Combined chronic lymphocytic leukemia and prolactinoma: a rare occurrence in a patient presenting with pituitary apoplexy

Case report

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The authors describe a rare case of combined pituitary chronic lymphocytic leukemia (CLL) and prolactinoma in a 77-year-old man presenting with apoplexy. This case highlights the importance of evaluating the pituitary gland in patients with CLL who present with clinical manifestations of apoplexy as well as the need to carefully evaluate pathological specimens from the gland for the presence of lymphocytic cells in those patients. This is the first reported case of a combined CLL–prolactinoma pituitary lesion presenting with apoplexy.

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Key Words • chronic lymphocytic leukemia • pituitary apoplexy • prolactinoma • transsphenoidal • cavernous sinus • small lymphocytic cells • flow cytometry • peripheral nerve

PITUITARY involvement in B-cell CLL and pituitary apoplexy, independently, are 2 rare events. Their co-occurrence in addition to the presence of prolactin-secreting adenoma cells, however, has never been described in the literature. We present the case of a combined pituitary CLL and prolactinoma apoplexy in a 77-year-old man to highlight the importance of imaging the brain in patients with CLL who present with signs and symptoms of pituitary apoplexy. To the best of our knowledge, there are only 2 other reported cases of CLL manifesting as a pituitary mass lesion.¹ ² The current case is the first instance of a combined pituitary CLL–prolactinoma presenting with apoplexy. This case illustrates the need to carefully evaluate pituitary tumor specimens from patients with CLL for small lymphocytic infiltration, notwithstanding the presence of pituitary adenoma cells.

Abbreviation used in this paper: CLL = chronic lymphocytic leukemia.

Case Report

History and Examination. This 77-year-old man with untreated CLL diagnosed 8 years earlier presented with a 2-day history of severe bifrontal headaches associated with nausea and vomiting, including left facial numbness and complete ophthalmoplegia of his left eye. Three weeks prior to his admission he was hospitalized at an outside hospital for a pulmonary embolus and discharged on a regimen of 5 mg of oral warfarin at bedtime along with subcutaneous injections of 115 mg of enoxaparin every 12 hours as a bridging therapy. At his initial examination at our institution, he was awake, alert, and fully oriented. Positive findings included complete dense ophthalmoplegia of the left eye, diminished facial sensation to all sensory modalities along the V1 and V2 distributions, and right eye blindness secondary to glaucoma. Visual acuity remained

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intact in his left eye. His international normalized ratio and prothrombin time on admission were 1.45 and 17.7, respectively. His white blood cell count was elevated at 189,500 \( \mu l \) (normal 3.2–10,600 \( \mu l \)). A CT scan of the patient’s head without contrast enhancement demonstrated a large, isodense, expansile sellar lesion with suprasellar extension and left cavernous sinus invasion, as well as erosion of the sellar floor and left sphenoid wing, including the foramen rotundum and vidian canal. In addition, there were patchy areas of hyperdensity within the sellar portion of the lesion, suggestive of acute hemorrhage consistent with apoplexy (Fig. 1).

On MRI, the tumor measured 4.0 \( \times \) 3.7 \( \times \) 3.7 cm; it was located within an expanded sella and extended into the adjacent suprasellar compartment, compressing both the pituitary stalk and optic chiasm, and into the left cavernous sinus space encasing the left internal carotid artery. The tumor had mixed areas of isointensity and hyperintensity on both T1- and T2-weighted images, consistent with acute and chronic hemorrhage of mixed ages with minimal contrast enhancement (Fig. 2).

Operative Course. After a Greenfield inferior vena cava filter was placed by the vascular surgeon, a microscope-assisted transnasal transsphenoidal approach was undertaken. Tumor was noted to be emanating from the sphenoid ostium on the left side. We gained entry into the sphenoid sinus through the eroded ostia and identified gross tumor within the sinus. A thickened membrane was sharply incised revealing more tumor, which was followed back to the sella. Tumor removal was accomplished with the use of various-sized Hardy ringed curettes and suction. The left carotid artery was found to be involved in the midportion of the sella. Tumor was carefully resected from around the internal carotid artery. At the completion of our resection, there was no evidence of CSF leak. A fat graft with fascia lata harvested from the patient’s right thigh was used to plug the sphenoid sinus.

