Hydrocephalus and Hyponatremia as the Presenting Manifestations of Primary CNS Lymphoma

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Dear Sir,

Although increasing incidence is reported, primary central nervous system lymphoma (PCNSL) is still uncommon in immunocompetent individuals. Accurate and timely diagnosis of PCNSL is often difficult because of its ambiguous clinical behaviors and inconsistent radiological findings [1–4]. We describe an unusual case of PCNSL whose clinical-radiological manifestations were first suggestive of idiopathic normal-pressure hydrocephalus (NPH) with hyponatremia.

Case Report

A 71-year-old man with an unremarkable medical history presented with progressive dementia and gait disturbance. He had been in good health until 8 months before admission, when he began to show the insidious onset of memory loss and unstable gait. Within the next 7 months, he continued to deteriorate to the point where he was markedly demented, could not walk alone, was completely dependent on his spouse for daily activities and finally developed urinary incontinence. His family noted recurrent episodes of somnolence and lethargy that lasted a few days. Brain CT obtained elsewhere showed a triventricular enlargement without an enhancing lesion. A radionuclide cisternography revealed a ventricular reflux and delayed migration to

the cerebral convexity. He was then referred to our institution for further evaluation of presumed NPH. On admission, he was awake but apathetic and unmotivated. Vital signs were normal. He was confused and disoriented to time and place. He showed profound memory impairment and a Mini-Mental Status Examination read 5 out of 30. Cranial nerve, motor, sensory and reflex functions were intact. Speech was slightly dysarthric and hypophonic. He was generally bradykinetic, accompanied by neither tremor nor rigidity. His gait disturbance was characterized by upright posture, wide-based short steps, gait initiation difficulty, shuffling, freezing and postural impairment. Routine blood works were normal except for mild hyponatremia (124 mmol/l). Serological tests for syphilis and AIDS were negative. Cerebrospinal fluid (CSF) examination disclosed normal opening pressure, 3 white cells/mm³, normal glucose and elevated total protein (142 mg/dl). There were no malignant cells. Three consecutive therapeutic CSF drainages of approximately 70 ml failed to show any clinical improvement. Subsequent CSF tests for virus, tuberculosis, mycoplasma, syphilis, fungi and parasites were negative. One week after admission, he became drowsy and somnolent, with declining responsiveness. Marked hyponatremia (110 mmol/l) was noted and his

mentality had gradually returned to baseline following correction of hyponatremia. Investigation for significant hyponatremia disclosed cortisol deficiency (1.1 µg/dl; normal range, 5–25) and complete hormonal evaluations suggested the presence of pan-hypopituitarism. Brain MRI at that time revealed a triventricular hydrocephalus that was comparable to the initial outside CT. After gadolinium enhancement, there were a thick homogenous enhancement along the ventricle lining and a focal enhancing lesion in the pituitary stalk (fig. 1a, b). A stereotactic biopsy of the lateral ventricle wall demonstrated atypical large lymphoid cells positive for CD20, indicating diffuse large B-cell lymphoma. A thorough systemic investigation including chest and abdominal CT, and bone marrow biopsy showed no evidence of systemic lymphoma. Finally, he was diagnosed as having PCNSL and a scheduled chemotherapy was commenced with dexamethasone, leucovorin, cytosine arabinoside and combined intravenous/intrathecal methotrexate (1 cycle for 3 weeks). Within 2 weeks after the initiation of chemotherapy, the encephalopathic symptoms of confusion, hallucination and somnolence improved to baseline. Repeat brain MRI after completing 2 cycles of chemotherapy revealed complete disappearance of ventricle wall enhancement

Fig. 1. Sagittal (a) and coronal (b) T₁-weighted MR images showing an enlargement of the lateral ventricle and a thick homogenous enhancement along the ventricle wall. A focal enhancing lesion was also found in the pituitary stalk with thickening (white arrowheads).

and a slightly diminished size of the lateral ventricle. Along with the radiological improvement, frontal gait disturbance gradually improved to standing alone and walking with a cane to some distance.

Discussion

In our patient the presenting symptoms manifested as progressive dementia, gait disturbance and urinary incontinence, in association with the radiological appearance of communicating hydrocephalus, were first suggestive of idiopathic NPH because no other identifiable causes of hydrocephalus were found. However, several findings were considered extraordinary for the idiopathic NPH: the rapid course of clinical deterioration, increased CSF protein and lack of improvement following CSF drainages. By the time the patient became lethargic, marked hyponatremia resulting from panhypopituitarism was found. Brain MRI documented a focal enhancing lesion in the pituitary stalk as well as diffuse ventriculitis with communicating hydrocephalus. These unique MRI features led to a brain biopsy, confirming a diagnosis of PCNSL.

PCNSL can present as single or multiple lesions within the brain and the clinical presentation is variable, depending largely on the location of the lesions or possibly related to raised intracranial pressure. The

site affected by PCNSL in our patient is very unusual. Although the most frequently involved site on MRI appearance is the periventricular one, only infiltration of ventricle walls in the form of isolated diffuse ventriculitis accompanied by communicating hydrocephalus has been rarely encountered [5, 6]. Therefore, it is important to recognize this rare presentation of PCNSL in the differential diagnosis of diffuse ventriculitis that can be seen in other tumors or in infectious conditions. The progressive dementia and frontal disequilibrium in our patient may be ascribed to hydrocephalus, but the cause of hydrocephalus remains elusive. We assumed that concomitant leptomeningeal involvement that was not evident on MRI may be responsible for the development of communicating hydrocephalus.

Another intriguing finding is lymphomatous involvement of the pituitary stalk. Cortisol deficiency and hypothyroidism presented with symptomatic hyponatremia that could account for the recurrent lethargy. Lymphomatous involvement of the pituitary gland with hypopituitarism is rare [7] and, to our knowledge, our patient is the first case of PCNSL involving the pituitary stalk with resultant panhypopituitarism that caused symptomatic hyponatremia in the elderly immunocompetent patient.

PCNSLs have heterogeneous T₁- and T₂-weighted signal abnormalities but the majority has a moderate to strong gadolinium enhancement on T₁-weighted MR images. Without enhanced MRI, the final diagnosis of our patient might be idiopathic NPH with hyponatremia [8] and thus emphasis should be placed on enhanced MRI in patients with hydrocephalus of undetermined etiology. Moreover, marked reduction or complete radiological disappearance of lymphoma lesions after short-term steroid treatment, as in our patient, is well described [9]. Given the PCNSL in the differential diagnosis, pathological confirmation should be established before starting steroid therapy, as it may elude the diagnosis.

The presented case is an example of PCNSL simulating other conditions. Heterogeneous radiological findings, together with diverse clinical manifestations and low diagnostic yield of CSF examination, pose a diagnostic challenge of PCNSL and a direct biopsy is mandatory for a correct diagnosis. Awareness that PCNSL can rarely present as hydrocephalus and hypopituitarism may shorten the interval between the clinical onset and diagnosis and prompt the clinicians to commence early treatment.

References

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