CASE REPORT

Late diagnosis of isolated central diabetes insipidus secondary to congenital toxoplasmosis—case report

Tahir Omer1,2,3,*,†, Mustafa Khan4,5 and Thomas Western6,4

1Department of Clinical sciences and nutrition, University of Chester, Chester, UK, 2Department of Life Sciences and Education, University of South Wales, Cardiff, UK, 3Department of Endocrinology and Diabetes, Northampton General Hospital, Northampton, UK, 4Department of Endocrinology and Diabetes, Bedford Hospital, Bedford, UK, 5Department of Biomedical and Life Sciences, Cardiff University, Cardiff, UK, 6Department of Internal Medicine, Rotorua Hospital, Rotorua, New Zealand

*Correspondence address. Northampton General Hospital Cliftonville, Northampton NN1 5BD, UK.
Tel: 01604 634700; Fax: 01604 545 819; E-mail: ometahir@gmail.com

Abstract

Congenital toxoplasmosis is an uncommon infection. Hypothalamic/pituitary involvement leading to isolated central diabetes insipidus is extremely rare. Making a correct diagnosis of this condition, albeit challenging, is crucial for adequate management. We present a 54-year-old female who developed central diabetes insipidus as a complication of congenital toxoplasmosis. She had polydipsia and hypernatraemia on presentation and responded to intranasal desmopressin with normalization of above-mentioned findings. Magnetic resonance imaging and cranial X-ray’s showed pronounced intracranial calcifications in both choroid plexuses. Thyroid function tests, serum cortisol level and anterior pituitary function were all normal. To the best of our knowledge, this is the first reported case of isolated diabetes insipidus due to congenital toxoplasmosis in literature diagnosed late in adulthood and gives an insight into the challenges of diagnosing central diabetes insipidus and the hypothalamic/pituitary involvement in cases of congenital toxoplasmosis.

INTRODUCTION

Toxoplasmosis is caused by an infection with the protozoan intracellular parasite ‘Toxoplasma gondii’ [1]. The parasite can be transmitted vertically to the foetus from a mother with no preceding exposure. The risk of congenital transmission depends on the timing of the maternal infection. It is <2% in the first trimester to >80% in the third trimester [2]. Congenital toxoplasmosis has a prevalence of 1–10 per 10 000 live births [3] and is typically subclinical. Acute presentation in neonates may include hydrocephalus, chorioretinitis, epilepsy, anaemia, thrombocytopenia, hepatosplenomegaly and jaundice [4]. Few infants may present with psychomotor delay. Involvement of the hypothalamic pituitary axis is uncommon and isolated hormonal deficiencies are rare [2, 3].

CASE REPORT

A 54-year-old woman was referred for evaluation for chronic hypernatraemia. She described struggling with a 45-year history of excessive thirst and polyuria. She was diagnosed with congenital toxoplasmosis as an infant and was previously investigated as a child in the early 1970s for the possibility of central diabetes insipidus (DI). However, due to normal urine osmolality and serum sodium level in the upper range of normal at that time, this was changed to a diagnosis of primary polydipsia. She was referred to an endocrinologist at the age of 36 due to polyuria and raised serum sodium level. However, due to lack of nocturia and random urine osmolality above 150 mOsmol/kg, it was thought that her condition was likely due to high water intake.
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Since then her serum sodium level had remained elevated at 148–150 mmol/L, and she presented to our clinic referred by her general practitioner. Her past medical history included cognitive developmental delay, bilateral chorioretinitis, profound sensorineural hearing loss and epilepsy. Her medical family history was unremarkable. She was delivered by normal vaginal delivery following an uneventful pregnancy. Her mother was exposed to dogs and cats able. She was then started on a single nocturnal dose of 10 mcg of nasal desmopressin. She made a remarkable recovery and was very satisfied with the treatment. The treatment has had a robust positive impact on her quality of life.

