Medulloblastoma presenting as dialysis disequilibrium syndrome

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Abstract

Dialysis disequilibrium syndrome (DDS) is a central nervous system disorder that occurs during or after hemodialysis. This is caused by brain edema that manifests as neurological symptoms that include headache, emesis, nausea, blurring of vision, disturbed consciousness, tremors and seizures, and in severe cases, death. The incidence of DDS is very high among patients with preexisting neurological diseases. There has been much debate about the origin of DDS. We report a case of DDS, as presenting syndrome of a medulloblastoma in a child aged 5 years, and discuss the pathogenesis and the possible role of DDS for an earlier detection of occult brain lesions in dialyzed patients.

Key words: Headache, renal dialysis, dialysis disequilibrium syndrome, hydrocephalus, medulloblastoma

INTRODUCTION

Dialysis disequilibrium syndrome (DDS) is the clinical manifestation of an acute neurological dysfunction, attributed to cerebral edema occurring during hemodialysis treatment. It is necessary to keep in mind that preexisting neurological conditions can reduce the intracranial compliance and consequently increase the probability of the hemodialysis-associated brain edema to become symptomatic, causing the so-called DDS.

CASE REPORT

A 5-year-old boy with end-stage renal disease, due to congenital anomalies of kidneys and urinary tract, was shifted from peritoneal dialysis, performed since the age of 6 months, to hemodialysis, because of recurrent peritoni-

Correspondence to: R. Dilena, MD, Department of Neurological Sciences Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, via Francesco Sforza 35, 20122 Milan, Italy. E-mail: robertino.dilena@policlinico.mi.it tis. During the previous year, two renal transplants had been performed and failed due to renal thrombosis. After his third hemodialysis treatment, the boy complained of headache during the session. The headache had frontal location and throbbing quality, onset 1 hour after the beginning of hemodialysis, of increasing intensity (the child often cried desperately), and ended with the end of treatment. Nausea and vomiting were sometimes associated with the headache.

Dialysis prescription (as regards small solutes removal) was adequate and predialysis blood urea nitrogen (BUN) was 140 mg/dL. Intradialytic mannitol infusion, sodium profiling, and reduction of blood flow rate proved unsuccessful in improving the symptoms.

One month after the first hemodialysis-related headache, short episodes of mild headache started to appear occasionally in between the hemodialysis sessions. Family history was positive for migraine (father and maternal grandmother). The neurological examination was normal. A diagnosis of dialysis headache, supported by familiar susceptibility to migraine, was at first considered (Table 1), but unusual headache intensity, occurrence of vomiting, and then initial signs of bilateral papilledema
 Table 1 Diagnostic criteria for dialysis headache according

 to the second edition of the International Classification of

 Headache Disorders³

Diagnostic criteria of dialysis headache

- A. At least three attacks of acute headache, fulfilling criteria C and D
- B. Patient is on hemodialysis
- C. Headache develops during at least half of hemodialysis sessions
- D. Headache resolves within 72 h after each hemodialysis session and/or ceases altogether after successful transplantation

suggested intracranial hypertension. Brain computed tomography (CT) scan revealed a triventricular dilatation related to an isodense mass in the posterior fossa. Brain magnetic resonance imaging (MRI) confirmed the presence of ventricular dilatation, showed transependymal absorption and a median large cerebellar mass, hypointense in T1, hyperintense in T2, having dishomogeneous gadolinium enhancement (Figure 1). A radical surgical resection of the mass was performed: the pathological diagnosis was "desmoplastic medulloblastoma with extensive nodularity." After surgery, no more headache or other symptoms of DDS occurred.

