

CENTRAL DIABETES INSIPIDUS DUE TO SARCOIDOSIS

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ABSTRACT. We describe a case of a 40-year old Caucasian male who presented with bihilar enlargement. Additional investigation revealed sarcoidosis. During hospitalization patient developed hypernatremia due to central diabetes insipidus. Central diabetes insipidus was caused by neurosarcoidosis. MRI-scan did not show abnormalities of the pituitary gland, but additional investigation showed hypopituitarism. He was treated with prednisolone, minrin and testosterone. Sodium- and testosterone levels normalised but suppletion is still required. (*Sarcoidosis Vasc Diffuse Lung Dis* 2017; 34: 191-193)

KEY WORDS: diabetes insipidus, sarcoidosis, hypogonadism

INTRODUCTION

Sarcoidosis is a systemic disease with formation of granulomas that can be present in multiple organs. Neuro-endocrine sarcoidosis, however, is rarely seen ($\pm 5\%$ of patients with sarcoidosis) and can lead to hypothalamic dysfunction and less often anterior pituitary hormone deficiency.

Here we describe a case of a patient with pulmonary sarcoidosis and central diabetes insipidus due to neuro-sarcoidosis.

CASE

A 40-year old Caucasian male with no relevant medical history presented at the emergency department with complaints of dyspnea and coughing. He had no fever and he had no history of tobacco use.

Furthermore, he lost 4 kg in the previous month. Physical examination revealed no abnormalities except for squeaky expirium. Laboratory results at admission were (normal values between brackets): sodium 137 mmol/L (135-145), creatinine 65 μ mol/L (70-110), calcium 2.34 mmol/L (2.20-2.60), albumin 37.5 g/L (35.0-50.0), c-reactive protein 150 mg/L (0-10), hemoglobin 9.2 mmol/L (8.5-11.0), leucocytes 5.9×10^9 /L (4.0-10.0). Arterial bloodgas analysis showed pH 7.30 (7.34-7.43), pCO₂ 30 mmHg (35-48), bicarbonate 14 mmol/L (23-28), base excess -10.6, pO₂ 79 mmHg (75-100), oxygen saturation 95% (92-98). Chest X-ray showed bihilar enlargement and reticular opacities in the upper lungfields.

He was hospitalized. Initially, he was suspected to have a respiratory tract infection for which treatment with antibiotics was started. The metabolic acidosis resolved spontaneously within 3 days and no cause for this temporal metabolic acidosis could be identified. Additional investigation revealed negative bacterial (Legionella and Streptococcal urinary antigen, serology for C. Burnettii, M. Pneumoniae, B pertussis and C pneumoniae) and viral serology as well as sputumculture. Quantiferon test was also negative. Computed tomography (CT) scan demonstrated bihilar lymphadenopathy and bilateral

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multiple pulmonary nodules with a perilymphatic distribution pattern suggestive for sarcoidosis (Figure 1). Soluble interleukin-2 receptor level (sIL-2R) was 9576 pg/mL (350-3154). Neopterin level was 2.2 ng/mL (0.3-2.5). Angiotensin converting enzyme level was 67 U/L (12-68). Positron Emission Tomography (PET)-CT scan showed increased uptake in the pulmonary hili, no other PET positive lesions were found (Figure 2). Pulmonary function test showed normal static lungvolumes, but a Tiffeneau-index 52%, FEV1 (forced expiratory volume in one second) value of 64% predicted and DLCO (diffusing capacity of the lung for carbon monoxide) of 68% predicted, respectively. Bronchoalveolar lavage fluid analysis showed a lymphocyte count of 40% in the alveolar fraction and a CD4/CD8 ratio of 3.8. Biopsies, which were obtained during bronchoscopy, revealed no granulomas. Uveitis was excluded by the ophthalmologist.



Fig. 1. HRCT-scan shows mediastinal lymphadenopathy at Naruke 4R and bilateral multiple pulmonary nodules with a perilymphatic distribution pattern

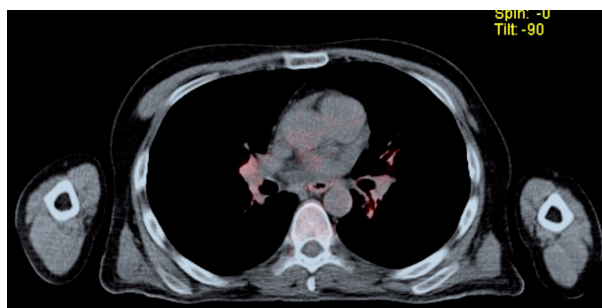


Fig. 2. PET-CT shows bilateral increased FDG-uptake

During hospitalization patient developed hypernatremia (155 mmol/L) with polyuria and polydipsia. Glucose levels were normal. Urine osmolality was very low (78 mOsm/kg). Fluid deprivation test was not performed because of the presence of the hypernatremia. Instead, a test dose of desmopressin was given after which polyuria decreased and urine osmolality normalised. Due to the concurrent diagnosis of sarcoidosis and the absence of other possible causes for central diabetes insipidus it was concluded that the central diabetes insipidus, was due to sarcoidosis. Treatment with desmopressin 10 microgram twice daily and prednisolone 30 milligram once daily was started.

Additional laboratory test results revealed hypogonadotropic hypogonadism: testosterone <0.4 nmol/L (8.4-28.7), LH <0.1 E/L (1.5-9.3) and FSH 0.6 E/L (1.4-18.1). Cortisol was low (08hrs) 0.20 μ mol/L (0.08-0.44) but because prednisone was started no additional testing of the pituitary-adrenal axis was performed. Thyroid hormone was normal: fT4 19.8 pmol/L (12.0-22.0), TSH 2.2 mE/L (0.27-4.2). Repeated anamnesis and physical examination revealed erectile dysfunction and loss of hair in armpits, secondary to the low testosterone levels for which he received suppletion with testosterone gel 25mg once daily. After administration of desmopressin sodium normalised, and polyuria as well as polydipsia resolved. Magnetic resonance imaging (MRI) of the pituitary gland showed no abnormalities (Figure 3).

