Ectopic Esthesioneuroblastoma of the Sphenoclivus: A Rare Entity

Farah Dayana Zahedi¹ · Balwant Singh Gendeh¹ · Salina Husain¹ ·
Ramesh Kumar² · Thean Yean Kew³

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Abstract Esthesioneuroblastoma is a rare malignant neoplasm of olfactory neuroepithelium and usually located at the olfactory cleft at superior nasal cavity. Ectopic localization of esthesioneuroblastoma is even rarer and usually posed with a diagnostic dilemma and delay in the diagnosis and management. We report a rare case of ectopic esthesioneuroblastoma of the sphenoclivus with the presentation of intermittent unilateral epistaxis, intermittent intractable headache without anosmia. Nasal endoscopy findings showed a pulsatile mass at the anterior face of the sphenoid sinus with extension posteriorly towards the clivus region and occupying the floor of the sphenoid sinus. Endonasal transclival endoscopic excision of tumour was performed which involved otorhinolaryngology surgeon and neurosurgeon with intraoperative navigation imaging and frozen section. The histopathological findings was esthesioneuroblastoma. Due to its rarity and unusual presentation, the diagnosis of ectopic esthesioneuroblastoma is difficult and can be misdiagnosed with the other type of malignancy. Therefore, the histopathological result is important in confirming the type of tumour and can lead to the next step of management.

Keywords Esthesioneuroblastoma · Olfactory neuroblastoma · Sphenoid sinus · Clivus · Nose neoplasm

Introduction

Esthesioneuroblastoma is an uncommon malignant neoplasm of olfactory neuroepithelium and usually located at the superior nasal cavity. It occurs equally in males and females and most common in the second and fifth decade of life, but can be seen at any age [1]. Ectopic localisation of esthesioneuroblastoma pose a dilemma and delay in the diagnosis due to its atypical presentation and extreme rarity of the disease. Only a few reports in the literature that mentioned about esthesioneuroblastoma from the ectopic regions. We report a rare case of an ectopic esthesioneuroblastoma of the sphenoclivus region. Imaging demonstrated a midline heterogenous enhancing mass at the clivus with the epicenter at the basisphenoid.

Case Report

History and Examination

A 71-year old man presented with intermittent left epistaxis associated with headache for 2 months duration. There was no other history of nasal and ocular symptoms. On nasal endoscopy examination, there was a mass at the left sphenothmoidal recess which was biopsied. The histopathological examination results were esthesioneuroblastoma (WHO grade 1). The computed tomography performed showed midline destructive lesion at the basisphenoid of the clivus. He defaulted follow-up since.

✉ Farah Dayana Zahedi
anna_firra82@yahoo.com.au

¹ Department of Otorhinolaryngology-Head and Neck Surgery, Universiti Kebangsaan Malaysia Medical Centre, Jalan Ya'acob Latif, Bandar Tun Razak, Cheras, 56000 Kuala Lumpur, Malaysia

² Neurosurgery Unit, Department of Surgery, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia

³ Department of Radiology, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia

Fig. 1 Computed tomography imaging showed a mass at the sphenoclivar region

Four years later, he presented again with 1 week history of intermittent intractable headache associated with intermittent left epistaxis. There was no other nasal, ocular symptoms or cranial neuropathies. On nasal endoscopy examination, there was a pulsatile mass at the anterior face of the sphenoid sinus with extension posteriorly towards the clivus region and occupying the floor of the sphenoid sinus. Cranial nerves were intact and there was no cervical lymphadenopathy.

As a pulsatile mass was seen on nasoendoscopy a repeat biopsy was not performed. Computed tomography imaging and magnetic resonance imaging study (Figs. 1, 2) was performed. Imaging demonstrated a midline heterogeneous enhancing mass at the clivus with the epicenter at the basisphenoid. Superiorly the mass had eroded the floor of the sella turcica and basisphenoid. There was no extension into the sella region. Inferiorly the mass extended to the level of nasopharynx. Laterally, the mass erodes the lateral wall of the sphenoid sinus and was in close proximity with the cavernous part of the internal carotid artery with no clear fat plane. Anteriorly, there was a destruction of the posterior wall of the sphenoid sinus with protrusion anteriorly into the anterior face of the sphenoid sinus. No enlarged cervical lymph nodes noted.

Operative Findings

Endonasal transclival endoscopic excision of tumour was performed which involved otorhinolaryngology surgeon and neurosurgeon with intraoperative navigation imaging and frozen section.

