

Clival Ectopic Pituitary Prolactinoma was Successfully Managed by Transsphenoidal Surgery: A Rare Case Report

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May 24, 2023

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ABSTRACT

Ectopic pituitary adenomas are isolated adenomas located outside the sella turcica (in variable locations) with a normal-appearing pituitary gland. These tumors are extremely rare and thought to often arise from embryological remnants along the route of Rathke's pouch migration. Ectopic pituitary adenomas can manifest in variable clinical ways depending on hormonal activity and involvement of adjacent structures, which can present a challenge in making a diagnosis and choosing most appropriate management. In this case study, we report a 47-year-old male who presented with visual disturbances, headache, generalised weakness and hyperprolactinemia. Magnetic Resonance Imaging showed a 2 cm mass located in the clivus invading the sphenoid sinus with an intact pituitary gland. The patient underwent uncomplicated endoscopic transsphenoidal surgery, during which the intersphenoid septum was removed to reach the posterior wall and eradicate the mass successfully, while maintaining integrity of the pituitary gland. Pathological studies were consistent with prolactinoma, with no cytological malignant features. Post-surgery, symptoms notably improved, serum prolactin level dropped, and patient's condition was satisfactory on follow-up with no long-term complications reported. The clival ectopic mass is a rare condition that it may be located adjacent to important structures and can be relatively difficult to reach. Therefore, surgery should be performed carefully to maintain the nearby structures and avoid any significant complications.

Key message: Ectopic pituitary adenoma is a rare neoplasm, located in the clivus and could mimic other clival tumors. Diagnosis and treatment could be challenging. It should be considered within the differential diagnosis of clival tumors.

Keywords: Ectopic pituitary adenoma; clival tumours; transsphenoidal surgery; prolactinoma; stalk effect; case report

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Introduction

Ectopic pituitary adenomas (EPAs) are isolated adenomas located outside the sella turcica with a normal intrasellar pituitary gland. EPAs are thought to be extremely rare tumours [1]. The location of EPAs can vary, with approximately 60% of reported cases found in the sphenoid sinus and suprasellar region, 30% in the clivus, nasal cavity, parasellar region, cavernous sinus, and sphenoid wing [2]. The origin of EPAs can take one of three forms, with the most common being adenomas derived from residual cells of Rathke's pouch which persist along the developmental pathway of the anterior pituitary gland. Clinical manifestations of EPAs usually depend on hormonal activity and involvement of adjacent structures. For example, tumours extending into the cavernous sinus or clivus can compress cranial nerves and cause visual disturbances and facial paresthesia, while sphenoid sinus EPA can result in headache, nasal obstruction and CSF leak [2]. The diagnosis and management of EPAs can be challenging and usually requires strong clinical suspicion along with magnetic resonance imaging (MRI) findings, including normal pituitary gland, and is confirmed by pathological studies. Computerized Tomograph (CT) can also provide useful information such as invasion of the sphenoid sinus, and therefore helps plan the endoscopic trans-sphenoidal surgery, which is considered the most appropriate management approach [3, 4]. In this case, we present a clival ectopic pituitary prolactinoma.

CASE PRESENTATION

A 47-year-old male presented to the ENT Department (Ear, Nose, and Throat) with a parietal and occipital headache, retro-orbital pain, transient blurry vision, fatigue, and difficulty completing routine tasks. The family and medical history were unremarkable. Laboratory findings showed elevated serum prolactin of 269ng/ml. MRI with contrast of sphenoid sinus and pituitary gland revealed a 2 cm mass within the clivus invading the sphenoid sinus. The mass showed moderate enhancement with peripheral calcifications. The pituitary gland and its stalk were normal, Fig.1 (A, B, C). The mass was totally resected via trans-sphenoidal endoscopic surgery. The posterior portion of the nasal septum was resected, and the inlet was expanded while maintaining the integrity of the sphenopalatine artery. The intersphenoid septum was removed to reach the posterior wall of the sphenoid, which was invaded by the tumour. However, the pituitary gland was notably intact. The neoplastic mass looked friable and it was carefully resected without any vascular or neurologic complications. The internal carotid arteries (ICAs), cranial nerves III/IV/V/VI, and the optic chiasm were all maintained Fig.2 (A, B, C, D). The postoperative period was uneventful. The gross examination revealed fragments of tan, white tissue measuring about 1.2×1×0.5 cm with bony chips. Microscopic examination showed a loosely infiltrating tumour composed of irregular cords and small nests of uniform small oval-to-polygonal-shaped cells surrounded by dense hyaline stroma and bone. In isolated areas, dystrophic calcifications are noted. Immunostains were performed for prolactin, Ki-67, CD138, Epithelial Membrane Antigen, CD45, CD34, S-100, protein, synaptophysin, chromogranin, and CD56. The tumour cells were strongly positive for prolactin, while the others were negative. No cytological malignant features were shown, Fig.3 (A, B, C, D, E, F). Postoperatively, the patient recovered rapidly, his symptoms notably improved, and serum prolactin level dropped to 26ng/ml. On an 18-month follow-up, the patient's condition was satisfactory with no long-term complications.

