Giant Prolactinoma Presenting with Neck Pain and Structural Compromise of the Occipital Condyles

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Abstract

Prolactinomas are the most common form of endocrinologically active pituitary adenoma; they account for ~ 45% of pituitary adenomas encountered in clinical practice. Giant adenomas are those > 4 cm in diameter. Less than 0.5% of pituitary adenomas encountered in neurosurgical practice are giant prolactinomas. Patients with giant prolactinomas typically present with highly elevated prolactin levels, endocrinologic disturbances, and neurologic symptoms from mass-induced pressure. Described here is an unusual case of a giant prolactinoma presenting with neck pain and structural compromise of the occipital condyles. Transnasal biopsy of the nasopharyngeal portion of the mass obtained tissue consistent with an atypical prolactinoma with p53 reactivity and a high Ki-67 index of 5%. Despite the size and invasiveness of the tumor, the patient had resolution of his clinical symptoms, dramatic reduction of his hyperprolactinemia, and near-complete disappearance of his tumor following medical treatment.

Keywords
► pituitary adenoma  
► giant prolactinoma  
► occipitocervical instability  
► occipital condyles  
► invasive adenoma

Introduction

Pituitary adenomas are common intracranial lesions; autopsy and radiographic studies find a prevalence of ~ 17%.1 Prolactinomas are the most common form of endocrinologically active pituitary adenoma; they account for ~ 45% of pituitary adenomas encountered in clinical practice.2 Prolactinomas are most often microadenomas (< 10 mm in diameter) and are diagnosed more frequently in women, who usually present with the hormonal sequelae of hyperprolactinemia including galactorrhea and oligomenorrhea. In men, macroprolactinomas (> 10 mm in diameter) are more commonly detected, and it has been hypothesized that the greater subtlety of male hormonal symptoms of hyperprolactinemia, gynecomastia, decreased libido, and impotence may account for the lower observed frequency and the larger size of clinically evident prolactinomas in men.3

Giant prolactinomas are > 4 cm in diameter. The true incidence is unknown; one case series reported that 0.5% of pituitary adenomas encountered in neurosurgical practice are giant prolactinomas.4 Patients with giant prolactinomas typically present with marked hyperprolactinemia (> 1000 ng/dL), hypogonadism, and neurologic symptoms from mass-induced pressure on or invasion of adjacent structures.
Described here is an unusual case of a giant prolactinoma presenting with neck pain and structural compromise of the occipital condyles.

**Case Report**

A 28-year-old man with no significant past medical history presented with 6 weeks of mild neck pain. The pain was worsened by cervical motion, with radiation to the occiput. The patient reported mild intermittent epistaxis and right nasal obstruction but denied headache, visual loss, diplopia, facial sensory abnormality, and endocrinological symptoms other than mildly decreased libido.

On examination, although the patient’s head at rest tilted to the left because of neck pain, his neck had full range of motion. Formal neuro-ophthalmologic examination revealed neither visual field deficit nor diplopia. Facial sensation was normal. Magnetic resonance imaging (MRI) of the brain revealed a 70 × 45 × 45-mm mass isointense with the clivus on T1- and T2-weighted images and homogeneously enhancing with gadolinium. It involved the clivus, sella, and both occipital condyles, extended into the posterior nasopharynx, and encased the cavernous and infraclinoid segments of both internal carotid arteries (Fig. 1A–F). Computed tomography showed severe bony destruction affecting both occipital condyles. An endoscopic transnasal biopsy of the nasopharyngeal portion of the mass was obtained during the first ears, nose, and throat clinic visit. Pathology revealed tissue consistent with an atypical prolactinoma with p53 reactivity and a high Ki-67 index of 5% (Fig. 1G–J). Endocrinologic studies were notable for prolactin 24,750 ng/dL, cortisol 5.4 μg/dL, free thyroxine 0.76 ng/dL, testosterone < 20 ng/dL, and insulinlike growth factor-1 of 89 ng/mL.

Medical therapy of cabergoline 1 mg/week, levothyroxine, and hydrocortisone was begun. Within 1 week, the patient’s neck pain resolved. Flexion-extension plain radiographs of the cervical spine did not demonstrate instability. However, the clinical signs of occipital condyles compromise and the risk of acute occipitocervical instability and neurologic decline consequent to the near-complete replacement of both occipital condyles by tumor, and its possible exacerbation by cabergoline-induced tumor lysis, prompted an elective occiput to C2 posterior fusion (Fig. 1K).

After an uncomplicated recovery from surgery, the patient remained free of neck pain. Throughout his first year of cabergoline therapy (3 mg/week), his only complaint was infrequent nasal moisture that was not believed to represent cerebrospinal fluid (CSF) rhinorrhea. One year after treatment, his prolactin had fallen to 36 ng/dL, and MRI showed a dramatic reduction in tumor size (Fig. 1L).

**Discussion**

This is an unusual case of a giant prolactinoma presenting with neck pain and near-complete destruction of the occipital condyles requiring occipitocervical fusion. Literature review reveals only three cases of prolactinoma invading the occipital condyles and requiring occipitocervical fusion; one patient with an unstable pathologic fracture underwent an occipitocervical fusion and 8 years later was diagnosed with a giant prolactinoma, one patient presented with acute neurologic deterioration due to compression of the brainstem and pons, and one had invasion of the occipital condyles and subsequent occipitocervical instability as a late sequela of a prolactinoma initially treated with radiation. However, this case represents the first report of a patient with a pituitary adenoma initially presenting with symptoms solely attributable to the invasion of the occipital condyles causing neck pain.

