

## CASE STUDIES

## Neurofibromatosis type 1 and lymphocytic hypophysitis: Single trigger and double shots?

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### Abstract

Lymphocytic hypophysitis, an inflammatory disorder of the pituitary stalk and gland, can cause multiple hormone deficiencies. The disease is considered to be of autoimmune etiology. We report here a case of lymphocytic hypophysitis with cortisol deficiency in an 18-year-old female who had been previously diagnosed with neurofibromatosis type 1. The case study also discusses the role of neurofibromin gene in autoimmunity and possible pathogenesis.

Keywords: Neurofibromatosis type 1, Lymphocytic hypophysitis

### Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominantly inherited disorder caused due to the loss of function of neurofibromin gene located on chromosome 17. This in turn causes the upregulation of p21 ras oncogene and the proliferation of melanocytes, endoneural fibroblasts, and Schwann cells (constitute the neural crest cells).<sup>1</sup> The clinical manifestations of the disease are various skeletal, neurological, and dermatological malfunctions. We report here a case of NF1 with lymphocytic hypophysitis and its pathogenetic possibilities.

### Case report

An 18-year-old female presented to the emergency medicine department with persistent vomiting and giddiness of one week duration. Her medical history revealed a previous diagnosis of NF1 and resection of right sided optic glioma around two years back. Her periods were regular. There was no history of any drug intake (including steroids). Physical examination revealed stable vitals, pulse rate of 86 per minute, and blood pressure of 108/78 mm Hg without postural fall. Her face was deformed with a neurofibroma. There were *café au lait* macules on her trunk (Fig. 1) and

freckling in the axillae. She was admitted in acute medical ward and was commenced on intravenous fluids and antiemetics. Her initial biochemical and hematological investigations were within normal limits, but the ESR level was 45 mm/hr. MRI scan showed an extracranial temporoparietal neurofibroma and nodular thickening (3.2 mm; normal <2 mm) with contrast enhancement of the infundibulum and the gland suggestive of lymphocytic hypophysitis (Fig. 2). Subsequent hormonal estimations revealed a very low random serum cortisol (0.46 ug/dl), elevated serum prolactin (57.12 IU/l), and normal TSH, gonadotropins, and free T3 and T4. She was negative for pregnancy test, and anti-thyroid peroxidase antibody (anti-TPO) and ANA estimations. Her serum calcium and ACE (angiotensin convertase enzyme) levels were normal. Chest X-ray and ultrasound abdomen did not reveal any abnormality. Mantoux test done prior to commencing steroids was negative.

Intravenous administration of hydrocortisone 100 mg three times daily was initiated. The subsequent follow-up of the patient in the outpatient department showed symptomatic improvement and the steroid was tapered to

maintenance dose of 20 milligrams per day. The patient is currently stable and is on daily dose of physiological replacement hydrocortisone therapy.

### Discussion

Lymphocytic hypophysitis (infundibular neurohypophysitis) is an autoimmune inflammation affecting the infundibular stalk, and the anterior and posterior lobes of pituitary. Around 80% of the affected patients have circulating anti-arginine vasopressin antibodies. In the current case, very low cortisol levels, elevated prolactin, enhanced pituitary stalk, and high ESR were suggestive of the diagnosis. Sarcoidosis was one of the differential diagnoses considered. A dramatic improvement in symptoms

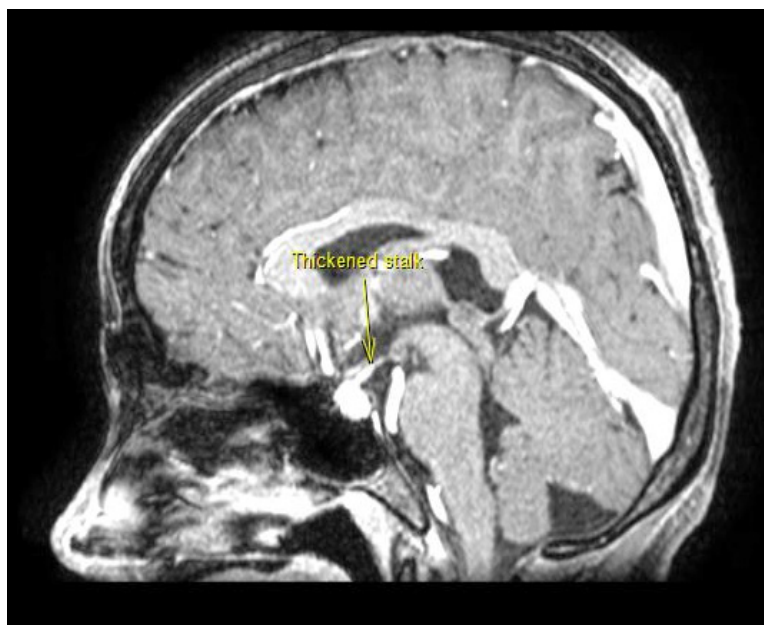
with treatment was observed and they did not recur on rapid tapering of hydrocortisone to physiological doses. In addition, absence of leptomenigeal or systemic involvement ruled out the possibility of sarcoidosis. A pituitary biopsy was necessary to confirm the diagnosis, but it was withheld, as the patient showed symptomatic improvement.

There is literature evidence on the conjoint occurrence of autoimmune conditions with NF. Yaccin *et al.* have reported a case of Hashimoto's thyroiditis and vitiligo in a patient with NF1.<sup>2</sup> Graves' disease and connective tissue diseases have also been previously diagnosed in patients with NF1.<sup>3,4</sup>

**Fig.1 : Café au lait spot on the abdomen**



**Fig. 2: The axial view of MRI scan showing the thickening of the pituitary stalk**



The pathogenesis of autoimmunity in NF1 is considered to be related to the malfunctioning neurofibromin gene. Suppression of Fas ligand expression by the defective neurofibromin causes lack of apoptosis of CD4+ T lymphocytes and the subsequent development of autoimmunity.<sup>5, 6</sup>

To the best of our knowledge, this is the first case of co-existence of NF1 and lymphocytic hypophysitis. This report further strengthens the possibility of the dual effect of the defective neurofibromin gene supporting its role in autoimmune diseases. Although not conducting a biopsy is the limitation of the case, there is enough evidence to conclude the diagnosis.

#### Competing interests

The authors declare that they have no competing interests.

#### Citation

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