DISCUSSION AND CONCLUSIONS

EPAs are rare extrasellar pituitary adenomas without any correlation with the components located inside the sella turcica. They are often found along the migration pathway of Rathke's pouch; however, the exact pathogenesis remains unclear [3, 4]. Unlike our case where the patient is a male, EPAs tend to present more in females, and most frequently between the fourth and seventh decades of life, with the mean age at diagnosis being 51.4 years old [3]. In this case, we report an EPA located in the clivus which represents the third most common location for EPAs, after the sphenoid sinus and suprasellar region [4]. Establishing the diagnosis of EPAs can be challenging as presentation varies widely depending on several factors, including anatomy, hormonal activity, and involvement/ invasion of surrounding structures [2]. When considering the differential diagnosis (DD), the clivus can be affected by a number of conditions, including lesions arising within the clivus or from adjacent structures with chordoma being the most common tumour of this

region, which can be usually differentiated from EPAs on imaging inspection. However, a biopsy is usually required to confirm the diagnosis [4, 5]. Other DD include intraosseous meningioma, chondrosarcoma, solitary plasmacytomas, myelomas, astrocytoma, craniopharyngioma, germ cell tumour, non-Hodgkin's lymphoma, melanoma, and metastases [1, 4]. Stalk effect due to a nonfunctional adenoma should be considered in DD of elevated prolactin levels. However, prolactin levels >200 - 250 ng/mL are suspected of prolactinomas whereas prolactin levels resulting from the pituitary stalk compression are generally <100 ng/mL and rarely exceed 250 ng/mL [6]. Consistent with the presenting complaints in our report, clival EPAs, similar to other clival lesions, are known to exhibit mass effect symptoms, such as headache and focal cranial nerve palsy [7, 5]. 58% of EPAs are functional tumours. In some clival diseases, endocrinopathy may result from the infiltration of the pituitary. Clival EPAs can invade adjacent structures causing destructive features such as bone erosion, in keeping with the tumour in our case which invaded the sphenoid sinus [4, 8, 9]. Due to the complexity of EPAs, several factors should be considered for treatment, including tumour size and location, clinical manifestations, hormone-secreting type and extent of invasion [4]. The majority of EPAs are definitively diagnosed following surgery and histopathological examination [10]. Herein, trans-sphenoidal endoscopic surgery was performed as a diagnostic and therapeutic procedure. Compared with other locations (cavernous sinus, suprasellar region and the sphenoid sinus), the clival EPAs are relatively more difficult to reach; thus, detect and confirm with an endoscopic biopsy. In addition, experience in EPAs treatment is often lacking considering how rare these tumours are [4]. In conclusion, ectopic pituitary prolactinomas in the clivus are rare and the diagnosis may be difficult. However, a histological study is necessary to confirm the diagnosis especially when there are no hormonal-related symptoms.

