Case Report

DIFFUSE LARGE B-CELL LYMPHOMA PRESENTING WITH DIABETES INSIPIDUS: A CASE REPORT

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ABSTRACT

Objective: To present a rare case of pituitary gland involvement in paranasal and central nervous system (CNS) lymphoma.

Methods: We describe the clinical presentation, laboratory data at presentation and follow-up, imaging studies, and management of the patient. A brief review of literature regarding pituitary involvement in lymphoma is also presented.

Results: A 53-year-old woman with a history of human immunodeficiency virus (HIV) infection was evaluated for 6-month history of polydipsia, high-volume polyuria, and headache. Laboratory work-up was consistent with diabetes insipidus. Magnetic resonance imaging showed a 6-mm lesion in the posterior pituitary and ill-defined decreased T1 signal in the clivus and sphenoid sinus. She was treated medically with desmopressin for her urinary symptoms, with symptomatic improvement. In the interim, she was admitted for acute visual loss. Repeat imaging revealed a soft tissue mass involving paranasal sinuses with intracranial extension to the sella and hypothalamus. Biopsy confirmed the diagnosis of diffuse large B-cell lymphoma. The patient was treated urgently with multidrug chemotherapy and intraventricular methotrexate, resulting in neurologic improvement. After 12 cycles, the patient did well, with regression of the tumor and marked improvement of her urinary symptoms with decreasing desmopressin requirement.

Conclusion: This is a rare case of hypothalamus-pituitary involvement in a diffuse, large B-cell lymphoma due to paranasal sinus involvement with CNS extension, presenting with central diabetes insipidus. Early detection with a high index of suspicion (particularly in patients with HIV) and treatment can lead to better outcomes. **(AACE Clinical Case Rep. 2015;1:e111-e114)**

Abbreviations:
AIDS = acquired immune deficiency syndrome; **CNS** = central nervous system; **DI** = diabetes insipidus; **HAART** = highly active antiretroviral treatment; **HIV** = human immunodeficiency virus; **MRI** = magnetic resonance imaging

INTRODUCTION

Pituitary involvement in lymphoma is rare. Most patients remain asymptomatic due to great reserve capacity of the anterior pituitary gland. When symptomatic, posterior pituitary deficiencies are more common than anterior, as the posterior pituitary is supplied directly by the systemic circulation. Therefore, diabetes insipidus (DI) seems to be the most frequent symptom of pituitary metastasis, although B-cell lymphoma itself represents a rare cause of DI (1).

Involvement of the pituitary gland with lymphoma of paranasal sinuses, which are very rare tumors with high tendency for central nervous system (CNS) extension, has rarely been described (1).

CASE REPORT

We present the case of a 53-year-old postmenopausal woman with a history of asthma, hypertension, and

Submitted for publication June 26, 2014
Accepted for publication October 11, 2014
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DOI:10.4158/EP14295.CR

chronic nonprogressing human immunodeficiency virus (HIV) infection of more than 10 years, who was evaluated in the endocrinology clinic for a 6-month history of polydipsia, polyuria (~3 liters per day), headaches, and a 30-pound weight loss. She denied visual changes, mood disorders, or history of lithium use. Physical examination was unremarkable, including visual fields and neurologic examination. Laboratory evaluation was suggestive of diabetes insipidus (Table 1), central hypogonadism, and central hypothyroidism (Table 2). Other pituitary hormone axes were uninvolved (Table 2). Brain magnetic resonance imaging (MRI) with and without contrast was done for further evaluation and showed a rounded area of limited enhancement measuring approximately 6 × 6.7 mm in the posterior aspect of the pituitary gland along with a focal defect in the floor of the sella at the same level. An ill-defined decreased T1 signal involving the superior and anterior aspect of the clivus was observed (Fig. 1). Mucoperiosteal thickening and partial opacification of the sphenoid sinuses and mucosal thickening of the maxillary and ethmoid sinus were also noted. The pituitary stalk and hypothalamus were unremarkable.

Given her symptoms and laboratory results, the patient was started on desmopressin, which resulted in improvement of urinary symptoms. She was referred for neurologic and neurosurgical evaluation in view of worsening headaches and abovementioned MRI findings. Her headaches were attributed to chronic sinusitis, and no surgical intervention was recommended. Over the next month, her headaches continued to worsen, and she was therefore referred for visual field evaluation and a repeat MRI. However, she was hospitalized for acute unilateral right-sided visual loss before she could get the recommended workup. Computed tomography of the head showed a large paranasal sinus mass with infiltration to the right optic nerve. MRI revealed a soft tissue mass involving the paranasal sinuses, with intracranial extension to the sella and hypothalamus. Biopsy was performed, which revealed a diffuse, large B-cell lymphoma with a Ki-67 index of more than 80%. Further imaging showed cervical and inguinal adenopathy and right upper- and lower-lobe lung nodules.

