

Central Diabetes Insipidus Associated with Orbital Apex Syndrome

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Orbital apex syndrome (OAS) manifests as multiple cranial nerve palsies caused by an abnormal nerve response to inflammation or other processes. Central diabetes insipidus (CDI) is characterized by deficient synthesis or secretion of antidiuretic hormone. A 62-year-old woman underwent myringotomy for otitis media with effusion. Two months after the procedure, symptoms of hearing loss had not improved, and she underwent left tympanoplasty and mastoidectomy. After surgery, she presented with left ocular pain and visual loss. Neurologic examination revealed ptosis, total ophthalmoplegia, and a relative afferent pupillary defect on the left eye. Magnetic resonance imaging showed an asymmetric contrast-enhancing lesion in the left orbital apex and left cavernous sinus, with adjacent dural thickening and enhancement. OAS was diagnosed, and steroid treatment was started. During the regular follow-up period, she reported polyuria, and CDI was diagnosed. Treatment with intranasal desmopressin 10 µg twice daily was started, and symptoms greatly improved. The mechanism underlying the association of CDI with OAS is unclear, and further research is needed. The present case suggests that polyuria in OAS should alert neurologists and ophthalmologists to possible CDI.

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Key words: orbital apex syndrome, central diabetes insipidus, malignant otitis externa, ophthalmoplegia

Introduction

The orbital apex is the posterior confluence of the orbit at the craniofacial junction. Many nerves, including the optic nerve, oculomotor nerve, trochlear nerve, abducens nerve, and the ophthalmic branch of the trigeminal nerve, and blood vessels, pass through this structure. Orbital apex syndrome (OAS) is an abnormal response of these nerves to inflammation or other processes, such as infection^{1–3}, trauma⁴, neoplasms⁵, and autoimmune disorders. Clinically characteristic symptoms include painful proptosis, ophthalmoplegia, and vision loss. A similar disease-cavernous sinus syndrome—does not affect the optic nerve and thus does not involve optic neuropathy. Treatment of the causative disease is necessary, and steroids can be used to treat neurological symptoms⁶.

Central diabetes insipidus (CDI) is characterized by deficient synthesis or secretion of antidiuretic hormone (also called arginine vasopressin or AVP) and can cause

symptoms of thirst and/or polydipsia, as well as increase in serum sodium and osmolality. Although there are several known causes of CDI⁷, it is idiopathic in approximately 30% to 50% of cases. CDI is associated with destruction of hormone-secreting cells in the hypothalamic nuclei⁸, and most such cases are treated with desmopressin.

In this report, we describe a case of CDI in OAS, which, to our knowledge, has not been previously reported.

Case Report

A 62-year-old woman was referred to the nephrology department for evaluation of polyuria. She had undergone myringotomy for otitis media with effusion at another hospital 1 year previously. For 2 months after that procedure, she was treated with third-generation cephalosporin antibiotics, even though microbiological findings

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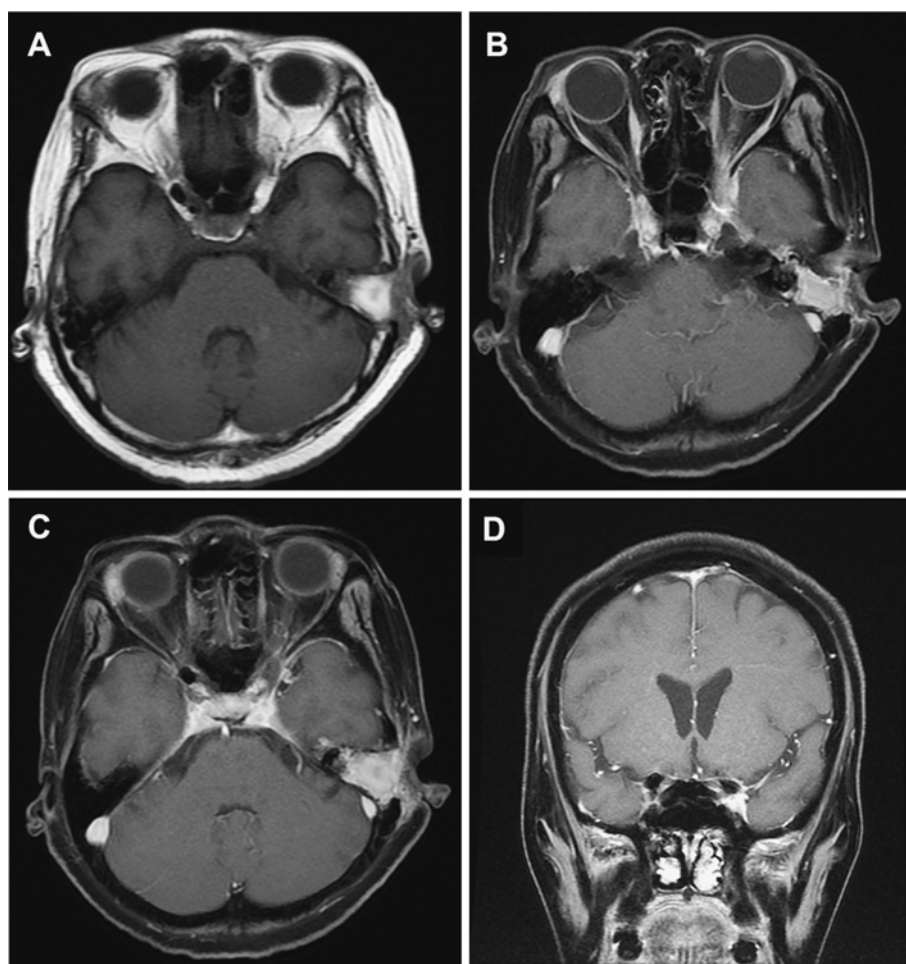


