Clin Pediatr Endocrinol 2009; **18**(1), 51-54


## Original Article

# Isolated Neurosarcoidosis Revealed by Diabetes Insipidus, Visual Loss and Diplopia in a Child Patient: A Diagnostic Problem

Rached Jomaa[1], Mohamed Habib Sfar[1], Samia Younes Mhenni[1], Saleh Jenzri[2], Saida Jerbi[3], Baha Zantour[1] and Riad Messoud[2]

[1]*Internal Medicine and Endocrinology Service, CHU Taher SFAR, Mahdia, Tunisia*

[2]*Ophthalmology Service, CHU Taher SFAR, Mahdia, Tunisia*

[3]*Radiology Service, CHU Taher SFAR, Mahdia, Tunisia*

**Abstract.** We report a case of 15-yr-old child that was presented with headache, polyuria, polydipsia, recent ocular motor and abducens nerve palsies and rapid visual loss. He had a long history of progressive symmetric muscular weakness predominant in the lower limb girdle. Water deprivation revealed central diabetes insipidus. Hormonal explorations demonstrated preserved pituitary function with mild hyperprolactinemia at 21.5 ng/ml (N: 2.6 to 13.1 ng/ml). Magnetic resonance imaging showed an extensive isosignal T1 and hyposignal T2 enhanced lesion infiltrating the pituitary gland, optic-chiasmal hypothalamic region, cavernous sinus, cerebrum tent and sphenoid and temporal meningeal spaces. The serum level of angiotensin converting enzyme and cerebrospinal fluid analysis were normal. No other systemic localisation was identified. Muscle biopsy objectified dystrophic changes. Genetic study identified a delT 521 mutation characteristic of Limb-girdle muscular dystrophy type 2C. Corticotherapy rapidly ameliorated the neurological symptoms. This patient was diagnosed as having neurosarcoidosis. Neurosarcoidosis is rarely reported in childhood. We discuss the problems related to diagnosis in such a situation below.

**Key words:** central diabetes insipidus, visual loss, hyperprolactinemia, neurosarcoidosis, limb-girdle muscular dystrophy

## Introduction

Sarcoidosis is a multisystem granulomatous disease usually diagnosed between the ages of 20 to 40 yr (1). The central nervous system is affected in 5 to 10% of cases. Leptomeninges, cranial nerves and the hypothalamic-pituitary axis are the most frequent localisations (1–4). Diabetes insipidus is the most frequently reported endocrine disorder (3, 5, 6). Patient age at endocrine manifestation varies from 10 to 66 yr (mean age: 33 yr) (7). Neurosarcoidosis is rarely reported in childhood (8). Classically, it is associated with other systemic manifestations (2, 8). Limb-girdele muscular dystrophy type 2C (LGMD 2C) is an autosomal recessive disease with early onset in childhood (9).

We report the case of a child with central

Received: September 17, 2008
Accepted: November 25, 2008
Correspondence: Dr. Rached Jomaa, Service de Médecine interne et Endocrinologie, CHU Taher SFAR Mahdia, 5100 Hiboun, Tunisia
E-mail: rached.jomaa@gmail.com

diabetes insipidus, mild hyperprolactinemia and cranial nerves lesions secondary to an isolated neurosarcoidosis, fortuitously associated with LGMD 2C.