Fig. 2 Magnetic resonance imaging showed a mass at sphenoclivar region

Fig. 3 Intraoperative findings of the tumour. The tumour was seen at the anterior face of the sphenoid sinus occupying the floor of the sphenoid sinus and extending posteriorly to the clivus region

Under general anaesthesia, the septum, middle and inferior turbinate were infiltrated with local anaesthesia. The right middle turbinate was displaced laterally and inferior half of the superior turbinate removed with Kerrison's forceps. Posterior ethmoidectomy, septectomy and sphenoidotomy was performed and the thin bone over sella removed up to the planum sphenoidale. The tumour was seen at the floor of the sphenoid sinus and extending to clivus (Fig. 3). A nasoseptal flap was raised to cover the

clival defect up to planum. The superior part of the nasopharynx was debrided using coblator exposing upper two-third of the clivus. The tumour was then exposed and removed in piecemeal. The clival carotids also exposed due to defect in the clival bone. Hemostasis was secured with floseal. Nasopore lubed with mupirocin was placed in the cavity. Silastic sheath was inserted and secured in both nostrils.

Histopathological Examination

Histopathological examination confirmed the diagnosis of esthesioneuroblastoma (WHO grade 1) (Fig. 4). The cellular tumour tissue arranged in lobules and nests with occasional Homer–Wright type rosettes seen. The immunohistochemical staining were positive for synaptophysin, neuron specific enolase (NSE), chromogranin and cytokeratin AE1/AE3 with low proliferation index (Ki67 <5 %).

The patient was offered post-operative radiotherapy, however he refused. He was well during the follow-up and there was no further epistaxis or headache.

Discussion

Esthesioneuroblastoma is an uncommon malignancy arising from olfactory neuroepithelium and it is thought to account for <5 % of malignant tumour of the nose and paranasal sinus [1]. Typically this tumour are found in the superior nasal cavity at the olfactory cleft. Ectopic site of esthesioneuroblastoma is very rarely reported in the

literature. To date, we only able to find a single case report of esthesioneuroblastoma from the sphenoclival region [2].

Due to its rarity and unusual presentation, the diagnosis of ectopic esthesioneuroblastoma is difficult and can be misdiagnosed with the other type of malignancy. Moreover, tumour of the sphenoid sinus and clivus are often subject to late diagnosis because of their deep location in the skull [3]. The diagnosis usually delayed until the tumour have invaded adjacent structures and cause consequence of symptoms. Our patient presented with atypical headache and intermittent epistaxis without any symptoms of nasal obstruction and hyposmia. Unilateral facial pain without any nasal and ocular symptoms was the clinical presentation in previously reported case of sphenoclival esthesioneuroblastoma [2]. The typical nasal and ocular symptoms of the usual location of esthesioneuroblastoma may not be the initial symptoms of ectopic esthesioneuroblastoma especially at the sphenoclival region. In fact our initial working diagnosis was that of a clival chordoma. Hence on the second presentation of our patient, the tumour was supposed to be rebiopsied. This will confirmed the initial diagnosis. Therefore, a careful nasal endoscopic examination, imaging and histopathological examination with proper staining is the crucial to diagnose this type of tumour.

The origin of esthesioneuroblastoma remains controversial [1]. Several theories proposed for the embryologic origin of the esthesioneuroblastoma. Majority of these tumour arise from the cribriform niche, therefore the proposed sources include the sphenopalatine ganglion, ectodermal olfactory placode, Loci's ganglion, autonomic ganglia in the nasal mucosa, olfactory epithelium and

Fig. 4 Histopathological examination shows a typical features of esthesioneuroblastoma

neural crest origin [4]. More recent studies link esthesioneuroblastoma to the basal progenitor cells of specialised olfactory mucosa [5]. Ectopic localization of esthesioneuroblastoma is more difficult to explain. One of the proposed theory is the tumour may arise from ectopic cell rests during embryologic development, although this theory remains speculative [6]. The concept of ectopic cell rests is supported by a case report of ectopic esthesioneuroblastoma in a patient with Kallman's syndrome characterised by absent of olfactory bulbs and pituitary hypoplasia caused by a defect in the embryologic migration of neurons from the olfactory placode [6, 7]. However, in our case the olfactory bulb and the pituitary gland are normal. The second theory that support the origin of ectopic esthesioneuroblastoma is the terminal nerve system theory. It was first suggested by Jakumeit in 1971 which the separate neuroendocrine cell population of the accessory olfactory systems. Embryologically, the olfactory placode divides into two systems. The first system contains the olfactory nerve and vomeronasal nerve; and the second system contains the terminal nerve that develops immediately caudal to the first. Both of them will degenerates in fetal life [8]. The terminal nerve ganglion located in the subarachnoid space caudal to the olfactory bulb and the neurons spread diffusely to rest in the lamina cribrosa, nasal septum, nasal mucosa, Bowman's gland, naris mucosa, crista galli and hypophthalmus [9]. Persistence of these cells beyond fetal life may provide origin of ectopic esthesioneuroblastoma. Either of these two theories may be the possible origin of the sphenoclivar esthesioneuroblastoma in our case.

