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Shunt nephritis: a rare and forgotten diagnosis

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ABSTRACT

Shunt nephritis is a rare complication of ventriculoatrial and ventriculoperitoneal shunt infection. The clinical manifestations are nonspecific and include asthenia, arthralgias, anorexia, weight loss, hematuria, proteinuria, and progressive renal impairment. Therefore, diagnosis can be delayed up to several years after the first clinical manifestations, which increases the risk of progressive renal impairment and neurological dysfunction. A 57-year-old woman who had undergone ventriculoperitoneal shunt placement in 1990 was admitted to the nephrology department to perform an elective kidney biopsy due to hematuria, proteinuria, and rapidly progressive renal failure. The patient presented with asthenia and weight loss with a duration of one year. No other symptoms were reported. The kidney biopsy was suggestive of infection-related glomerulonephritis: since an exudative, membranoproliferative pattern was seen in light microscopy and immunoglobulin M (IgM) and C3 staining were predominant on immunofluorescence. During the hospital stay, the patient developed neurological symptoms. Cerebrospinal fluid (CSF) examination showed pleocytosis. Shunt nephritis was suspected, and antibiotic treatment was initiated. Due to the patient's worsening of neurological status, an urgent shunt removal surgery was performed. Two months later, her renal function was normal, and the urinalysis result was unremarkable, even though her neurological status did not improve. Although rare, shunt nephritis should be considered in patients that have a history of ventriculoperitoneal shunt placement and present with a proliferative or membranoproliferative glomerulonephritis and prominent IgM deposits in immunofluorescence. Early diagnosis and shunt removal are critical for improving the neurological and renal prognosis.

Implication for health policy/practice/research/medical education:

Although rare, shunt nephritis should be considered in patients that have a history of ventriculoperitoneal shunt placement and present with a proliferative or membranoproliferative glomerulonephritis and prominent IgM deposits in immunofluorescence. Early diagnosis and shunt removal are critical for improving the neurological and renal prognosis.

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Introduction

Ventriculoatrial (VA) and ventriculoperitoneal (VP) shunts are used to treat hydrocephalus in order to relieve intracranial pressure (1). The most common causes of shunt failure in both pediatric and adult populations are shunt obstruction followed by infection, with infection occurring in 8–15% of patients who undergo VP shunt placement (2,3). Shunt nephritis is an even rarer complication of shunt infection, and its incidence has been declining since its first description in 1965 (4,5).

The clinical manifestations of shunt nephritis are

nonspecific and include asthenia, arthralgias, skin rash, anorexia, weight loss, and recurrent fever. Consequently, diagnosis can be delayed by up to several years after the first clinical manifestations (5-7). Bacteremia may be intermittent, and negative results are initially obtained in 56% of cerebrospinal fluid (CSF) cultures and 27% of blood cultures (6). The most frequent microorganism involved is *Staphylococcus epidermidis*, but other microorganisms that might be mistaken for contaminants in blood cultures can occur, such as *Propionibacterium acnes* (7,8).

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Clinical workup may show anemia, an elevated sedimentation rate, decreased C3 complement levels, and often positive results for cryoglobulins, antineutrophil cytoplasmic autoantibodies (ANCA), rheumatoid factor, and antinuclear antibodies (ANA). Hepatosplenomegaly may appear in ultrasonography (5,8). Hematuria is present in 90% of cases, and proteinuria can range from mild to nephrotic. Renal function can vary from normal to rapidly progressive loss (5-7).

A membranoproliferative pattern is the most common pattern found in kidney biopsies, but there can be isolated mesangial proliferation, as well as extra-capillary proliferation with crescents in some cases (8,10). Immunofluorescence microscopy demonstrates subendothelial and mesangial granular deposits containing polyclonal immunoglobulin M (IgM), immunoglobulin G (IgG), and C3 (6,8,10,11). Electronic microscopy shows electron-dense deposits in subendothelial and mesangial regions (8,10,11). Treatment requires antibiotic therapy and prompt shunt removal. Delayed diagnosis and consequent delays in shunt removal are associated with poor neurological and renal prognosis, even if appropriate antibiotics are administered (5-7).