Histological Evaluation. The frozen histological section showed pieces of ischemic and necrotic pituitary adenoma with foci of viable tumor associated with acute and chronic hemorrhage. Within the fragments of clotted blood as well as in the adenoma were islands of predominantly small, round, monotonous lymphocytes. On permanent tissue sections, immunohistochemical stains with appropriately reactive controls revealed strong immunoreactivity for CD5 and CD20 involving the small lymphocytes with occasional scattered CD3-positive T-cells. The pituitary adenoma cells were positive for prolactin and negative for growth hormone and adrenocorticotropic hormone (Fig. 3). A final diagnosis of intermixed apoplectic pituitary prolactinoma and CLL was determined.

Postoperative Course. The patient’s postoperative course was uneventful, with slow resolution of his left eye ophthalmoplegia and left facial numbness. He was evaluated by the endocrinology service shortly after surgery and was placed on hydrocortisone and thyroid hormone.

![Fig. 1. Axial CT scans of the patient’s head. A: Images without contrast enhancement demonstrating a large isodense expansile sellar lesion with patchy areas of hyperdensity within the sellar portion of the lesion, suggestive of acute hemorrhage. B: Images showing suprasellar extension and left cavernous sinus invasion, as well as erosion of the sellar floor and left sphenoid wing, including the foramen rotundum and vidian canal.](image-url)
replacement therapies. A week after surgery, his inferior vena cava filter was removed, and he restarted warfarin with enoxaparin bridging therapy. At routine follow-up 6 weeks after surgery, he was noted to be doing well, with complete resolution of his cranial nerve IV and VI palsies and continued improvement in his oculomotor nerve palsy.

**Discussion**

**Pituitary Apoplexy**

Pituitary apoplexy is an uncommon event that occurs most notably secondary to hemorrhage within a preexisting pituitary lesion or an expanding anterior pituitary gland resulting from postpartum hypopituitarism. Pituitary apoplexy is usually heralded by an abrupt onset of severe headache, nausea, vomiting, deterioration of vision, restriction of visual fields, ophthalmoplegia, or, infrequently, altered sensorium. The unique clinical manifestation was first described by Bleibtreu in 1905, while the term currently ascribed to the condition (pituitary apoplexy) was first coined in 1950 by Brougham et al., who described 5 patients who died suddenly, in whom postmortem autopsy revealed hemorrhage and necrosis of a pituitary adenoma. The incidence of pituitary apoplexy ranges from 0.6% to 22%. The symptomatology usually falls into 3 main categories: pressure effects from fulminant expansion of the gland and the tumor; meningismus, headache, nausea, and vomiting from leakage of blood into the subarachnoid space; or panhypopituitarism secondary to destruction and infarction of the gland. The clinical sequelae of pressure depend on the direction of the tumor expansion, which may exert pressure on the cranial nerves within the cavernous sinus causing ocular motility deficits or on the optic apparatus within the suprasellar space causing both

![Fig. 2.](image-url) Magnetic resonance imaging obtained in the patient. Coronal and axial T1-weighted MR images with Gd enhancement (A) demonstrate a large, minimally enhancing tumor measuring $4.0 \times 3.7 \times 3.7$ cm located within an expanded sella and extending into the adjacent suprasellar compartment, compressing both the pituitary stalk and optic chiasm, and into the left cavernous sinus space, encasing the left internal carotid artery. Axial and sagittal T1-weighted (B) and axial T2-weighted MR images without contrast enhancement (C) reveal acute and chronic hemorrhage of mixed ages.