In this case, we faced a diagnostic dilemma due to the atypical presentation and the location of the tumour although the initial histopathological examination showed esthesioneuroblastoma. The usual tumours in this location include meningioma, chordoma, neurilemoma, epidermoid, chondroma, chondrosarcoma and metastases. Esthesioneuroblastoma was the last consideration in our list of the differential diagnoses. Despite the initial biopsy showing confirming the diagnosis of esthesioneuroblastoma our suspicion was still a chordoma or chondrosarcoma. As a pulsatile mass was initial seen a biopsy was not performed. The pulsations seen was most likely a transmitted pulse. Clival chordoma was the initial working diagnosis since the computed tomography and magnetic resonance imaging studies showed the tumour was mainly located at the clivus with the epicenter was at the basisphenoid. Therefore, multiple discussions was carried out with our pathologist, radiologist and neurosurgeon to establish the accurate diagnosis and treatment plan for this patient.

Histopathological examination with immunohistochemical staining is essential for the diagnosis of this tumour. The typical histologic appearances include the presence of

characteristic cells separated into nests or components by fibrovascular septae, neurofibrillary intercellular matrix and rosette formations [10]. The classical Homer–Wright rosettes are nearly pathognomonic for esthesioneuroblastoma, however, care must be taken to avoid mistaking rosette-like arrangements of cells surrounding collagen or foci of necrosis [11]. Immunohistochemical staining usually positive for neuroendocrine markers including synaptophysin, chromogranin and neuron specific enolase [10]. In our case, he was diagnosed with esthesioneuroblastoma (WHO grade 1) based on the histopathological examination and immunohistochemical staining.

The mainstay treatment for esthesioneuroblastoma are surgery with adjuvant or neoadjuvant radiotherapy [6]. The surgical approach and the extend of surgery is dictate by the localisation of the tumour and the involvement of the surrounding structures. Traditionally, the treatment of choice for esthesioneuroblastoma is a combined approach with craniofacial resection. However, in the advances of endoscopic skullbase surgery with neuronavigational guidance, equal or better surgical clearance with significant lesser morbidity and mortality can be achieved when the tumour is located in the trajectory of the endoscope. Sphenoclivar lesions lends themselves to a transnasal endoscopic approaches [2]. Multidisciplinary team consisting of otorhinolaryngologist and neurosurgeon is an absolute necessity in dealing with tumour at the sphenoclivar region [2, 12]. The used of intraoperative navigation system for surgery involving the anterior skullbase is already well established. Wiltfang et al. [13] evaluated the suitability and usefulness of intraoperative image guided surgery of the anterior skullbase and stated that navigation reliably allowed to visualize the extent of tumour configuration and risk zones. Therefore, neuronavigation allowing more radical resection associated with less morbidity.

In previous reports, endonasal endoscopic resection combined with postoperative radiotherapy offers a good quality of life and excellent outcomes for disease control [14, 15]. Dulguerov et al. [16] in their study document 92 % disease free tumour control in those treated with a combination protocol as compared to 14 and 40 % disease free tumour control for surgery alone and radiotherapy alone respectively. However, a study by Biller et al. [17] maintain that an adequate surgical resection has a results superior to combination therapy and reserve the radiotherapy for recurrences, unresectable tumours and cases of incomplete excision. Our patient refused radiotherapy at the moment, therefore, we followed him up and planned for serial imaging to monitor if there is any recurrence of the tumour. The role chemotherapy remains unclear and has been used as an adjunct in advanced cases or as a combination with radiotherapy in unresectable tumour.

Conclusion

Ectopic esthesioneuroblastoma of the sphenoclivus is extremely rare. Due to its rarity and unusual presentation, the diagnosis of ectopic esthesioneuroblastoma is difficult and can be misdiagnosed with the other type of malignancy. Therefore, the histopathological result is important in confirming the type of tumour and can lead to the next step of management.

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Compliance with Ethical Standards

Conflict of interest Dr. Farah Dayana Zahedi, Professor Dato' Dr. Balwant Singh Gendeh Associate Professor Dr. Salina Husain and Associate Professor Dr. Ramesh Kumar and Dr. Kew Thean Yean declare that they have no conflict of interest.

Ethical Approval This case reports only involved a review on a patient's case. This article does not contain any experimental studies with human participants or animals performed by any of the authors.

Informed Consent Informed consent was obtained from the individual included in this case report.

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