The patient was treated urgently with multidrug chemotherapy with "EPOCH-R" (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab), with intravenous methotrexate, resulting in neurologic improvement after the first treatment. After 12 cycles, the patient did well, with regression of the tumor seen on follow-up positron emission tomography scan. In the meantime, she was also started on highly active antiretroviral treatment (HAART). She had marked improvement of her symptoms, with decreasing desmopressin requirements (Fig. 2). The results of repeat thyroid function tests were within the normal range; she did not require thyroid hormone replacement.

DISCUSSION

Pituitary gland involvement with lymphomas can occur as a primary pituitary lymphoma and as CNS involvement in diffuse B-cell lymphoma. Mechanisms of the latter include hematogenous or meningeal spread and direct extension from the juxtasellar and skull base lesions, as seen in our case. A vast majority of the cases are asymptomatic due to the great reserve capacity of the pituitary gland (1,2). When symptomatic, posterior pituitary deficiencies are more common than anterior (2). This may be explained by the blood supply of the pituitary gland, as the posterior pituitary is supplied directly by the systemic circulation through hypophyseal arteries, whereas the anterior pituitary is supplied through the portal vessel system to allow delivery of hypothalamic prohormones. Also, the posterior pituitary has a larger area of contact with the adjacent dura. DI has been reported as the most common symptom associated with metastatic pituitary disease (2,3). It can be transient or intermittent due to regeneration of neuro-hypophyseal fibers and obliteration of symptoms because of adrenocorticotropic hormone deficiency until corticosteroid replacement is initiated. Hypothyroidism and hypoadrenalism are the other frequent hormonal deficiencies (2,3). B-cell lymphoma is one of the rare differential diagnoses for anterior or posterior pituitary hormonal deficiency. B-cell lymphoma should be kept on the list

Table 1
Laboratory Results Before and After DDAVP Treatment – Consistent with a Diagnosis of Diabetes Insipidus

Parameter	Before DDAVP	After DDAVP
Serum Na (mg/dL)	145	136
Serum osmolality (mOsm/kg)	309	--
Urine osmolality (mOsm/kg)	125	--
Urine Na (mEq/L)	25	34
Urine specific gravity	1.003	1.010

Abbreviations: DDAVP = desmopressin; Na = sodium.

Table 2
Comparison of Laboratory Work Before and After Chemotherapy

	Initial evaluation	Postchemotherapy	Normal range
FSH (IU/L)	2.08	4.8	1.5-14.0
LH (IU/L)	1.0	3.6	0.8-7.6
Free T_4 (ng/dL)	0.78	0.98	0.84-1.68
TSH (mIU/L)	0.131	1.53	0.4-4.0
Cortisol (μg/dL)	10.5	11.2	7-25
ACTH (pg/mL)	30	--	5-27
Prolactin (ng/mL)	57.7	3.2	1.9-25.0

Abbreviations: ACTH = adrenocorticotropic hormone; FSH = follicle-stimulating hormone; LH = luteinizing hormone; T_4 = thyroxine; TSH = thyroid-stimulating hormone.

for differential diagnosis for new-onset DI, especially in patients with HIV/acquired immune deficiency syndrome (AIDS), as it may represent a potentially reversible cause of DI.

Pituitary adenoma and other sellar lesions, including granulomas, abscesses, cysts, aneurysms, traumas, and apoplexy, can mimic the clinical as well as radiologic presentation of metastatic pituitary disease. It is difficult but important to distinguish metastasis from these conditions in order to make appropriate management decisions. The presence of DI and ophthalmoplegia, specifically abducens nerve palsy, along with rapidity of symptom onset have been suggested to differentiate infiltration of lymphoma or leukemia from adenomas but are nonspecific. Radiologic findings are also usually not helpful (3).

The presented case describes pituitary involvement in a paranasal sinus lymphoma, which has rarely been described in the literature (1). Lymphoma of paranasal sinuses itself is a rare tumor, with an incidence of approximately 1% in North America, where the histology is almost exclusively diffuse, large B-cell lymphoma (4). It has an aggressive nature, with a tendency to involve the CNS; leptomeningeal spread and CNS relapses are common, possibly due to its proximity to the brain. Diagnosis of this type of lymphoma is usually late because of a paucity of symptoms caused by the tumor and normal or subtle changes seen on the imaging studies (5,6). Thus, patients present with locally advanced disease, as seen in our case, where the patient was initially thought to have sinus headaches, with minimal changes in MRI, which delayed the diagnosis and treatment. MRI may be normal or may show iso- or hypodense T1 or T2 signals in the pituitary. Posterior pituitary involvement may cause absence of the pituitary bright spot (2).

