ADULT ONSET CNS LANGERHANS CELL HISTIOCYTOSIS: EARLY DIAGNOSIS MAY PREVENT PERMANENT PANHYPOPITUITARISM

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OBJECTIVE

To emphasize the importance of early suspicion and detection of CNS Langerhans Cell Histiocytosis (LCH) in a symptomatic patient with Diabetes Insipidus (DI) and discuss the evolution, progression and treatment of CNS LCH.

INTRODUCTION

LCH is a rare disease with an annual incidence of 3-5 cases per million. It is characterized by aberrant proliferation of specific dendritic (Langerhans) cells belonging to the monocyte-macrophage system. These cells can infiltrate virtually any organ without necessarily inducing dysfunction. LCH shows a particular predilection for involvement of the Hypothalamo–Pituitary Axis (HPA), leading to DI. The incidence in adults may be underestimated due to the fact that many cases likely remain undiagnosed.

CASE PRESENTATION

A 53 year old post-menopausal female presented to her primary care physician with complaints of headache and blurry vision for 2-3 months. MRI of the brain revealed a lobulated enhancing mass centered in the suprasellar location measuring 2.8 cm (AP) x 2.4 cm (Transverse) x 1.6 cm with hyper intensity on FLAIR (see fig 1). During this time frame the patient was diagnosed with hypothyroidism. A review of systems revealed that the patient had polyuria, compensated with polydipsia for a few years preceding the headache. MRI guided right fronto-temporal craniotomy with biopsy was performed during hospitalization. Prior to the biopsy, her sodium was normal (140 mmol/L). Post-operatively, while in the recovery room, the patient was noted to have greater than 800 ml of urine output over the course of three hours. Overnight, the patient developed respiratory failure and was intubated. In the interim she had a urine output of approximately nine liters over a 12 hour period, and as a result, her serum sodium increased to 166 mmol/L. Endocrinology was then consulted to manage her DI. Patient was initially treated with DDAVP 1 mcg subcutaneously every eight hours with resultant improvement in her polyuria. Fluids were replaced first with a combination of quarter Normal Saline and Half Normal Saline with free water via naso-gastric feeding tube and later with Half-normal saline only. Her serum Sodium normalized (145 mmol/L) in 48 hours. The biopsy findings revealed LCH (see fig 2). Peri-operatively, she had received dexamethasone. Additional work up revealed panhypopituitarism (see table 1). Dose of levothyroxine was increased to 112 mcg (from 50 mcg pre-op) by mouth daily. Physiological hydrocortisone replacement was started at 20mg in the morning and 10mg in the evening.

DI was managed with DDAVP 0.2 mg by mouth twice daily. Oncology was consulted who recommended chemotherapy (Cladarabin) as outpatient Currently she has completed treatment with Cladarabin with more than 33% shrinkage in tumor size and mass symptoms.

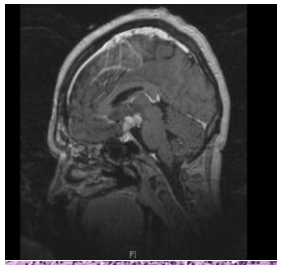

Fig1. MRI of the brain showing the lobulated enhancing mass centered in the suprasellar location measuring 2.8 cm (AP) x 2.4 cm (Transverse) x 1.6 cm with hyperintensity on flare.

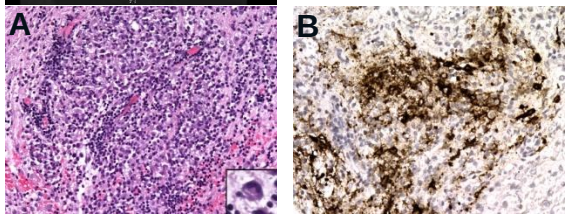

Fig 2. A) A biopsy from the suprasellar mass contained patchy areas of a cellular lymphohistiocytic infiltrate, including scattered Langerhans cells with typical C-shaped nuclei (lower right, insert; hematoxylin and eosin, original magnification x200) along with a few small CD20 positive lymphocytes among the numerous T-cells (not pictured). B. Numerous Langerhans cells were also confirmed immunohistochemically (anti-CD1a, original magnification x200).

Cortisol-AM	Latest Range: 6.7-22.6 MCG/DL	1.0
FSH	No range found	0.7
Luteinizing Hormone	No range found	0.2
T4-Free	Latest Range: 0.6-1.6 NG/DL	1.0
TSH	Latest Range: 0.35-5.00 MCU/ML	0.070 (L)
T3-Free	Latest Range: 2.1-3.9 PG/ML	2.6

Table 1: Post-op pituitary hormonal work up revealing panhypopituitarism.

DISCUSSION

•LCH is rare in adults and most often presents with symptoms related to bone, lung and skin.
•Our case is unique as her symptoms are related only to pituitary involvement.
•Despite being symptomatic for years, the patient was diagnosed only after the suprasellar lesion exhibited mass effect, leading to further work up. By this time, she had lost both anterior and posterior pituitary function.
•The mean time from symptomatic onset to diagnosis of DI is 6.25 years and from DI to anterior pituitary involvement is 5 years.
•MRI guided biopsy is needed for definitive diagnosis.
•Chemotherapy decreases the size of tumor, but does not necessarily reverses DI.

CONCLUSION

•Delay in diagnosing LCH as a cause of DI is in part due to very low incidence of LCH, particularly in adults.
•This case highlights the importance of including LCH as the etiology of DI.
•An increased awareness could lead to possible early diagnosis and treatment.
•High index of suspicion, early diagnosis, and treatment of LCH in cases of central DI in adults may prevent development of panhypopituitarism

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