## Case Report

A 15-yr-old child was presented with a 4 wk history of headache, polyuria, polydipsia and recent diplopia and rapid visual loss. He had a long history of progressive symmetric muscular weakness predominant in the lower limb girdle. No personal or familial history of tuberculosis was noted. He drank 10 to 13 litres of water per day. His daily urine volume was 12 l/day. This polyuria and polydipsia evolved since 4 mo. In a physical examination, his blood pressure was 80/50 mmHg, his wt was 27 kg (–3 SD) and his height was 140 cm (–3 SD). His penis measurement was 4 cm and his testicular volume was 4 ml. A neurological examination found partial bilateral palpebral ptosis, bilateral reflected mydriasis, convergent strabismus related to the ocular motor and abducens nerve palsies, proximal and distal weakness predominantly in the lower limb girdle and diffuse areflexia. Intellectual function was preserved. The heart, lungs and abdomen were normal. Neither lymphoadenopathy nor skin nodules were detected. An ophthalmologic evaluation revealed bitemporal hemianopsia in the visual ground without any anomaly in the retinol examination. Visual evoked potentials showed bioptical alteration. Glycaemia, natremia, kalemia, calcemia and other routine laboratory investigations were normal. His serum creatine kinase level was 657 IU/L (N: 25 to 195). The results of hormonal tests were as follows: TSH was 0.8 mIU/L (N: 0.34–5.6), free $T_4$ was 0.7 ng/dl (N: 0.58–1.64), cortisol was 204 $\mu$g/L, cortisol peak after intravenous injection of corticotropin (1 $\mu$g) was 537 $\mu$g/L, peak of GH after glucagons injection was 16.5 ng/mL, IGFI was 175 ng/mL (N: 50–170), IGF-BP3 was 3565 ng/mL (N: 1000–3300), Prolactinemia was 21.5 ng/mL (N: 2.6–13.1), FSH was 4.47 mIU/L and LH was 0.73 mIU/L with T at 0.28 ng/mL. Water deprivation followed by administration of vasopressin analogue revealed a central diabetes insipidus (maximal urine osmolality before vasopressin was 212 M). Cerebrospinal fluid (CSF) analysis was normal, and a tuberculin test was negative. The serum level of angiotensin converting enzyme (ACE) was 50.3 IU/l (N: 8 to 52). Magnetic resonance imaging (MRI) with a gadolinium injection showed an extensive lesion infiltrating the pituitary gland, optic-chiasmal hypothalamic region, cavernous sinus, cerebrum tent and sphenoid and temporal meningeal spaces. The lesion was visible in isosignal T1 and hyposignal T2 and was enhanced after gadolinium injection (Fig. 1). The normal hyperintense signal in the neurohypophysis was absent in the T1 image. Chest computed tomography, pulmonary function tests and an electrocardiogram were normal. Skeleton radiography and abdominal ultrasound did not find any anomalies. Electromyography showed a myogenic pattern. Muscle biopsy confirmed dystrophic changes with variability in fibre diameter without any granuloma. Genetic study identified a delT 521 mutation characterising the LGMD 2C.

The patient received intravenous methylprednisolone pulse therapy at a rate of 500 mg/d for three days, followed by daily oral prednisolone therapy (1 mg/kg/d) and nasal spray of desmopressin. During the first wk of treatment, we observed an improvement in vision and disappearance of strabismus and headache. Three, 8 and 18 months later, MRI follow-up showed an important regression of the previously described lesion with appearance of some necrosis in the last exam. Ophthalmologic examinations were normal for the left eye, but we noted an altered right visual ground with atrophy of the right optic nerve. We also noted that prednisolone treatment improved muscular function. The serum ACE level was 15 IU/l (N: 8 to 52). Prednisolone was gradually reduced to 10 mg/d with clinical stabilisation.