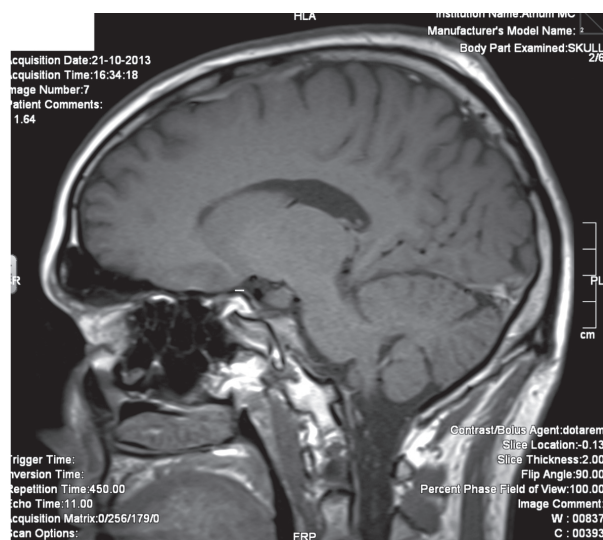


Fig. 3. MRI (T1-image) of the pituitary gland demonstrated no abnormalities

He was discharged after two weeks of hospitalization with prednisolone maintenance-therapy. The dosage was tapered from 30 mg to 5 mg daily and desmopressin was tapered to 10 µg once daily during the following eighteen months. sIL-2R level decreased to 5292 pg/mL. During follow-up, sodium levels remained within the normal range, testosterone level increased, but supplementation is still required.

In conclusion, the diagnosis of hypogonadotropic hypogonadism and central diabetes insipidus due to neurosarcoidosis was made.

DISCUSSION

In this report we described a middle-aged man who presented with hypogonadism and central diabetes insipidus due to neurosarcoidosis.

In a previously published review article, a mean age of 33 years old for patients presenting with endocrine manifestation was described (1). Neurological manifestations of sarcoidosis include aseptic meningitis, cranial neuropathy, myopathy, hydrocephalus, peripheral neuropathy and hypothalamo-pituitary involvement (2). Hypopituitarism is a rare complication in sarcoidosis although the hypothalamus and pituitary gland are the most susceptible endocrine organs (3). Prevalence of hypothalamic-pituitary involvement is estimated at 2.5% in patients with neurosarcoidosis (4). In 2007 Miyoshi et al. described a patient with panhypopituitarism due to sarcoidosis. (5) That patient was treated for two years with corticosteroids. After that period a complete regression of neurohypophysial swelling was present. Defects of the anterior pituitary responses, however, were only marginally alleviated. This is in line with the results of a study which demonstrated the effectiveness to restore function of the anterior pituitary gland is not

to be expected in patients with diabetes insipidus due to neurosarcoidosis (6). Nevertheless, complete recovery of hypothalamic sarcoidosis with hypopituitarism has been described (7).

Although therapy in our patient could be tapered during follow-up, it remains unclear whether complete remission will occur in the future.

In our patient no swelling of the pituitary gland was present. 10% of patients with neurosarcoidosis have a normal MRI of the hypophysis. Hypopituitarism in the absence of pituitary pathology or an identifiable cause is rare.

In patients with multiple anterior pituitary hormone deficiencies, sarcoidosis should be included in the differential diagnosis (8).

REFERENCES

1. Murialdo G, Tamagno G. Endocrine aspects of neurosarcoidosis. *J Endocrinol Invest* 2002 Jul-Aug; 25(7): 650-62.
2. Chen RC, McLeod JG. Neurological complications of sarcoidosis. *Clin Exp Neurol* 1989; 26: 99-112.
3. Loh KC, Green A, Dillon WP, Jr, Fitzgerald PA, Weidner N, Tyrrell JB. Diabetes insipidus from sarcoidosis confined to the posterior pituitary. *Eur J Endocrinol* 1997 Nov; 137(5): 514-9.
4. Zajicek JP, Scolding NJ, Foster O, Rovaris M, Evanson J, Moseley IF, Scadding JW, Thompson EJ, Chamoun V, Miller DH, McDonald WI, Mitchell D. Central nervous system sarcoidosis-diagnosis and management. *QJM* 1999; 92(2): 103-17.
5. Miyoshi T, Otsuka F, Takeda M, Inagaki K, Otani H, Ogura T, Ichiki K, Amano T, Makino H. An elderly patient with sarcoidosis manifesting panhypopituitarism with central diabetes insipidus. *Endocr J* 2007 Jun; 54(3): 425-30.
6. Tabuena RP, Nagai S, Handa T, Shigematsu M, Hamada K, Ito I, Izumi T, Mishima M, Sharma OP. Diabetes insipidus from neurosarcoidosis: long-term follow-up for more than eight years. *Intern Med* 2004 Oct; 43(10): 960-6.
7. Hidaka N, Takizawa H, Miyachi S, Hisatomi T, Kosuda T, Sato T. A case of hypothalamic sarcoidosis with hypopituitarism and prolonged remission of hypogonadism. *Am J Med Sci* 1987 Nov; 294(5): 357-63.
8. Wilson V, Mallipedhi A, Stephens JW, Redfern RM, Price DE. The causes of hypopituitarism in the absence of abnormal pituitary imaging. *QJM* Jan; 107(1): 21-4.