DISCUSSION

To our knowledge, this is the first report of a medulloblastoma presenting with DDS. DDS, first described in 1962 by Kennedy et al.,¹ is a clinical manifestation of an acute neurological dysfunction attributed to cerebral edema occurring during hemodialysis treatment or within 24 hours following hemodialysis. DDS manifests as variable combination of symptoms of different severity that include headache, nausea, vomiting, disorientation, blurred vision, tremors, muscle twitching, hypertension, seizures, coma.² When DDS is mild and characterized by headache, it needs to be distinguished by dialysis headache (as defined by the diagnostic criteria of the International Classification of Headache Disorders,³ Table 1). When severe, it can lead to death, due to massive cerebral edema. New patients, just being started on hemodialysis, are at higher risk to develop DDS, particularly if the BUN is markedly elevated (above 175 mg).⁴ Also, young age is a risk factor for DDS. Important predisposing factors² are the preexisting neurological conditions, particularly intracranial lesions (subdural hematoma, head trauma, recent stroke, hydrocephalus, brain tumors) or conditions associated with cerebral edema (hyponatremia, hepatic encephalopathy, malignant hypertension, rapid elevation of pCO₂, severe metabolic acidosis, severe sepsis). Several cases of DDS in patients with intracranial lesions, such as head injury,5 intracerebral hemorrhage6 and hydrocephalus,7 have been reported and the direct measurement of intracranial pressure (ICP) in these patients has shown that ICP increases significantly during hemodialysis. Animal experimental studies^{8,9} have shown that DDS is caused by brain edema, as a result of rapid hemodialysis, which determines an osmotic gradient between brain and plasma. Data from neuroimaging in humans support this finding. Brain CT scans in uremic patients undergoing intermittent hemodialysis have shown a decreased density,



Figure 1 Brain magnetic resonance imaging: (a) FLAIR sequence, ventricular dilatation with transependimal absorption; (b) T2 sequence, hyperintense cerebellar mass sized $4.5 \times 3.5 \times 3$ cm; (c) T1 sequence, dishomogeneous gadolinium enhancement.



Figure 2 The pressure (P)–volume (V) curve of the intracranial compartment is exponential. If intracranial pressure (ICP) is within the normal range (point a), small volume increases leave the ICP substantially unchanged. If basal ICP is high (point b), similar small volume increases determine a steep rise of ICP (point c).

which gives evidence of an increased brain water content.10 Diffusion-weighted MRI in nephrectomized animals and humans after an initial hemodialysis treatment has shown the presence of interstitial brain edema.^{10,11} Regarding the pathogenesis, the current evidence¹² suggests that urea disequilibrium (according to the so-called "reverse urea effect theory") and perhaps (to a minor degree) organic osmolytes contribute to cerebral edema. According to the first theory ("the reverse urea effect"), during hemodialysis the clearance of urea is slower across blood-brain barrier than across dialytic membrane (from plasma to dialysate), generating an osmotic gradient that produces water movement into brain tissue, finally causing brain edema.¹³ This theory has been demonstrated in experimental animals.^{8,9} In peritoneal dialysis, where the clearance of urea is more gradual, DDS never happens. The second proposed mechanism for brain edema related to hemodialysis, the so-called "idiogenic osmoles theory", states that an osmotic gradient between brain and plasma develops during rapid dialysis because of newly formed brain organic osmolytes.13 However, according to some more recent evidence,¹⁴ it is unlikely that organic osmolytes (like glutamine, glutamate, taurine, and myoinositol) can have an important contribution to cerebral edema in DDS, because they do not significantly rise after hemodialysis.

In our patient, the DDS was caused by the combined effects of an occult brain tumor and the added brain edema caused by hemodialysis. Pathogenesis is easily understood looking at the exponential pressure–volume relationship of the intracranial compartment (Figure 2). The raising of ICP reflects the relationship between alterations of the craniospinal content volume and the compliance, which is the ability of craniospinal axis to accommodate added volume.¹⁵ Considering that the brain is enclosed in a nonexpandable case of bone and that the brain parenchyma is nearly incompressible, a new slowly

growing intracranial volume (like a tumor) displaces venous blood and cerebrospinal fluid (CSF), initially producing a little change in ICP and no symptoms. However, in doing so, the ability to accept other volumes and even the cerebral blood flow component of the cardiac cycle is decreased and becomes clear where other volume is added.¹⁵

In other words, compared with normal intracranial system (Figure 1, point a) in patients with a pathological intracranial mass, like our patient, the compensatory reserve of intracranial system is low (Figure 2, point b). Consequently, while in normal intracranial systems the modest parenchymal swelling added by hemodialysis treatment is compensated and asymptomatic, in pathological intracranial systems (Figure 2, point c) it is sufficient to cause a steep rise of ICP, producing acute symptoms of DDS.