Fig. 1 Axial and coronal T1-weighted brain magnetic resonance images without contrast (A) and with contrast (B-D) show a soft-tissue enhancing lesion at the left orbital apex and left cavernous sinus, as well as fluid collection and contrast enhancement involving the left mastoid and left middle ear.

showed no growth of any pathogen. However, symptoms of hearing loss did not improve, and she underwent left tympanoplasty and mastoidectomy. After surgery, she presented with left ocular pain and vision loss. Neurologic examination revealed ptosis, total ophthalmoplegia, and a relative afferent pupillary defect in the left eye. Magnetic resonance imaging (MRI) showed an asymmetric contrast-enhancing lesion in the left orbital apex and the left cavernous sinus, with adjacent dural thickening and enhancement (Fig. 1). The results of a cerebrospinal fluid examination were normal. OAS was diagnosed, and the patient was treated with high-dose systemic steroids (intravenous methylprednisolone 1 g for 5 days and sequential oral prednisolone) and antibiotics. Ocular pain, ptosis, and ophthalmoplegia improved during treatment, and the patient underwent regular follow-up. Five months after initiating steroid therapy, she complained of polyuria and intermittent thirst and, 3 months later, was transferred to the nephrology department for evaluation.

The patient's daily urine output was 3 L, and the specific gravity of a urine specimen was less than 1.005. Urine osmolality was 165 mOsm/kg H₂O, and plasma osmolality was 345 mOsm/kg H₂O. Serum sodium was 166 mEq/L (135-145). Blood urea nitrogen and creatinine levels were 7.3 and 0.6 mg/dL, respectively. Pituitary hormones-including human growth hormone, thyroid stimulating hormone, adrenocorticotropic hormone, luteinizing hormone, follicle stimulating hormone, and prolactin-were within normal ranges. A water deprivation test showed a low urine osmolality of 92 mOsm/kg H₂O, which increased to 385 mOsm/kg H₂O after subcutaneous administration of 5 units desmopressin (Table 1). Sellar MRI showed no posterior pituitary bright spot (Fig. 2). We diagnosed CDI, and treatment with intranasal desmopressin (10 µg twice daily) resulted in marked improvement in symptoms.

Table 1 Results of the vasopressin challenge test

Time	Before Desmopressin	30 min after Desmopressin	60 min after Desmopressin	90 min after Desmopressin
Serum osmol (mOsmol/kg)	304	304	301	302
Urine osmol (mOsmol/kg)	92	62	385	337



Fig. 2 Sagittal section of a T1-weighted sellar dynamic magnetic resonance image shows no posterior pituitary bright spot.

Discussion

We describe a case of CDI in a patient who initially had only OAS, which suggests that polyuria in OAS should alert neurologists and ophthalmologists of possible CDI. OAS consists of multiple cranial neuropathies secondary to infiltration of the orbital apex, typically resulting from infectious, inflammatory, or neoplastic processes. The present case of OAS was most likely caused by inflammation of the otitis media, with effusion sequelae of surgery. However, the onset and worsening of CDI are difficult to explain.

The relation of CDI with OAS is not known. However, the orbital apex and cavernous sinus are successive structures, and the cavernous sinus and pituitary gland are adjacent. Lesions below the median eminence of the hypothalamus, including posterior pituitary lesions, rarely cause permanent CDI since antidiuretic hormone is produced in the hypothalamus and can be secreted into circulation via the portal capillaries in the median eminence. The clinical severity of CDI depends on the extent

of neuronal destruction⁹. Typically, 80% to 90% of magnocellular neurons of the hypothalamus must be destroyed before symptoms manifest¹⁰. The pituitary gland lies in the sella turcica, while the paired cavernous sinuses are venous structures that are positioned laterally and contain the cavernous portion of the internal carotid artery. The blood supply to the posterior pituitary is arterial, via the superior and inferior hypophyseal arteries, and drains into the cavernous sinus via the hypophyseal veins. Thus, inflammation of the orbital apex might affect the pituitary gland. In particular, orbital apex inflammation could lead to decreased blood supply to, or compression of, the hypophysis. Of course, inflammation or disturbance of blood drainage in the cavernous sinus might directly affect the posterior pituitary gland. However, although cases of cavernous sinus usually affect cranial nerves III, IV, V, and VI, the present patient had visual loss that was a symptom of cranial nerve II (optic nerve) involvement. Therefore, cavernous sinus syndrome was not suspected or considered in the present patient. No posterior pituitary bright spot was observed, which supports a diagnosis of CDI but is not diagnostic. A recent case study reported that fibrosis of the dura mater over the anterior cranial fossa led to CDI, which was diagnosed as a bright spot in the posterior portion of the pituitary gland on gadolinium-enhanced MRI¹¹. This imaging finding was reported to be present as a normal finding in 20% to 30% of the population, and in the early stages of CDI^{12,13}. Ultimately, we were unable to determine the exact mechanism underlying the association between CDI and OAS, and further research is thus needed.

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Conflict of Interest: None declared.

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