List of Abbreviations

PAs: Pituitary Adenomas

EPAs: Ectopic Pituitary Adenomas

CD: Cluster of Differentiation

CSF: Cerebrospinal fluid

DD: Differential Diagnosis

CT: Computed Tomography

MRI: Magnetic Resonance Imaging

ACTH: Adrenocorticotrophic Hormone

ICAs: Internal Carotid Arteries

CNs: Cranial Nerves

REFERENCES LIST

1. Kohno, M., Sasaki, T., Narita, Y., Teramoto, A., & Takakura, K. (1994). Suprasellar ectopic pituitary adenoma—case report. *Neurologia medico-chirurgica* , 34 (8), 538–542. <https://doi.org/10.2176/nmc.34.538>
2. Agely, A., Okromelidze, L., Vilanilam, G. K., Chaichana, K. L., Middlebrooks, E. H., & Gupta, V. (2019). Ectopic pituitary adenomas: common presentations of a rare entity. *Pituitary* , 22 (4), 339–343. <https://doi.org/10.1007/s11102-019-00954-y>
3. Yang, B. T., Chong, V. F., Wang, Z. C., Xian, J. F., & Chen, Q. H. (2010). Sphenoid sinus ectopic pituitary adenomas: CT and MRI findings. *The British journal of radiology* , 83 (987), 218–224. <https://doi.org/10.1259/bjr/76663418>
4. Zhu, J., Wang, Z., Zhang, Y., Li, X., Liu, J., Deng, K., Lu, L., Pan, H., Wang, R., Yao, Y., & Zhu, H. (2020). Ectopic pituitary adenomas: clinical features, diagnostic challenges and management. *Pituitary* , 23 (6), 648–664. <https://doi.org/10.1007/s11102-020-01071-x>

5. Shuman, W., Loewenstern, J., Pai, A., Bederson, J., & Shrivastava, R. (2019). Variability in Clinical Presentation and Pathologic Implications of Ectopic Pituitary Tumors: Critical Review of Literature. *World neurosurgery* , 122 , 397–403. <https://doi.org/10.1016/j.wneu.2018.10.200>
6. Vilar, L., Fleseriu, M., & Bronstein, M. D. (2014). Challenges and pitfalls in the diagnosis of hyperprolactinemia. *Arquivos brasileiros de endocrinologia e metabologia* , 58 (1), 9–22. <https://doi.org/10.1590/0004-2730000003002>
7. Hou, L., Harshbarger, T., Herrick, M. K., & Tse, V. (2002). Suprasellar adrenocorticotrophic hormone-secreting ectopic pituitary adenoma: case report and literature Review. *Neurosurgery* ,50 (3), 618–625. <https://doi.org/10.1097/00006123-200203000-00035>
8. Thompson, L. D., Seethala, R. R., & Müller, S. (2012). Ectopic sphenoid sinus pituitary adenoma (ESSPA) with normal anterior pituitary gland: a clinicopathologic and immunophenotypic study of 32 cases with a comprehensive review of the english literature. *Head and neck pathology* , 6 (1), 75–100. <https://doi.org/10.1007/s12105-012-0336-9>
9. Horiuchi, T., Tanaka, Y., Kobayashi, S., Unoki, T., & Yokoh, A. (1997). Rapidly-growing ectopic pituitary adenoma within the sphenoid sinus—case report. *Neurologia medico-chirurgica* , 37 (5), 399–402. <https://doi.org/10.2176/nmc.37.399>
10. Tajudeen, B. A., Kuan, E. C., Adappa, N. D., Han, J. K., Chandra, R. K., Palmer, J. N., Kennedy, D. W., Wang, M. B., & Suh, J. D. (2017). Ectopic Pituitary Adenomas Presenting as Sphenoid or Clival Lesions: Case Series and Management Recommendations. *Journal of neurological surgery. Part B, Skull base* , 78 (2), 120–124. <https://doi.org/10.1055/s-0036-1592081>

FIGURE LEGENDS

Fig.1 (A, B, C): MRI with contrast of sphenoid sinus and pituitary gland in sagittal (A), transverse (B), and coronary (C) sections showing a mass in the clivus with moderate enhancement and peripheral calcifications.

Fig.2 (A, B, C, D): Endoscopic images of transsphenoidal surgery showing the neoplastic mass adjacent to the intact pituitary gland (A), the neoplastic mass adjacent to both the right and left ICAs (B, C), and the pituitary gland after complete resection of the mass (D).

Fig.3 (A, B, C, D, E, F): Histological images of the resected mass showing small nests of uniform small oval-to-polygonal-shaped cells surrounded by dense hyaline stroma (A, B), negative staining for synaptophysin, chromogranin, and CD56 respectively (C, D, E), positive staining for prolactin (F).