In conclusion, when evaluating patients who develop neurological symptoms during hemodialysis, DDS must be differentiated from dialysis headache, the former presenting with symptoms of intracranial hypertension. DDS suggests a reduced compliance of intracranial compartment, especially when it persists despite optimal hemodialysis prescription: in these cases, a neuroimaging study needs to be urgently performed. Therefore, hemodialysis can paradoxically allow an earlier diagnosis of unknown and potentially treatable intracranial lesions.

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REFERENCES

- Kennedy AC, Linton AL, Eaton JC. Urea levels in cerebrospinal fluid after haemodialysis. *Lancet.* 1962; 1:410– 411.
- 2 Arieff AI. Dialysis disequilibrium syndrome: Current concepts on pathogenesis and prevention. *Kidney Int.* 1994; **45**:629–635.
- 3 Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia*. 2004; **24**(Suppl 1):9–160.
- 4 Lopez-Almaraz E, Correa-Rotter R. Dialysis disequilibrium syndrome and other treatment complications of extreme uremia: A rare occurrence yet not vanished. *Hemodial Int.* 2008;12:301–306.
- 5 Bertrand YM, Hermant A, Mahieu P, et al. Intracranial pressure changes in patients with head trauma during haemodialysis. *Intensive Care Med.* 1983; **9**:321–323.
- 6 Yoshida S, Tajika T, Yamasaki N, et al. Dialysis dysequilibrium syndrome in neurosurgical patients. *Neurosurgery*. 1987; **20**:716–721.

- 7 Flannery T, Shoakazemi A, McLaughlin B, et al. Dialysis disequilibrium syndrome: A consideration in patients with hydrocephalus. *J Neurosurg Pediatr.* 2008;**2**:143–145.
- 8 Pappius HM, Oh JH, Dossetor JB. The effects of rapid hemodialysis on brain tissue and cerebrospinal fluid of dogs. *Can J Physiol Pharmacol*. 1967; **45**:129–147.
- 9 Silver SM, De Simone JA Jr, Smith DA, et al. Dialysis disequilibrium syndrome (DDS) in the rat: Role of the "reverse urea effect. *Kidney Int.* 1992; **42**:161–166.
- Dettori P, La Greca G, Biasoli S, et al. Changes of cerebral density in dialyzed patients. *Neuroradiology*. 1982; 23:95–99.
- 11 Chen CL, Lai PH, Chou KJ, et al. A preliminary report of brain edema in patients with uremia at first hemodialysis:

Evaluation by diffusion-weighted MR imaging. *AJNR Am J Neuroradiol*. 2007; **28**:68–71.

- 12 Galons JP, Trouard T, Gmitr AF, et al. Hemodialysis increases apparent diffusion coefficient of brain water in nephrectomised rats measured by isotropic diffusionweighted magnetic resonance imaging. *J Clin Invest*. 1996; **98**:750–775.
- 13 Patel N, Dalal P, Panesar M. Dialysis disequilibrium syndrome: A narrative review. Semin Dial. 2008; 21:493– 498.
- 14 Silver SM, Sterns RH, Halperin ML. Brain swelling after dialysis: Old urea or new osmoles? *Am J Kidney Dis.* 1996; 28:1–13.
- 15 Andrews PJ, Citerio G. Intracranial pressure. Part one: Historical overview and basic concepts. *Intensive Care Med.* 2004; **30**:1730–1733.