Delayed recovery of adipsic diabetes insipidus (ADI) caused by elective clipping of anterior communicating artery and left middle cerebral artery aneurysms

Jeffrey Tan, Samuel Ndoro, Uchenna Okafo, Aoife Garrahy, Amar Agha, Danny Rawluk

ABSTRACT

Adipsic diabetes insipidus (ADI) is an extremely rare complication following microsurgical clipping of anterior communicating artery aneurysm (ACoA) and left middle cerebral artery (MCA) aneurysm. It poses a significant challenge to manage due to an absent thirst response and the co-existence of cognitive impairment in our patient. Recovery from adipsic DI has hitherto been reported only once. A 52-year-old man with previous history of clipping of left posterior communicating artery aneurysm 20 years prior underwent microsurgical clipping of ACoA and left MCA aneurysms without any intraoperative complications. Shortly after surgery, he developed clear features of ADI with adipsic severe hypernatraemia and hypotonic polyuria, which was associated with cognitive impairment that was confirmed with biochemical investigations and cognitive assessments. He was treated with DDAVP along with a strict intake of oral fluids at scheduled times to maintain euonatremia. Repeat assessment at six months showed recovery of thirst and a normal water deprivation test. Management of ADI with cognitive impairment is complex and requires a multidisciplinary approach. Recovery from ADI is very rare, and this is only the second report of recovery in this particular clinical setting.

Case report

A 52-year-old city council worker with a history of clipping of left posterior communicating artery aneurysm 20 years prior was electively admitted for clipping of ACoA and left MCA aneurysm, which were found on surveillance imaging. He has a strong family history of intracranial aneurysms, with his mother and three other siblings diagnosed with the same. He had no other medical comorbidities and was on no regular medications. Preoperatively, he was cognitively intact with no neurological deficits. He had a normal baseline urea and electrolytes, and his other pre-operative investigations were unremarkable.

The patient underwent a left pterional craniotomy and clipping of ACoA and left MCA aneurysms without any intraoperative complications. Shortly after surgery, he developed clear features of ADI with adipsic severe hypernatraemia and hypotonic polyuria, which was associated with cognitive impairment that was confirmed with biochemical investigations and cognitive assessments. He was treated with DDAVP along with a strict intake of oral fluids at scheduled times to maintain euonatremia. Repeat assessment at six months showed recovery of thirst and a normal water deprivation test. Management of ADI with cognitive impairment is complex and requires a multidisciplinary approach. Recovery from ADI is very rare, and this is only the second report of recovery in this particular clinical setting.
complications. On the first post-operative day he was found to be disorientated to place and time but not to person, with some impairment of his short-term memory. On further assessment, he was dysphasic and this was characterised by perseveration, paraphonia and difficulty following commands.

On the second post-operative day, his plasma sodium concentration rose to 160mmol/l (pre-operative sodium=137mmol/l) with a plasma osmolality of 338 mosm/kg (normal 290–295mosm/kg) and urine osmolality of 200mosm/kg. Twenty-four hour urine output was greater than 2,800ml. He had normal blood glucose, potassium and calcium levels. Despite the persistent hypernatremia, he denied thirst (he rated his thirst as one or two out of ten on a visual analogue scale with one being no thirst and ten maximum thirst) and did not drink unless prompted by the nursing staff. He was therefore diagnosed with ADI. Morning cortisol, gonadal and thyroid function were normal.

He was treated with S/C desmopressin (DDAVP) and intravenous 5 % dextrose at a rate of 125mls/hour with an additional oral fluid target of two litres per 24 hours. His plasma sodium corrected over the following five days and he was subsequently switched to oral DDAVP 0.2mgs twice daily and an oral fluid target of two litres per day.

His recovery was further complicated with a tonic clonic seizure on the fifth post-operative day, which necessitated treatment with phenytoin, lorazepam and maintenance dosages of levetiracetam as seizure prophylaxis. CT brain revealed a new infarct in the left anterior frontal lobe. Cerebral angiography showed good occlusion of the previously clipped aneurysms, but moderate vasospasm in the terminal left internal carotid, left A1, M1 and M2 segments with no stasis or vessel occlusion demonstrated.

His dysphasia improved considerably and he suffered no further seizures. Formal cognitive testing with the Galveston Orientation and Amnesia Test (GOAT) and the Montreal Cognitive Assessment (MoCA) demonstrated significant impairment (score of 58/100 and 21/30 respectively).

He was subsequently transferred to the National Rehabilitation Centre on a maintenance dose of DDAVP. He required ongoing prompting to maintain a fluid intake of 1.5–2 litres. His sodium remained normal.

He was readmitted six months later for a water deprivation test (DDAVP was held for 36 hours before the test). The test showed normal concentration of urine with a peak urine osmolality of greater than 700mOSm/kg, reduction in urine output to 30mls in the last hour together with normal thirst score of seven on a ten point thirst visual analogue scale. His plasma sodium remained unchanged and in the normal range throughout the test (Table 1).