Invasive clival masses can pose a diagnostic challenge. Considerations include pituitary adenoma, atypical meningioma, chordoma, chondrosarcoma, osteosarcoma, plasmacytoma, sinonasal malignancy, mucocoele of the sphenoid sinus, intraosseous lymphoma, neuroenteric cyst, craniopharyngioma, and metastasis. It is not always possible to differentiate chordoma from pituitary adenoma. Both are typically contrast enhancing. When assessed with MRI, chordomas are typically very T2 hyperintense, whereas pituitary adenomas are typically T2 isointense; however, macroadenomas may have heterogeneous T2 signal. In this case, the lesion was largely T2 isointense with some heterogeneous T2 signal that is consistent with the pathologic diagnosis of pituitary adenoma. Many pituitary adenomas that invade the clivus are initially misdiagnosed as chordomas. This case highlights the importance of maintaining a broad differential diagnosis for clival masses and particularly including pituitary adenoma for lesions involving the sella turcica that are T2 isointense.

Based on the 2004 World Health Organization (WHO) classification of pituitary adenomas, this tumor met the criteria for an atypical adenoma. These tumors are distinguished by a Ki-67 proliferative index > 3%, excessive p53 immunoreactivity, and increased mitotic activity, and such atypical adenomas are described as intermediate between benign pituitary adenomas and pituitary carcinomas. The incidence of atypical pituitary adenomas in surgical series ranged from 2.7% in the German Pituitary Tumor Registry to 15% in the series of Zada et al. Prolactinomas represented 8% and 11% of atypical adenomas in these two series, respectively. The classification of atypical pituitary adenomas has engendered significant controversy. Notably, the WHO classification does not include invasiveness as a criterion for designation as atypical. The implications of immunohistochemical findings are also controversial; conflicting reports support18–20 and discount21–23 the value of Ki-67 proliferative indexes and p53 immunoreactivity in predicting the behavior of pituitary adenomas. In the largest case series of atypical pituitary adenomas published to date, Zada et al found atypical adenomas were significantly more likely to be invasive on MRI imaging than are typical adenomas. The atypical tumor in our case was highly invasive.

Neither our case nor those of Zada et al had the long-term follow-up required to link atypical histology and invasiveness with risk of recurrence. But a study of 410 patients who underwent resection of a pituitary adenoma, including 116 patients who underwent resection of a prolactinoma,
suggests that tumors that are invasive and “proliferative” (assessed by Ki-67 positivity, mitoses per high-powered field, and p53 positivity) had 25- and 12-fold rates of residual tumor and tumor progression after 8 years of postoperative follow-up when compared with noninvasive, nonproliferative adenomas. However, neither of these studies specifically addressed giant prolactinomas treated nonoperatively.

Despite the large size and invasive nature of this patient’s prolactinoma, dramatic reductions of tumor size and prolactin level were achieved with medical therapy alone. This is consistent with prior reports in the literature regarding the sensitivity of giant prolactinomas to dopamine agonists. Recent case series of surgical treatment of giant adenomas report rates of gross total resection of only 14 to 61%, of significant complications of up to 18%, and of mortality of 0 to 4.6%. In contrast, medical therapy has significantly lower complication rates and no mortality. Nonetheless, treatment of giant prolactinomas with

Fig. 1 (A–C) T1-weighted postcontrast magnetic resonance imaging (MRI) scan displays a large contrast-enhancing mass. (D) T-2 weighted noncontrast MRI scan shows a large isointense mass with areas of heterogeneous and hyperintense signal. (E, F) Axial and sagittal noncontrast computed tomography CT scans show destruction of both occipital condyles. (G) Hematoxylin and eosin, prolactin, (I) Ki-67, and (j) p53 stained slides of biopsy tissue from the intranasal portion of the tumor display morphology and staining consistent with an atypical prolactinoma. (K) Postoperative lateral X-ray shows posterior occipit-C2 instrumented fusion. (L) Sagittal T1-weighted postcontrast MRI scan following 1 year of cabergoline therapy demonstrates significant reduction in tumor volume.
dopamine agonists is not without potential complications including CSF fistula,\(^1\)\(^3\)\(^5\)\(^6\)\(^8\)\(^9\) pneumocephalus,\(^7\)\(^9\) pituitary apoplexy,\(^3\)\(^8\) optic chiasm herniation,\(^3\)\(^8\)\(^9\) and brainstem angulation.\(^3\)\(^4\) However, given the high efficacy and low relative morbidity of dopamine antagonism, medical therapy should remain the first-line treatment for giant prolactinomas.

**Conclusion**

This is the first reported case of a giant prolactinoma presenting with neck pain secondary to invasion of the occipital condyles and only the fourth reported case of a prolactinoma causing structural compromise of the occipital condyles requiring occipitocervical fusion. Pituitary adenoma should be included in the initial differential diagnosis of all lesions in or about the sella. Despite the size and invasiveness of the tumor, the patient had resolution of his clinical symptoms, dramatic reduction of his hyperprolactinemia, and near-complete disappearance of his tumor following medical treatment with a dopamine agonist.

**References**


