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*Case report***Membranoproliferative glomerulonephritis type 1 secondary to an infected ventriculoperitoneal shunt: a case report**

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**Abstract**

Ventricular shunting is the usual method for treatment of congenital or acquired hydrocephalus. Immune-mediated glomerulonephritis (shunt nephritis) is a rare but life-threatening complication of this neurosurgical technique. Intraglomerular deposition of circulating immune complexes and the subsequent activation of the classical pathway of serum complement's cascade result in glomerular inflammation. Membranoproliferative glomerulonephritis is the most common histologic pattern observed in renal biopsy. The diagnosis needs high suspicion and is based on clinical and laboratory findings. Deterioration of renal function in association with signs of infection and low levels of serum complement's proteins C3 and C4 make the diagnosis possible. The prognosis is variable and depends on the time of diagnosis after the onset of glomerular injury. The optimal treatment includes timely removal of the infected shunt in combination with aggressive antibiotic therapy. In this paper we present the case of a membranoproliferative glomerulonephritis type 1 in a patient with a ventriculoperitoneal shunt. Although this type of shunting is considered safer than the ventriculoatrial one, the risk of complications such as an immune-mediated glomerulonephritis still exists.

**Key words:** hypocomplementemia; membranoproliferative glomerulonephritis; shunt nephritis; ventriculoperitoneal shunt

**Introduction**

Ventricular shunting is the usual method for treatment of congenital or acquired hydrocephalus. Ventriculoatrial (VA) and ventriculoperitoneal (VP) shunts are commonly used for the drainage of CSF into the right atrium or the peritoneal cavity, respectively. Each type of shunting presents a series of potential complications. Among them, infections are frequent with an average incidence of 10-15% [1]. They usually occur during the first months after surgery. Clinical manifestations of an infected shunt may

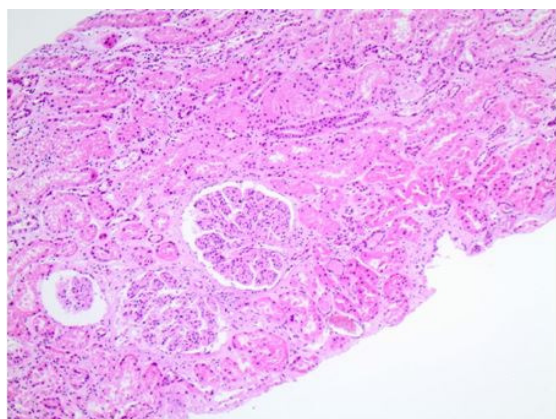
be variable, ranging from an asymptomatic infection to severe clinical conditions such as sepsis, ventriculitis, intraabdominal collections, peritonitis, glomerulonephritis (GN) or cor pulmonale [2]. However, in terms of durability and severity of complications, the VA shunt is considered to be a safer choice than the VP one [2-4]. Shunt nephritis, an immune-mediated GN, is a relatively rare complication of an infected shunt, with an estimated incidence of 0.7-2.25% [5]. Since its first description in 1965 [6], several hundreds of cases have been reported in the literature, mostly associated with an infected VA shunt [7,8]. However, its frequency tends to be lower in the last years, mostly due to better preventive measures taken perioperatively. In this report we describe a case of a shunt nephritis which complicated an infected VP shunt.

**Case report**

A 51-year-old female patient was admitted to the Nephrology Department for investigation of low-grade fever, headache and acute renal failure. Her medical history included hydrocephalus with intracranial hypertension syndrome secondary to CNS echinococcosis and placement of the first VP shunt 10 years earlier. Since then the patient underwent multiple neurosurgical operations for shunt malfunction, including placement of two new shunts, one VA 9 years ago and one VP 4 years ago, respectively, as well as various revisions of the latter. The VP shunt was still functional on her admission. The patient was presented in our outpatient department well orientated in time and space, hemodynamically stable (BP 120/80 mmHg, 90 pulses/min) and with low-grade fever. She reported recurrent episodes of fever and headache during the last six months responding to simple antipyretics and analgesics. The clinical examination was unremarkable with the exception of mild dysarthria and generalized muscle weakness. No edema, rash or palpable lymphadenopathy was present. The initial laboratory workup revealed anemia (Hb 8.6 g/dl, Hct 26.5%) with high erythrocyte sedimentation rate (59 mm/h) and moderate renal dysfunction (urea=64 mg/dl, creatinine 2.05 mg/dl). On urinalysis there was