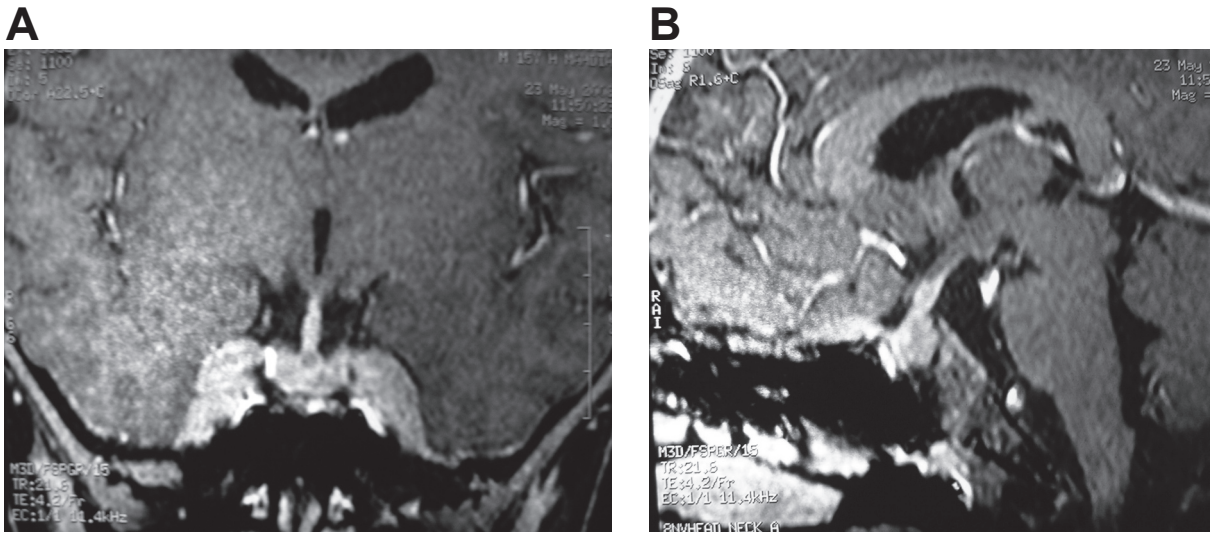


**Fig. 1** Coronal (panel A) and sagittal (panel B) T1-weighted MR images after i.v. gadolinium administration demonstrates enhanced lesions infiltrating the hypothalamus, pituitary stalk, pituitary gland, cavernous sinus, chiasmatic region, cerebrum tent and meningeal spaces.

## Discussion

In this report, we described a child presented with polyuria, polydipsia, rapid installation of visual loss and abducen and ocular motor palsies secondary to an isolated neurosarcoidosis.

This clinical presentation poses a problem in diagnosis. Indeed, isolated cases of neurosarcoidosis are uncommon (1, 2, 10) and occur late (2). Chapelon found 6/30 cases with isolated neurosarcoïdosis, mostly presenting with myopathy or polyneuropathy, but only one presented endocrine dysfunctions alone (2). Many investigations can point towards or support a diagnosis of possible neurosarcoidosis, but only biopsy proves it. In the absence of positive nervous system histology, the diagnosis is supported by a clinical picture compatible with neurosarcoidosis and exclusion of other similar neurological disease, with or not histological confirmation of disease elsewhere (1, 3, 4). In our patient, muscular biopsy eliminated sarcoidosis myopathy.

Among the various symptoms attributed to neuroendocrine sarcoidosis, polyuria and polydipsia are the most frequent manifestation, as reported in approximately 30% of patients with sarcoidosis involving the central nervous system (5, 7, 8). Cranial neuropathies are the commonest manifestation and are seen in approximately 50 to 70% of adults (1) and 31% of children with neurosarcoidosis (8). Association of such abnormalities in our patient suggests the diagnostic of neurosarcoidosis.

A periventricular distribution of lesions and leptomeningeal enhancement are the two most common abnormal findings in neurosarcoidosis (8, 11). In our case, MRI findings with the negativity of others radiological procedures are especially helpful to differentiate neurosarcoidosis from histiocytosis, which is a frequent cause of diabetes insipidus in young patients (12). The images also exclude multiple sclerosis, lymphocytic infundibuloneurohypophysitis and lymphocyctic hypophysitis (5).

The serum levels of ACE are raised in 35 to 75% of patients with neurosarcoidosis (1, 2, 10). Normal ACE levels, such as those seen in our patient, do not exclude a diagnosis of neurosacrcoidosis (1, 10). Normal CSF analysis

helps to exclude infectious diseases, particularly tuberculosis, and some tumours such as lymphoma (1, 10).