### DISCUSSION

Intracranial involvement in cases of congenital toxoplasmosis is uncommon [1]. Typically, this includes the triad of hydrocephalus, chorioretinitis and brain calcifications and is categorized by multiple areas of expanding necrosis with periaqueductal and periventricular vasculitic changes [3].

The protozoon can invade the pituitary gland and was found in the sella turcica without provoking inflammatory changes [5]. Involvement of the hypothalamus/pituitary axis usually results in multiple hormonal deficiencies due to the involvement of anterior pituitary. Isolated central DI due to involvement of the posterior pituitary is extremely rare [2, 3, 6, 7]. DI in these cases is usually identified early and responds well to vasopressin [8].

The pathogenesis of toxoplasma-induced DI, however, remains poorly understood [6, 7]. Antidiuretic hormone deficiency leads to the control of osmolality of body fluids being solely dependent upon the operation of an intact thirst mechanism [8].

The diagnosis of DI depends on a careful and comprehensive clinical evaluation, followed by basic metabolic profile, plasma and urine osmolality, and provocative testing for confirmation. Reaching a diagnosis and correct classification of DI is crucial for management, yet it can be challenging [9].

The universal water deprivation test can be very useful. Dehydration results in elevation of plasma osmolality, stimulating vasopressin secretion, which then causes appropriate concentration of urine. The test needs to be performed in a controlled setting under direct medical supervision due to the risk of severe hypernatraemia, which can develop within hours and could potentially be life threatening. Inability to raise the urine osmolality above that of plasma in response to fluid deprivation indicates DI. Patients with central DI usually respond to vasopressin administration leading to urine concentration. Unfortunately, the interpretation of the test is not always straightforward, particularly if the patient has chronic polydipsia or partial central or nephrogenic DI [8, 9].

The gold standard radiological test is an MRI of the sella. The absence of a bright spot in the posterior pituitary on T1 images can help in the diagnosis of central DI. This bright spot represents the neuro-granules containing vasopressin and can be absent in patients with central DI [10].

Our patient has the classical central nervous system involvement. Due to intact compensatory thirst mechanism, she was able to compensate to some degree by excessively increasing

### Table 1: The patient’s initial laboratory results

| Laboratory          | Results | Reference range |
|---------------------|---------|-----------------|
| Urine sodium        | 32 mEq/L| –               |
| Urine chloride      | 25 mEq/L| –               |
| Urine osmolality    | 195 mOsm/kg | –       |
| Sodium              | 150 mmol/L | 133–146 mmol/L |
| Potassium           | 3.8 mmol/L | 3.5–5.3 mmol/L  |
| Creatinine (Jaffe method) | 66 umol/L | 50–90 umol/L |
| ALP                 | 118 u/L | 30–120 u/L      |
| Albumin             | 44 g/L  | 35–50 g/L       |
| Serum osmolality    | 320 mOsm/kg | 275–295 mOsm/kg |
| TSH                 | 4.09 mU/L | 0.25–4.00 mU/L  |
| Free T4             | 16 pmol/L | 12–22 pmol/L    |
| 9:00 cortisol       | 164 nmol/L | 135–550 nmol/L  |
| Prolactin           | 138 µIU/L | <499 µIU/L      |
| Oestradiol          | 65 pmol/L | 80–1400 pmol/L  |

ALP = Alkaline phosphatase; TSH = Thyroid stimulating hormone.

### Table 2: The patient’s water deprivation test

| Time       | Serum osmolality (mOsm/kg) | Urine osmolality (mOsm/kg) | Sodium (mmol/L) | Urine output (ml) |
|------------|-----------------------------|-----------------------------|-----------------|-------------------|
| 08:00      | 312                         | 145                         | 335             |                   |
| 09:00      | 309                         | 80                          | 539             |                   |
| 10:00      | 315                         | 146                         | 458             |                   |
| 11:00      | 315                         | 95                          | 148             | 385               |
| 12:00      | –                           | –                           | 316             |                   |
| 13:00      | –                           | –                           | –               | 292               |
| 14:00      | 313                         | 332                         | 150             |                   |
| 15:00      | 313                         | 542                         | 94              |                   |
| 16:00      | 317                         | 494                         | 86              |                   |
| 17:00      | 316                         | 496                         | 87              |                   |
| 09:00 next day | 306                         | 652                         | 146             |                   |

A pituitary magnetic resonance imaging (MRI) (Fig. 2) showed gross dilation of both lateral ventricles, with atrophy of the left temporo-parieto-occipital region, which are characteristic findings in congenital toxoplasmosis. The sella turcica showed a small pituitary gland. There was normal gadolinium enhancement of the anterior pituitary.