Discussion

Water balance and osmolality are finely controlled via hypothalamic integration of signals from osmoreceptors, which leads to a corresponding neurosecretory vasopressin response. The organum vasculosum laminae terminalis (OVLT) is the site of the putative osmoreceptor\(^2\) in the anterior hypothalamus that detects increase in plasma osmolality. Specifically, neurons in the dorsal cap of the OVLT in animal models are able to detect these changes in plasma osmolality and/or angiotensin II or relaxin in the bloodstream.\(^3\) It derives its vascular supply from small perforating branches of the anterior

<table>
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<th>Time (minutes)</th>
<th>Plasma sodium (mmol/L)</th>
<th>Plasma osmolality (mosm/kg)</th>
<th>Urine osmolality (mosm/kg)</th>
<th>Urine output (mls/hr)</th>
<th>Thirst score</th>
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cerebral artery and ACoA. Excitatory connections are said to project from the OVLT to the supraoptic nucleus (SON), which is the site of vasopressin synthesis, which then secretes vasopressin into the bloodstream from the posterior pituitary. A deficient thirst sensation is also known to occur after damage to osmoreceptors in the anterior hypothalamus, which has neural connections to the cerebral cortex centres for thirst appreciation. Therefore, clipping of the anterior communicating artery aneurysm would potentially compromise the blood supply to these osmoreceptor cells. The combination of diabetes insipidus with the absence of thirst in response to hypernatremia but preservation of other hypothalamic function would suggest dysfunction of the osmoreceptor cells rather than the SON, but possibly both.

ADI is a potentially life-threatening condition and is associated with increased mortality compared to DI with intact thirst. The principal features are central diabetes insipidus due to vasopressin deficiency and absence of the normal physiological thirst response to plasma hyperosmolality (plasma sodium or tonicity). In a normal subject, in order to maintain water homeostasis, even a small increase in plasma osmolality will trigger a compensatory thirst response (resulting in increased water intake) and vasopressin secretion which increases renal water re-absorption thus restoring plasma osmolality to within its very narrow normal range. Patients with cranial DI are highly dependent on an intact thirst perception to stimulate compensatory water intake to replace urinary losses, and this explains why most patients with cranial DI but normal thirst have plasma sodium within or near the normal range if they have free access to water. Our patient clearly had adipsia (as evident by lack of drinking despite a very high plasma sodium and reporting a thirst score of one or two over ten despite significant dehydration) with absent or blunted vasopressin response (as evident by hypotonic polyuria despite a very high plasma sodium level). The response to exogenous vasopressin administration confirms this to be cranial DI. Most recently, copeptin, which is a glycosylated peptide that is released from the hypothalamus, is being described as a novel biomarker in the diagnosis of polyuria-polydipsia syndromes. It is being evaluated in a multi-centre international study (NCT01940614) comparing it with the current gold standard water deprivation test.

ADI is also strongly associated with obesity and sleep-related disorders like apnoea, which can lead to progressive respiratory stress and compromise. This should be evaluated in all ADI patients with an Epworth sleepiness score, and these patients may benefit from early weight management programs if clinically indicated.

There have only been a limited number of reported cases of adipsic/hypodipsic cranial DI or cognitive deficits relating to ACoA surgery in the literature. The true incidence of adipsic/hypodipsic DI following elective clipping of an ACoA aneurysm is unknown. Recovery of adipsic DI resulting from clipping of ACoA aneurysm is an exceptionally rare event, and to our knowledge has only been described once before. In a recently published case series of 12 patients with DI, Cuesta et al described a 51-year-old male had recovery of osmoregulated thirst and AVP secretion ten years post-clipping of ACoA aneurysm in the setting of a subarachnoid haemorrhage. The difference in interval between onset and recovery in these two cases highlights the heterogenous pattern of recovery seen in ADI and emphasises the importance for long-term surveillance.

There are several proposed mechanisms for recovery of thirst in ADI. In a case series of three paediatric patients with DI post-resection of craniopharyngioma in which recovery of thirst (and persistence of DI) occurred within nine months, the authors proposed that adipsia was demonstrative of neuronal contusion with the capacity to recover after time. However, recovery of thirst perception after a much longer interval has also been described and attributed to neural regeneration in the infarcted anterior hypothalamus supplied by the small perforating braches of the ACoM aneurysm. Adipsia may also be exacerbated by, if not itself a manifestation of, cognitive impairment post-operatively.
Our patient responded well to DDAVP and hypotonic fluid intake, which is the first line treatment in cranial diabetes insipidus. The dosage of DDAVP varies among individuals but generally a low dose is advised initially, which can be increased as necessary. Chlorpropamide, which acts by increasing renal tubule’s responsiveness to endogenous vasopressin and has been postulated to stimulate vasopressin secretion from the posterior pituitary, could be supplemented in patients with residual ability to secrete Vasopressin, although in modern clinical practice, almost all patients with DI can be managed long-term with oral or nasal Desmopressin. Regular measurements of plasma sodium are essential. Scheduled targeted intake of water is to be based on daily changes to body weight akin to another form of medication, however, this was made difficult by his cognitive impairment.

Conclusion

Management of ADI with cognitive impairment is complex and requires a multidisciplinary approach. Recovery from ADI is very rare, and this is only the second report of recovery in this particular clinical setting.

Competing interests:
Nil.

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