



# CASE REPORT

## Langerhans Cell Histiocytosis Presenting with Headache and Sellar Mass in an Adult

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### Introduction

Langerhans Cell Histiocytosis (LCH) is a rare disease characterized by aberrant proliferation of a specific dendritic (Langerhans) cell belonging to the monocyte macrophage system.<sup>1</sup> These cells can infiltrate virtually any organ without inducing dysfunction.<sup>2</sup> LCH is encountered more often in children, with a peak age range of 1-3 years and an incidence of 3-5 cases per million per year and a male to female ratio of 2:1.<sup>3</sup> LCH is rare in adults and the incidence may be underestimated due to the fact that many cases likely go undiagnosed.

In order of decreasing frequency, the presenting symptoms are skin rash, dyspnea or tachypnea, polyuria and polydipsia, bone pain, lymphadenopathy, weight loss, fever, gingival hypertrophy, ataxia, and memory problems.<sup>4</sup> Regarding the endocrine system, LCH has a particular predilection for involvement of the hypothalamo-pituitary axis (HPA), leading to diabetes insipidus (DI) in up to 50% of cases. In a recent analysis, DI was the most common and permanent consequence of LCH, occurring in 24% of patients.<sup>5</sup> Other endocrine deficiencies can develop in up to 20% of patients.<sup>5,6</sup> Endocrine manifestations include DI followed by growth hormone deficiency with a median latency of about one year, followed by gonadotropin deficiency with a median latency of about seven years from the

diagnosis of DI. ACTH and TSH deficiency also have been described.<sup>7</sup>

The length of time from the first symptom(s) to diagnosis is frustratingly long. Many patients wait one to four years before the correct diagnosis is made, and others have symptoms for 5 to 20 years.<sup>8</sup> The difficulty in making an accurate diagnosis is reflected in the long time from symptom onset to diagnosis, lack of clinical suspicion, and the variable characteristics of the disease. Diagnosis is based on electron microscopy or immunohistochemistry (positivity for S100 protein and CD1a).<sup>9-11</sup> Treatment is based on the extent of the disease and the site of involvement.<sup>12</sup>

We report a case of a woman who had symptoms of diabetes insipidus for many years before she presented with headache and subsequently was diagnosed with LCH.

### Case Report

A 53-year-old post-menopausal female presented to her primary care physician with complaints of headache and blurry vision for two to three months. An MRI of the brain revealed an enhancing lesion in the suprasellar hypothalamic area extending into the brain stem measuring 2.8 cm (AP) x 2.4 cm (transverse) x 1.6 cm with hyperintensity on FLAIR (see Figure 1). During this time frame, the patient also was diagnosed with hypothyroidism. In retrospect, the patient had

polyuria, compensated with polydipsia, for a few years preceding the headache. An MRI-guided right fronto-temporal craniotomy was completed with guided biopsy.

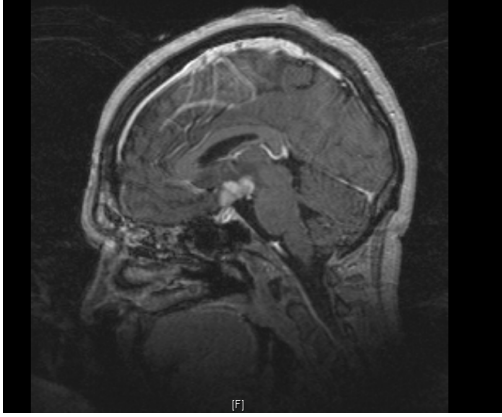


Figure 1. MRI of the brain showing the lobulated enhancing mass centered in the suprasellar location.

Pre-biopsy biochemical evaluation revealed normal sodium (140 mmol/L). Post-operatively, while in recovery room, the patient had greater than 800 ml of urine output over the course of three hours. Over the next two hours, she became lethargic, developed respiratory acidosis, and was intubated for respiratory failure. She had urine output of about nine liters over a period of 12 hours. Her blood chemistry 12 hours post-biopsy revealed hypernatremia with serum sodium of 166 mmol/L. An endocrinologist was consulted to manage diabetes insipidus.

The patient initially was treated with DDAVP 1 mcg subcutaneously every eight hours with resultant improvement in polyuria. Fluids were replaced first with a combination of quarter-normal saline and half-normal saline with the addition of free water via naso-gastric feeding tube and later replaced with half-strength saline only. With these measures, her sodium improved to 146 mmol/L over a span of 48 hours. At this point, she was extubated. Serum sodium was maintained in normal range with oral

maintenance fluids and DDAVP 0.2 mg by mouth twice daily. Perioperatively while she was intubated, she received dexamethasone, and IV levothyroxine 50 mcg daily.