microscopic hematuria (60 dysmorphic red blood cells per high-power field with few erythrocyte casts) and proteinuria (+++) without leucocyturia. Twenty-four hours urine collection revealed proteinuria within nephrotic range (4349.1 mg/24h). The immunological tests showed mildly increased IgG (1786 mg/dl, normal 700-1600), positive rheumatoid factor (44.3 IU/ml, normal <20) and decreased serum complement's proteins C<sub>3</sub> (35 mg/dl, normal 82-17) and C<sub>4</sub> (6 mg/dl, normal 10-40). The rest of the immunological tests (ANA, anti dsDNA, anti ENA, c-ANCA, p-ANCA, HBs Ag, anti-HCV, cryoglobulins, Coombs' tests) were negative. The renal ultrasound showed kidneys and cortex of normal size, with diffuse hyperechogenicity without signs of obstruction. The chest X-ray was normal and the echocardiogram excluded infective endocarditis showing only a small pericardial effusion. All the initial blood cultures as well as the urinary culture were negative.

Based on the medical history and the clinical and laboratory findings the suspicion of shunt nephritis was set. Thus, the patient underwent renal biopsy which showed hypertrophic glomeruli with lobular appearance and endocapillary hyperplasia. Glomerular basement membranes (GBM) appeared segmentally thickened and reduplicated (double contour) (Figure 1). Immunofluorescence revealed granular, mesangial and intra-membranous deposits of IgM, C<sub>3</sub>, C1q and  $\lambda$  light chains. There were a few atrophic tubules and interstitial fibrosis to a small extent (<10% of the cortex). The histologic pattern was type 1 membranoproliferative GN.



**Fig 1.** Two glomeruli with increased lobulation and hypercellularity. Hyperplasia of endothelial and mesangial cells (H-E staining x 62,5).

Three days after the admission the clinical condition of the patient was deteriorated with high fever (40°C) and signs of intracranial hypertension (vomiting, headache and confusion). The cranial CT scan showed dilatation of the third and fourth ventricles secondary to shunt's malfunction (Figure 2). The examination of cerebrospinal fluid (CSF) revealed marked leucocytosis and hypoglycorrhachia (1600 cells/mm<sup>3</sup>, PMNn=90%, glucose=64 mg/dl, protein=12.5mg/dl). Cerebrospinal fluid and blood cultures were sent for analysis while an empirical antibiotic therapy was initiated (Vancomycine 1 gr / 48h

iv and Rifampicin 600 mg / 24h iv). In the meantime the obstructed shunt was removed and a temporary external CSF drainage was placed.



**Fig. 2.** Cranial CT

*Staphylococcus aureus* in both blood and CSF cultures as well as at the tip of the shunt was detected. Progressively a decline of the number of cells was observed in the CSF examination and a new cranial CT scan showed decongestion of the ventricles and thus a new ventriculoperitoneal shunt was placed. Renal function and proteinuria were normalized on the 17th and 36th day, respectively. After 68 days in the ICU the patient was transferred to the Internal Medicine Department in stable condition.

## Discussion

Shunt nephritis is an immune-mediated GN, which rarely complicates an infected ventricular shunt. Colonization of the distal tip of the shunt and passage of the nephritogenic strains into the bloodstream are the initial pathophysiological events. Persisting bacteremia stimulates the formation of circulating immune complexes. Intrglomerular deposition of the complexes and the subsequent activation of the classical pathway of the serum complement induce glomerular injury [7]. The presence of bacterial antigens in the renal tissue has been described [9].