Case Report

A 57-year-old Caucasian woman presented with a history of dyslipidemia, depression, and cerebral hemorrhage complicated by hydrocephalus, which required ventriculoatrial shunt placement 30 years ago in Venezuela and three shunt surgeries in France. The woman had developed progressive weight loss and asthenia for the past year and was referred to the nephrology department because of persistent hematuria and proteinuria, as well as rapidly progressive renal impairment. She was normotensive (blood pressure: 134/64 mm Hg) and had no fever, peripheral edema, arthritis, or cutaneous lesions. The cardiopulmonary examination was normal.

The initial investigation revealed a normocytic normochromic anemia (hemoglobin 8.5 g/dL) with normal haptoglobin, a negative Coombs test, and normal

levels of ferritin, folic acid, and vitamin B12. Her serum creatinine (sCr) level was 2.0 mg/dL (one year prior, sCr was 1.2 mg/dL), and her blood urea level was 114 mg/dL. Urinalysis revealed numerous red blood cells (>25 per high power field) and proteinuria (protein-to-creatinine ratio 1.6). ANA, anti-dsDNA, and ANCA results were negative, complement levels (C3 and C4) were decreased, and the results for rheumatoid factor and cryoglobulins type III (polyclonal IgG and IgM) were positive. Her serology results were negative for hepatitis B and C and for HIV.

An abdominal ultrasound showed hepatosplenomegaly, and renal ultrasound showed normal-sized hyperechogenic kidneys without hydronephrosis. The patient was admitted to the nephrology department, and a kidney biopsy was performed. The biopsy revealed 23 glomeruli, including 9 with diffuse mesangial hypercellularity (6 of which with polymorphonuclear cells), and 4 with glomerular basement membrane duplication, diffuse endocapillary hypercellularity and subendothelial deposits suggestive of a membranoproliferative pattern (Figures 1A, 1B, and 1C). Immunofluorescence microscopy showed 3+ diffuse granular mesangial and glomerular basement membrane IgM and C3 staining, while IgG, IgA, C1q, lambda, and kappa chains were negative.

Blood cultures were then obtained, and treatment with antibiotics was started. *Staphylococcus epidermidis* was isolated in blood cultures. The transthoracic echocardiography result was normal, and thoracic, abdominal, and pelvic computed tomography (CT) scans showed hepatosplenomegaly but otherwise normal results. One week after admission, the patient developed fever and an altered mental state with a Glasgow Coma Scale (GCS) score of 6. An urgent head CT scan was performed and showed hydrocephalus. An examination of the CSF showed pleocytosis (leucocytes 286/ μ L), no erythrocytes, normal glucose (CSF-to-serum glucose ratio was not available), and elevated proteins (86 mg/dL). CSF cultures were negative.

The obstructed VP shunt and the old VA shunt

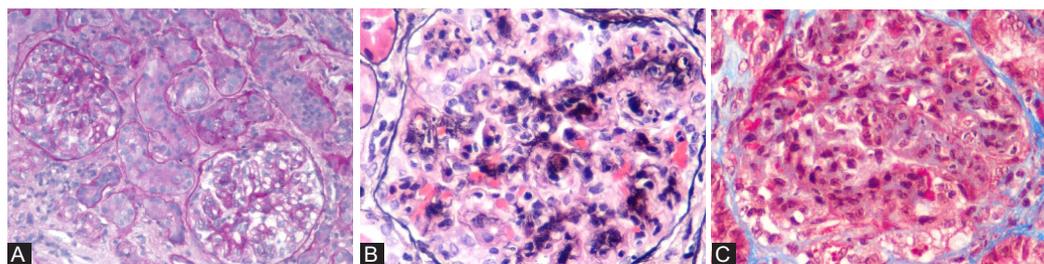


Figure 1. (A) Two glomeruli with mesangial and endocapillary hypercellularity (PAS stain, 200x). (B). One glomerulus with mesangial and endocapillary hypercellularity and polymorphonuclear cells (Silver stain, 400x). (C). One glomerulus with endocapillary hypercellularity and subendothelial deposits (Masson's trichrome stain, 400x).