Although randomized controlled trials are not available due to the rarity of paranasal sinus lymphoma, previous reviews have suggested multidrug chemotherapy followed by local irradiation (unless the area of irradiation is

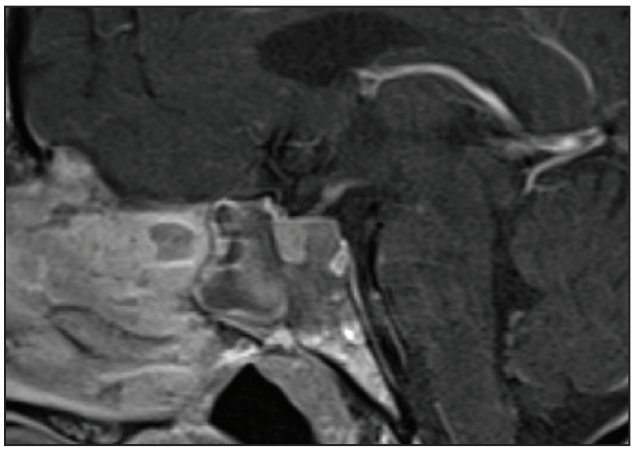

Fig. 1. Initial magnetic resonance imaging showing limited enhancement in posterior pituitary and decreased T1 signal in clivus.

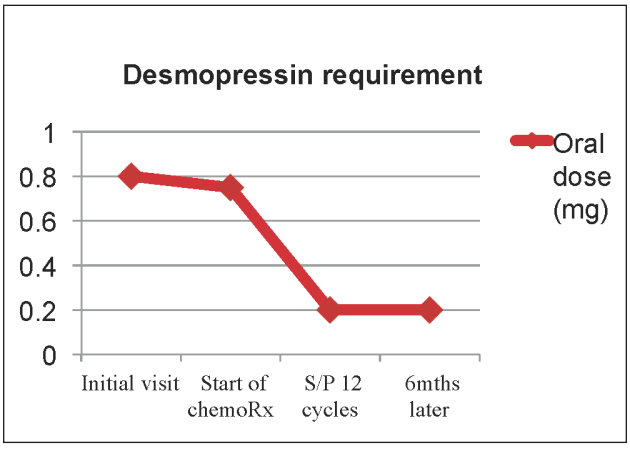

Fig. 2. Desmopressin dose requirement over time.

too large) with or without intrathecal chemoprophylaxis. A review of 44 patients with primary paranasal sinus lymphoma treated with the abovementioned regimen showed 5- and 10-year overall survival rates of 48 and 41% and disease-specific survival rates of 62 and 62%, respectively (4). Doxorubicin-based chemotherapy combinations such as "CHOP" (adriamycin, cyclophosphamide, vincristine, and prednisone) or "ACVBP" (doxorubicin, cyclophosphamide, vindesine, bleomycin, and prednisone) are recommended. The role of CNS prophylaxis is controversial; however, intrathecal chemoprophylaxis has been suggested for aggressive paranasal sinus lymphomas (4,7). In addition to improving survival, chemotherapy has been shown in previous case reports to at least partially reverse the hormonal deficiency, which was seen in our case as well (8). Complete restoration of pituitary function has also been reported (2).

Introduction of HAART has decreased the incidence of AIDS-related non-Hodgkin lymphoma. Immune recovery induced by HAART leads to improvement in patient survival (9). In a retrospective study of 192 patients, the complete response rate and the median overall survival for AIDS-related lymphoma improved to 57% and 43.2 months, respectively, in the HAART era, compared with 32% and 8.3 months in the pre-HAART era (10). The appropriate timing of institution of HAART in relationship to chemotherapy has been evaluated in several clinical trials but still remains a topic of debate. Suggested approaches include either continuing or briefly withholding HAART while on multidrug chemotherapy. HAART may be beneficial when given concurrently with chemotherapy for patients with low CD4 cell counts at the time of diagnosis of lymphoma, those with a history of opportunistic infections or other AIDS-related complications, those who appear likely to adhere to taking multiple oral medications, and those patients who would likely achieve an undetectable HIV viral load with HAART. HAART either during or shortly after completion of chemotherapy may ameliorate the increased toxicity of concurrent immunotherapy, thereby improving survival of patients with AIDS-related lymphoma (11).

CONCLUSION

This is a rare case of hypothalamus-pituitary involvement in a diffuse, large B-cell lymphoma of the paranasal sinus with CNS extension, presenting with central DI. Early differentiation of lymphoma from other sellar lesions is important to plan appropriate treatment. Timely detection with a high index of suspicion (particularly in patients with HIV) and treatment can lead to better outcomes.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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