Title: Primary pituitary lymphoma: An unusual cause of hypopituitarism, case report and literature review.

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Abstract:

Background:

The most common cause of hypopituitarism is pituitary adenoma. However, in the case of intrasellar masses different etiologies are possible. We report an unusual case of primary pituitary lymphoma presented with hypopituitarism.

Case presentation:

A 26 year old woman presented with amenorrhea, galactorrhea and neurological disorders. In addition the laboratory work-up revealed partial hypopituitarism. The magnetic resonance imaging of the head showed a sellar mass. A presumptive diagnosis of granulomatous processes was made and the patient was given steroid therapy. Repeat brain MRI detected new lesions in the brain with regression of the pituitary mass. The biopsy of the parasellar mass revealed the diagnosis of B-cell lymphoma.

Conclusion:

Lymphoma of the pituitary stalk is extremely rare and represents a diagnostic challenge. Medline review reveals only nineteen similar cases. This report highlights the role of MRI and biopsy in the case of pituitary mass to set the accurate diagnosis.

Key words:

Hypopituitarism, sellar mass, pituitary lymphoma, primary central nervous system lymphoma.
Background:

The sellar and parasellar region is an anatomically complex area where a number of neoplastic, infectious, inflammatory, developmental and vascular pathologies can occur. The most common etiology of hypopituitarism is the pituitary adenoma, accounting for 10 to 15% of intracranial neoplasms [1]. Differentiation among various etiologies may not always be easy, since many of these lesions may mimic the clinical, endocrinologic and radiologic presentations of pituitary adenomas. The diagnosis of sellar lesions involves a multidisciplinary effort. We report an unusual case of primary pituitary lymphoma presenting as hypopituitarism.

Case presentation:

A 26 year-old-woman, with a history of infertility for five years (treated by ovulation induction medications), was admitted to the hospital for evaluation of amenorrhea, galactorrhea and neurological disorders. She was well until 6 months before her admission in the neurology department of the University Hospital of Rabat, when she developed weakness, headaches associated with nausea and vomiting, shaking chills, night sweats, an 8-pound weight loss and diplopia. Computed tomography scan (CT scan) of the brain showed a hyperdense mass in the sellar and parasellar region (figure 1). Magnetic resonance imaging (MRI) of the brain revealed an enhancing sellar mass with suprasellar extension (figure 2). Laboratory findings showed: microcytic anemia (10 g/dl), hyponatremia (130mEq/L), elevated erythrocyte sedimentation rate (40 mm in first hour) with an increased alpha-2-gobulin in serum protein electrophoresis. An endocrinological evaluation revealed low levels of follicle stimulating hormone (2.5 IU/L) and luteinizing hormone (0.5 IU/L), serum prolactin level was greatly increased (145 ng/ml), and thyroid function tests were normal. She
underwent an extensive biological work-up evaluation including: skin testing for tuberculosis; serological tests for HIV, panel hepatitis and syphilis; lumbar puncture and salivary gland biopsy; all were unrevealing. Chest x-ray and abdominal echography were normal. Initially, the diagnosis of granulomatous processes was suggested, on the basis of the patient’s presentation and imaging findings (the mass was in the pituitary stalk and the hypophyseal parenchyma was normal also because predilection sites of granulomatous processes are the leptomeninges especially the sellar and suprasellar region, such as the pituitary stalk). Then the patient was given prednisolone 60 mg/day with clinical improvement. However, subsequent head MRI detected new lesions of the brain in contrast of the regression of the pituitary mass (figure 3). She underwent stereotactic biopsy of the parasellar lesion. Histological examination revealed infiltrative large-sized lymphocytes with occasional mitotic figures. The immunohistochemical tests confirmed the diagnosis of large B-cell lymphoma (the B-cell marker CD20 was positive and the CD3 T-cell marker was negative) (Figure 4). The patient died rapidly before the initiation of treatment two weeks after the diagnosis.