were surgically removed. After surgery, the patient's neurological status worsened (GCS; 4), and she was admitted to the intensive care unit. Magnetic resonance imaging of the head showed mesencephalic and bulge hemorrhage and edema suggestive of ventriculitis. She was treated with antibiotics for 8 weeks. Two months after shunt removal, apyrexia was sustained, her renal function was normal (sCr=0.6 mg/dL), and urinalysis showed neither proteinuria nor hematuria, although her neurological prognosis remained poor (GCS; 8).

Discussion

Shunt nephritis is a rare complication of shunt infection, and renal injury results from persistent antigenemia due to chronic bacteremia, subsequent immune complex glomerular deposition, classical pathway complement activation, and direct injury to glomerular cells. This is supported by a high frequency of circulating immunocomplexes, cryoglobulinemia, and rheumatoid factor, as well as the preferential localization of deposits in the mesangium and sub-endothelial region (8,11,12). Usually, shunt nephritis occurs at six months after shunt placement. Risk factors for infection include young age, frequent revisions, and certain causes of hydrocephalus, such as post-infectious hydrocephalus, post-hemorrhagic hydrocephalus, or hydrocephalus due to spina bifida or other neurologic defects resulting in communication of the CSF with skin (13). Most cases have a subacute course with constitutional symptoms, and neurological symptoms are often absent, especially when microorganisms such as *Staphylococcus epidermidis* and *Staphylococcus aureus* are involved (5-7,13).

Our patient initially did not present neurological symptoms, hence the diagnosis of shunt infection was not forthcoming. Since constitutional symptoms were the most noticeable, other hypotheses such as occult neoplasia or an autoimmune disease were first considered. The kidney biopsy was a valuable clue for the diagnosis of shunt nephritis due to the membranoproliferative pattern and IgM deposit on. Membranoproliferative glomerulonephritis is the most common pattern in subacute infections, particularly shunt nephritis, and IgM deposits are typically found in shunt nephritis (6,10-12).

Up to a third of adults with infection-related glomerulonephritis (IRGN) have decreased C3 and C4, and cryoglobulins and rheumatoid factor are also frequently positive in IRGN associated with shunt infection and endocarditis (10). Blood cultures, transthoracic echocardiography, and thoracic, abdominal, and pelvic CT scans were performed to exclude an occult infection. As soon as the patient developed neurological symptoms, shunt nephritis became the most probable diagnosis.

Shunt infection is generally defined by the identification of a bacterial pathogen on the CSF in conjunction with CSF pleocytosis, fever, neurological symptoms, and signs of shunt malfunction (2,3,13). Our patient had CSF results compatible with pleocytosis, but the CSF cultures were negative as antibiotics had already been started. The head CT scan revealed hydrocephalus, so ventriculoperitoneal malfunction was suspected, and shunt removal was performed. Initially, an external ventricular drainage was placed, but it was then substituted with a new ventriculoperitoneal shunt. As our patient had already been subjected to 3 shunt revision procedures, surgery was difficult, and her mental status never improved. The renal prognosis is generally favorable since 36.7% of such patients experience partial remission, and 40% have complete remission, as with our patient (6,7).

Conclusion

Although rare, a diagnosis of shunt nephritis should be considered in patients with a history of VA or VP shunt placement who present with renal failure, hematuria, and proteinuria. This consideration is important even if patients present without fever or neurological complaints, particularly if the renal biopsy shows a proliferative or membranoproliferative pattern with prominent IgM deposits. Thus, in these cases, a high index of suspicion is crucial to prevent delays in diagnosis, which worsen the neurological, renal, and overall prognosis.

Conflict of interest

The authors have no conflicts of interest to declare.

Ethical considerations

Ethical issues including plagiarism, double publication, and redundancy have been completely observed by the authors. A written informed consent for publication was obtained from a relative of the patient.

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