In our case *Staphylococcus aureus* was isolated from blood and CSF cultures. *Staphylococcus* species are responsible for the majority of shunts' infections. *Staph. epidermidis* accounts for about 40% and *Staph. aureus* for another 20% of all cases respectively [2]. *Staphylococcus* has a high affinity for the material of the shunt and produces a biofilm which protects the strains from the bactericide antibiotic effect [10]. Other bacteria of the normal skin flora such as gram positive cocci, gram

positive anaerobic bacilli, gram negative bacilli or yeasts may also infect a ventricular shunt causing nephritis [11,12]. The clinical condition of our patient was initially dominated by renal dysfunction in the context of recurrent febrile episodes but rapidly complicated by intracranial hypertension. Indeed, the clinical picture of shunt nephritis includes signs and symptoms of infection such as recurrent fever, purpuric rash, hepato-splenomegaly or arthritis [13] as well as cerebral manifestations (vomiting, changes of behavior, seizures). The renal manifestations are variable, including microscopic or macroscopic hematuria (88-100%), non-nephrotic range proteinuria (64-100%) or nephrotic syndrome (28-43%), arterial hypertension (10-64%) and renal failure (46-61%) [7,8]. The laboratory work-up is helpful for the diagnosis. Anemia and increased markers of inflammation (leucocytes, CRP and erythrocyte sedimentation rate) are observed. A characteristic finding is hypocomplementemia (C3, C4, CH50), which reflects the activation of the classical pathway of the serum complement. Antinuclear antibodies and serological markers suggestive of circulating immune-complexes such as rheumatoid factor or cryoglobulines may be positive. Cases of shunt nephritis with positive titers of proteinase-3 ANCA have also been reported [14]. Blood and cerebrospinal fluid cultures as well as cultures of the removed shunt's tip can determine the causative agent, guiding accordingly the antibiotic therapy. Brain imaging (CT or MRI scan) can confirm the presence of shunt obstruction.

Histologically, the membranoproliferative pattern is dominant in renal biopsy. Hypertrophic glomeruli with mesangial expansion and hypercellularity, duplication of the GBM and granular, mesangial, subendothelial or intramembranous depositions, predominantly of IgM, IgG and C3 are common findings. Pure mesangioproliferative lesions as well as endocapillary hyperplasia or extracapillary proliferation with crescents have also been reported [11].

Shunt nephritis must be differentiated from subacute infective endocarditis, glomerulopathies with low serum complement levels such as poststreptococcal GN, lupus nephritis or C3 glomerulopathy as well as other secondary causes of membranoproliferative GN (i.e. HCV-related cryoglobulinemic GN or light chain deposit disease). Although the initial colonization of the shunt usually occurs within the first months after the operation, glomerulonephritis may develop after several months or even years. In our case the diagnosis was made 4 years after the last operation for shunt's placement. The patient complained of low-grade fever and intermittent episodes of headache during the previous six months. This clinical information in association with the histologic finding of the preponderance of IgM glomerular depositions was suggestive of a relatively recent inflammatory process with good prognosis.

In general, the time of removal of the shunt after the onset of the infection has influence on the prognosis of

the disease. The optimal treatment consists of complete shunt removal and temporary external drainage of CSF, in combination with the appropriate antibiotics administered intravenously and intraventricularly for at least 10 days [8]. A new shunt must be placed only after clinical remission. In our patient the removal of the infected ventriculoperitoneal shunt and the antibiotic course rapidly normalized her renal function.

## Conclusions

Although the therapy of hydrocephalus with placement of a VP shunt has fewer complications in comparison with a VA one, glomerulonephritis should be considered in patients with VP shunt, signs of infection and coexisting deteriorated renal function. The therapeutic approach includes removal of the shunt combined with aggressive antibiotic therapy. The aforementioned may improve the prognosis of the renal injury.

*Conflict of interest statement.* None declared.

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