The pathology report revealed gliosis with scattered atypical cells, patchy chronic inflammation, and Rosenthal fibers. Histiocytic infiltrate was present consistent with Langerhans cell histiocytosis. A patchy polymorphous inflammatory infiltrate consists of small lymphocytes, plasma cells, eosinophils, sometimes multiple per high power field, and larger histiocytes with clefted "C" to horseshoe-shaped nuclei (immunoreactive with CD1a). A few multinucleated cells including one Touton-type giant cell was noted, but no well-formed granulomas were found. No emperipolesis was noted. No necrosis was detected. CD1a stains were positive for multiple of the cells with abundant cytoplasm and C-shaped nuclei. S100 highlighted frequent immunoreactive cells, inclusive of, yet more than, the CD1a population of cells (see Figure 2). CD20 highlighted multiple small lymphocytes (see Figure 3). No CD117 immunoreactive cells were identified ruling out CNS germinoma. CNS lymphoma was ruled out with appropriate stains. The consulting oncologist recommended chemotherapy as an outpatient.

Additional workup during hospital stay revealed panhypopituitarism. Dexamethasone was discontinued post-extubation and the 8 am cortisol level, more than 48 hours later, was 1.0 mcg/dl indicating adrenal insufficiency. FSH and LH were low at 0.7  $\mu$ U/mL and 0.2  $\mu$ U/mL respectively, which in a post-menopausal female was suggestive of pituitary dysfunction. TSH was 0.07  $\mu$ U/mL and free T4 was 1.0 ng/dL presenting a picture of central hypothyroidism. The dose of levothyroxine was changed from 50 mcg intravenously daily to her home dose of 112 mcg daily by mouth. Physiological hydrocortisone replacement was started at 20

mg in the morning and 10 mg in the evening. DI was treated with a maintenance dose of DDVAP 0.2 mg by mouth twice daily. Eventually she underwent rehabilitation and was discharged home.

After discharge, the patient was treated

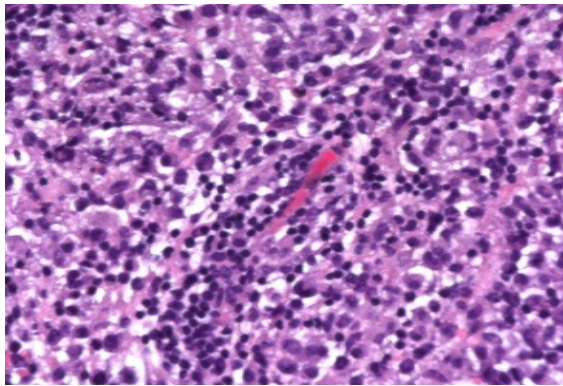


Figure 2. Numerous Langerhans cells were confirmed immunohistochemically (anti-CD1a, original magnification x200).

### Discussion

LCH is a rare disorder characterized by idiopathic proliferation of specialized bone marrow derived Langerhans cells. LCH may be systemic or localized and its clinical manifestations are variable. In adults, infiltration is seen most frequently in bones (52%), lungs (40%), and skin (7%); whereas involvement of liver, spleen, lymph nodes and bone marrow is less frequent.<sup>4,13,14</sup> In view of the non-specific symptoms, LCH usually is misdiagnosed or under diagnosed.

This case was unique as her symptoms of LCH were related only to pituitary involvement. The patient had symptoms of DI for a few years, but the diagnosis was delayed until the patient had symptoms from the pituitary mass including headache and visual complains. By then, the patient had lost anterior and posterior pituitary hormone functions including antidiuretic hormone, thyroid, gonadotropic hormones, and cortico-

with chemotherapy. Following treatment, she had about 33% shrinkage of the tumor size on MRI. Her visual symptoms have resolved but she continued to have pan-hypopituitarism and was on adequate pituitary hormone supplements.

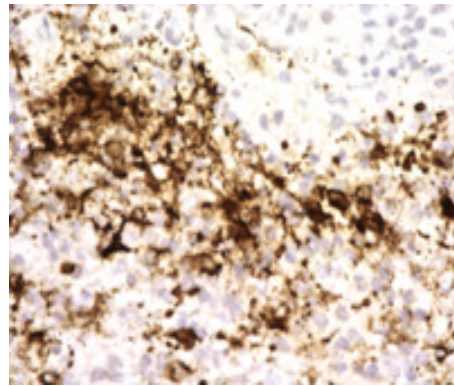


Figure 3. A biopsy from the suprasellar mass contained patchy areas of a cellular lymphohistiocytic infiltrate, including scattered Langerhans cells with typical C-shaped nuclei.

trophin hormones. The long mean time from symptom onset to diagnosis was due, in part, to lack of clinical suspicion related to the low incidence of the disease.

Diagnosis of LCH is based on electron microscopy or immunohistochemistry (positivity for S100 protein and CD1a). Treatment is based on the extent and site of disease involvement. Options include conservative therapy with topical steroids, hormone replacement therapy, or local excision versus aggressive therapy including radiation, chemotherapy, anti-CD1a mono-clonal antibodies and/or organ or stem cell transplantation.<sup>15-17</sup>

This report attempted to identify evolution of pituitary dysfunctions, histopathological picture, and progress of the disease. Health care professionals should be aware of LCH as a possible cause of DI. An increased awareness could lead to early

diagnosis and treatment before more permanent damage occurs. The quality of life may be impaired by long-term sequelae including orthopedic problems, deafness, pituitary insufficiency, neurological defects, and impaired liver function. Most reported cases have systemic involvement.<sup>8,15</sup>

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