Her prolonged history, the typical MRI findings of congenital toxoplasmosis, the lack of radiological evidence of an alternative hypothalamic or pituitary pathology in addition to the normal anterior pituitary hormonal profile support that her central DI is very likely due to involvement of the hypothalamus by T. gondii in early childhood.

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CONCLUSION

This case report highlights a rare neuroendocrine complication of congenital toxoplasmosis diagnosed in an adult patient and aims at bringing the healthcare providers attention to the subject. It also highlights the difficulties encountered in making a correct diagnosis of DI, which is crucial for adequate management.

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CONFLICT OF INTEREST

None declared.

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ETHICAL APPROVAL

Not applicable.
CONSENT FOR PUBLICATION

The authors obtained written informed consent from the patient for this publication.

GUARANTOR

Dr T.O. is the nominated guarantor of this paper.

REFERENCES

1. Robert-Gangneux F, Darde M. Epidemiology of and diagnostic strategies for toxoplasmosis. Clin Microbiol Rev 2012;25:264–96. doi: 10.1128/CMR.05013-11.
2. Mohamed S, Osman A, Al Jurayyan N, Al Nemri A, Salih M. Congenital toxoplasmosis presenting as central diabetes insipidus in an infant: a case report. BMC Res Notes 2014;7:184. doi: 10.1186/1756-0500-7-184.
3. Nitta A, Suzumura H, Kano K, Arisaka O. Congenital toxoplasmosis complicated with central diabetes insipidus in the first week of life. J Pediatr 2006;148:283. doi: 10.1016/j.jpeds.2005.05.030.
4. Thiebaut R, Leproust S, Chene G, Gilbert R, SYROCOT (Systematic Review on Congenital Toxoplasmosis) Study Group. Effectiveness of prenatal treatment for congenital toxoplasmosis. Lancet 2007;369:115. doi: 10.1016/S0140-6736(07)60072-5.
5. Remington JS, Klein JO. Infectious disease of the foetus and newborn infant. In: Remington JS, McLeod R, Thulliez P eds. Toxoplasmosis, 4th edn. Philadelphia, PA: Saunders, 2001, 205–346.
6. Oygür N, Yılmaz G, Ozkaynak C, Guven AG. Central diabetes insipidus in a patient with congenital toxoplasmosis. Am J Perinatol 1998;15:191–2. doi: 10.1055/s-2007-993924.
7. Karadag A, Erdeve O. Isolated central diabetes insipidus in a newborn with congenital toxoplasmosis. J Pediar Endocrinol Metab 2006;19:173–5.
8. Di Iorgi N, Napoli F, Allegri A, Olivieri I, Bertelli E, Gallizia A, et al. Diabetes insipidus; diagnosis and management. Horm Res Paediatr 2012;77:69–84. doi: 10.1159/000333333.
9. Fenske W, Quinkler M, Lorenz D, Zopf K, Haagen U, Papassotiriou J et al. Copeptin in the differential diagnosis of the polydipsia-polyuria syndrome—revisiting the direct and indirect water deprivation tests. J Clin Endocrinol Metabol 2011;96:1506–15. doi: 10.1210/jc.2010-2345.
10. Shin J, Lee H, Choi C, Suh D, Kim C, Hong S et al. MR imaging of central diabetes insipidus: a pictorial essay. Korean J Radiol 2001;2:222. doi: 10.3348/kjr.2001.2.4.222.