In neuroendocrine sarcoidosis, there is no relationship between imaging findings and hormonal status (6). This statement applicable to our patient, who had preservative anterior pituitary function. Hyperprolactinemia is reported to occur in 3-32% of patients (6).

In our patient, corticotherapy rapidly improved the clinical picture within a few days of the start of treatment. This outcome supports the diagnosis of neurosarcoidosis and has discouraged biopsy. It is well known that glucocorticoids have beneficial therapeutic roles in the treatment of muscular dystrophies (13).

In conclusion, we report a case of a child with diabetes insipidus, mild hyperprolactinemia and rapid installation of cranial nerve lesions. A diagnosis of neurosarcoidosis was made on the basis of the clinical presentation, MRI findings and elimination of others similar neurological diseases; however, the absence of histological proof prevents a definitive diagnosis. Corticotherapy has rapidly ameliorated the patient's neurological symptoms.

## Acknowledgements

We are grateful to Dr. Mourad Said for his collaboration during treatment of this patient.

## References

1. Joseph FG, Scolding NJ. Sarcoidosis of the nervous system. Pract Neurol 2007;7:234–44.
2. Chapelon C, Ziza JM, Piette JC, Levy Y, Raguin G, Wechsler B, *et al.* Neurosarcoidosis: signs, course and treatment in 35 confirmed cases. Medicine (Baltimore) 1990;69:261–76.
3. Marangoni S, Argentiero V, Tavolato B. Neurosarcoidosis: Clinical description of 7 cases with a proposal for a new diagnostic strategy. J Neurol 2006;253:488–95.
4. Zajicek JP, Scolding NJ, Foster O, Rovaris M, Evanson J, Moseley IF, *et al.* Central nervous system sarcoidosis—diagnosis and management. QJM 1999;92:103–7.
5. Bullmann C, Faust M, Hoffmann A, Heppner C, Jockenhövel F, Müller-Wieland D, *et al.* Five cases with central diabetes insipidus and hypogonadism as first presentation of neurosarcoidosis. Eur J Endocrinol 2000;142:365–72.
6. Bihan H, Christozova V, Dumas JL, Jomaa R, Valeyre D, Tazi A, *et al.* Sarcoidosis: clinical, hormonal, and magnetic resonance imaging (MRI) manifestations of hypothalamic-pituitary disease in 9 patients and review of the literature. Medicine (Baltimore) 2007;86:259–68.
7. Murialdo G, Tamagno G. Endocrine aspects of neurosarcoidosis. J Endocrinol Invest 2002;25:650–62.
8. Baumann RJ, Robertson WC Jr. Neurosarcoid presents differently in children than in adults. Pediatrics. 2003;112(6 Pt 1):e480–6.
9. Kefi M, Amouri R, Driss A, Ben Hamida C, Ben Hamida M, Kunkel LM, *et al.* Phenotype and sarcoglycan expression in Tunisian LGMD 2C patients sharing the same del521-T mutation. Neuromuscular Disorders 2003;13:779–87.
10. Sharma OP. Neurosarcoidosis: a personal perspective based on the study of 37 patients. Chest 1997;112:220–8.
11. Dumas JL, Valeyre D, Chapelon-Abric C, Belin C, Piette JC, Tandjaoui-Lambiotte H, *et al.* Central nervous system sarcoidosis: follow-up at MR imaging during steroid therapy. Radiology 2000;214:411–20.
12. Maghnie M, Cosi G, Genovese E, Manca-Bitti ML, Cohen A, Zecca S, *et al.* Centra diabetes insipidus in children and youg adults. N Engl J Med 2000;343:998–1007.
13. Pradhan S, Ghosh D, Srivastava NK, Kumar A, Mittal B, Pandey CM, *et al.* Prednisolone in Duchenne muscular dystrophy with imminent loss of ambulation. J Neurol 2006;253:1309–16.