis, osteomyelitis, and some viral infections.2,4-6,13,18,20,22,26,30,32,33 The pathological changes seen in shunt nephritis were similar to those in animals with experimental nephritis induced by injection of foreign proteins over long periods of time. The injected antigen stimulated the production of immune complexes that are removed from the blood by the reticuloendothelial system, the smaller complexes being deposited within the kidney.

Laboratory analyses have shown low serum C3 concentrations not necessarily corresponding to the severity of the disease, the presence of cryoglobulins, and a positive rheumatoid factor test, all of which were reversible when the shunt was completely removed.2,33 The return of depressed serum C3 and C4 protein complement to normal levels coincides with the recovery of infection and clinical remission of the glomerulonephritis.2

Twice-weekly determinations of C3 and C4 levels were carried out in patients being treated for shunt nephritis until normal levels were restored. Failure of these levels to return to normal were thought to indicate continued infection and failure of the treatment regimen being implemented.12,36 An infected shunt may similarly seed the bloodstream and induce antigen-antibody complexes which are later trapped in the kidney. Indeed, circulating antigens to S. epidermidis were found in the serum and kidneys of these patients. The hepatosplenomegaly that was found was thought to be due to the removal of larger complexes by the reticuloendothelial system.

Renal Biopsy

Renal tissue biopsies show characteristic endothelial proliferation with mesangial expansion and prolifer-
tion of cellular elements. Hyperlobulated, tufted, and enlarged glomeruli with a reduced number of open capillary lumina are seen.\(^2\) These have been found by electron microscopy to contain electron-dense material between the capillary endothelium and the basement membrane. Immunofluorescence antibody studies have demonstrated IgG, IgM, and IgA, and C3, C4, and C1q fixation of the glomerular basement membrane.\(^3\)

### Treatment

It has been suggested that the clinical signs of shunt nephritis, including the nephrotic syndrome, revert with adequate treatment of the shunt infection without removing the system.\(^2\)\(^,\)\(^3\)\(^,\)\(^4\) Intraventricular antibiotic injection with external drainage or periodic removal of shunt fluid as intracrural pressure increases may be carried out as the first mode of treatment in patients with shunt nephritis.\(^2\)\(^,\)\(^2\)\(^,\)\(^9\)\(^,\)\(^12\)\(^,\)\(^19\)\(^,\)\(^29\)\(^,\)\(^34\) Daily doses may be given of one of the following drugs: 100 gm methicillin, 4 to 8 mg gentamicin, 25 to 100 mg cephalosporin, 75 mg nafcillin, or 50 mg ampicillin; simultaneous monitoring of trough ventricular CSF antibiotic concentrations should be performed to ensure effective levels in relation to the minimum inhibitory concentration for the organism.\(^9\)\(^,\)\(^11\)\(^,\)\(^29\)\(^,\)\(^34\) Perioperative antibiotic prophylaxis in the insertion of the VA shunt may further lower the incidence of shunt nephritis.

If this mode of therapy fails to achieve shunt sterilization within 2 weeks, Wald and McLaurin\(^4\) proposed that the complete shunt should be replaced and a 2-week intensive course of intraventricular antibiotics started immediately postoperatively. They reported no toxic reactions with intraventricular antibiotic injection. Such toxicity was sought, but not found, in the form of anaphylactoid reactions, bone marrow depression, or seizures. The only positive finding at the time of treatment was a rise in CSF protein values, the exact amount of which was not reported.

Immediate removal of the shunt, replacement with a new shunt system in a different location, and simultaneous administration of systemic and intraventricular antibiotics have been advocated by several authors.\(^1\)\(^,\)\(^3\)\(^,\)\(^33\)\(^,\)\(^33\) Following removal of the shunt, 51% of the reported patients made a complete recovery. As a result of these studies, careful follow-up monitoring with periodic urinalysis and serum immunoglobulin profiles is recommended in shunted children, since early diagnosis and treatment of shunt nephritis can prevent irreversible renal damage in these patients.\(^2\)

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