![Fig. 3.](image-url) Photomicrographs demonstrating fragments of pituitary adenoma surrounded by acute hemorrhage (A) as well as intermingled, small, monotonous lymphocytic cells (B); H & E. Immunohistochemical analysis revealed all of the lymphocytes to be positive for CD5 (C), and the majority were CD20 positive. The pituitary adenoma cells were prolactin positive (D) but negative for adrenocorticotropic hormone and growth hormone. Original magnification ×400 (A–D).
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visual acuity and field deficits. Multiple endocrine deficiencies manifesting as weakness, lethargy, depressed mental status, nausea, and vomiting secondary to the destruction of the gland may occur less frequently because of the great functional reserve of the pituitary gland, which can function with as little as 10% of viable tissue.5,20,24,26

Chronic Lymphocytic Leukemia

Chronic lymphocytic leukemia is a monoclonal disorder characterized by a progressive accumulation of functionally incompetent lymphocytes. The most indicative feature of CLL is a peripheral lymphocytosis (> 5.0 × 10⁹/L). Accounting for approximately 30% of all leukemias in the US, CLL is the most common form of leukemia affecting the adult population in Western countries. The incidence rate is 2–6 cases per 100,000 person-years, and the median age at diagnosis is 65 years. The male-to-female ratio is 2 to 1.13,14,19,20 The affected lymphocytes are of B-cell lineage in 95% of cases that carry CD5. Onset is insidious, and the diagnosis is occasionally discovered after a blood cell count is obtained for another reason. Enlarged lymph nodes are the single most common presenting symptom. Diagnosis is made from a series of tests including the absolute peripheral lymphocyte count, the presence of smudge cells (artifact produced by damaged lymphocytes) on a peripheral smear with evident lymphocytosis, and peripheral blood flow cytometry detecting the presence of circulating clonal B-lymphocytes expressing CD5, CD19, and CD20.13,18,20,23 A bone marrow aspirate is usually not necessary unless a diagnosis is difficult to establish. Other tests include liver and spleen ultrasonography that may demonstrate organomegaly.13,14,19,20 Chemotherapy is not required in patients with CLL until they become symptomatic.

Chronic Lymphocytic Leukemia Infiltration of the Pituitary Gland

With the exception of a large autopsy series by Barcos et al.,2 showing an incidental finding of CLL infiltration of the CNS in 20% of cadavers, cases of CNS involvement in B-cell CLL have rarely been reported. The majority of established cases include leptomeningeal spread and spinal cord involvement.10,12,16,17,19,22,27,28 Among sellar and parasellar metastases, CLL comprises a minute proportion.1 In the largest retrospective study by Bower et al.,7 only 8 of 962 patients with CLL demonstrated CNS involvement. In the majority of those cases, however, involvement was restricted to the leptomeninges. Only 2 of 8 cases showed isolated brain involvement: one case presenting as a mass involving the hypothalamus and the other case presenting as a pituitary adenoma. In 2004, Nimubona et al.21 reported the case of a 43-year-old woman with CLL who presented with symptoms of a growing sellar mass. In 2001, Rye et al.25 reported postmortem histological findings of CLL infiltration of the pituitary gland extending into the posterior pituitary stalk in a 61-year-old man with known CLL who died of complications of hyponatremia and lower respiratory tract infection. According to Barcos et al.,2 CLL infiltration of the pituitary gland associated with apoplexy had not been reported previously, although Kindon et al.18 described a case of pituitary apoplexy in a patient with a pituitary abscess secondary to hypogammaglobulinemia from known CLL. The histopathology revealed squamous tissue and inflammatory changes consistent with an abscess with no evidence of direct CLL involvement. Our case is the first to describe CLL infiltration of the pituitary gland presenting with apoplexy. What is also interesting about our case is that the histopathology revealed evidence of a coexisting prolactinoma, which is also a novel finding not previously described.

Clinical and Histopathological Implications

Specimens from patients with known CLL who present with the typical compressive and metabolic signs and symptoms of a growing sellar mass should be examined closely and, if a small lymphoid infiltrate is present, should be evaluated completely to determine whether it is neoplastic, keeping in mind that pituitary CLL may coexist with pituitary adenoma.

Co-occurrence of pituitary involvement in B-cell CLL, in addition to the presence of prolactin-secreting adenoma cells, has never been described in the literature. This unusual finding in a 77-year-old man highlights the need for careful evaluation of pituitary tumor specimens from patients with CLL for small lymphocytic infiltration, notwithstanding the presence of pituitary adenoma cells.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Couldwell. Acquisition of data: Krisht. Analysis and interpretation of data: Krisht, Palmer. Drafting the article: Krisht. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Couldwell.

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References