Discussion:

We described an unusual presentation of lymphoma revealed by hypopituitarism. Our patient presented a partial hypopituitarism with a sellar mass in brain MRI. The sella and parasella region may be affected by a wide variety of tumors. Pituitary adenoma is the most common cause of sellar mass [1]. Primitive germ cell tumors, vascular lesions, benign tumors, infections and granulomatous processes are others common differential diagnosis [1]. But lymphoma of the pituitary stalk is extremely rare and represents a diagnostic challenge. To our knowledge, only nineteen similar cases have been previously reported (tableau 1) [2-20]. In the present case the diagnosis of granulomatous processes has been made, on the basis of patient presentation and imaging findings. The treatment was subsequently initiated with
steroid therapy and showed clinical improvement and sellar mass regression. Though, subsequent head MRI detected new lesions in the cerebellum and periventricular region (figure 3). Then the diagnosis of primary central nervous system lymphoma (PCNSL) was strongly support according to neuroimaging work-up, because the vast majority of PCNS tumors arise in the deep hemispheric periventricular white matter, the corpus callosum, cerebellum, orbits, and cranial nerves [21].

In the series of patients with pituitary lymphomas reported, only in one case was the presumptive diagnosis lymphoma of the brain. In the large majority of cases presumptive diagnosis was pituitary adenoma. Confirmation of diagnosis was most frequently obtained with surgery [2-20].

In our review of 20 cases of pituitary lymphoma including our patient, we found that the mean age of patients was 55.5 years (range 26 - 86 years). The most common presentation was hypopituitarism (75%), followed by headache (55%), diplopia (40%), diabetes insipidus (31%) and hyperprolactinemia (25%). Histologically, similar to PCNSL, most lymphomas of the pituitary gland are B-cell non-Hodgkin lymphoma. The MRI of the head demonstrated enhancing parasellar masses with diffuse enlargement of the pituitary gland (95%), suprasellar extension (45%), cavernous sinus extension (35%), and stalk thickening (20%). Differential diagnosis is difficult on MRI findings. The enhancing parasellar masses with diffuse enlargement of the pituitary gland appears to be suggestive of a pituitary lymphoma (table 1).

Nevertheless, primary central nervous system lymphoma (PCNSL) represents approximately less than 2% of primary brain tumors. Its incidence has increased over the last 30 years [19]. So far, despite recent therapeutic advances, PCNSL exhibit one of the worst prognoses among all non-Hodgkin lymphomas (median survival < 6 months) [22]. However, primary pituitary lymphomas seem to have a better prognosis according to the cases published
up to now (median survival > 6 months; range 11 days - 21 months). Our patient died two weeks after diagnosis.

For a long time, radiotherapy (RT) has been the standard treatment, producing a response rate of 60–65% and a notable neurological improvement in most cases of PCNSL. However, relapse usually occurred within a few months after RT. Although the introduction of systemic chemotherapy based on CHOP (cyclophosphamide, doxorubicin, vincristin and prednisone) regimen and high-dose methotrexate followed by radiation therapy has consistently improved survival, the prognosis of PCNSL still dismal, with high rates of local relapse and consequent death. About half of the patients with pituitary lymphoma received chemotherapy, only in three cases without cranial radiation [22]. Regimens used were different and were in the most cases extrapolated from the protocol used in PCNSL. Despite the increasing number of studies published since a decade on PCNSL and recent therapeutic advances, several questions still remain unanswered about the optimal management of these tumors.

**Conclusion:** This case presentation reports a rare case of primary pituitary lymphoma and highlights the importance of biopsy to confirm the pathological diagnosis of pituitary tumors associated with hypopituitarism. The imaging of the brain and the histopathology including detailed immunohistochemistry is of vital importance in making an accurate diagnosis of the pituitary lymphoma. Finally, lymphoma must be kept in mind in the differential diagnosis of lesions in the sellar and parasellar region.
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Figure 1: CT scan of the brain with contrast showing the pituitary tumor.
Figure 2: MRI of the brain performed at the first presentation shows the pituitary tumor; coronal (A) and sagittal (B) T1-weighted images with contrast enhancement.
Figure 3: Four months later after steroid treatment, MRI of the brain shows new process developed in the CNS.
Figure 4: The histological examination confirmed the diagnosis of pituitary lymphoma. Figures A and B show infiltrative large-sized lymphocytes with occasional mitotic. The immunohistochemical tests were positive for the B-cell CD20 marker (C) and negative for the T-cell marker CD3 (D).
Additional files provided with this submission:

Additional file 1: Table 1.doc, 53K
http://www.biomedcentral.com/imedia/4405638374425475/supp1.doc