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Case Report of Combined Sixth and Twelfth Cranial Nerve Palsy: A Rare Case of Clival Syndrome Arising from Thymoma

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Abstract

Godtfredsen syndrome or clival syndrome is a rare syndrome of abducens and hypoglossal nerve palsies (cranial nerve 6th and 12th respectively) that localizes to a clival mass. There are few reported cases of this clinical presentation. The aim of this case report is to describe this rare manifestation observed in a woman with clival metastases arising from a thymoma. A previously well 34-year-old native lady presented to a district hospital in Sabah, Malaysia, with history of blurring of vision and headache for 1 month. Cranial nerve examination reveals right abducens nerve palsy (right 6th CN) and right hypoglossal nerve palsy (right 12th CN). Initial imaging with CT brain reveals a subtle extra-axial hyperdense mass adjacent to the clivus and a routine chest x-ray reveals a mediastinal mass. Further imaging of thorax showed right anterior mediastinal mass, which then proceeded with Video-Assisted Thoracoscopic Surgery (VATS) guided biopsy. The biopsy result was consistent with the finding of thymoma, type B2. She was then diagnosed with aggressive form of thymoma, which unfortunately has metastasized to the bone, lung, liver and brain. Despite prognosis at the time of diagnosis is guarded, she still opted to undergo chemotherapy. Despite the completion of 6 cycles of chemotherapy, her disease progressed, and she eventually succumbed to the illness. In short, the presence of combined 6th and 12th palsy should alert clinician to the possibility of clival mass or metastases and hence could earlier workup with appropriate imaging can lead to earlier diagnosis and better treatment outcome.

Keywords

Clival Syndrome, Godtfredsen Syndrome, Abducens and Hypoglossal Nerve

Palsies

1. Introduction

Back in 1947, Godtfredsen described an ophthalmo-neurological symptom in connection with malignant nasopharyngeal tumours [1]. The cases described were patients with malignant nasopharyngeal tumours presented with ophthalmoplegia and trigeminal neuropathy due to invasion into the cavernous sinus. The ophthalmoplegia was found to be usually due to abducens nerve palsy. In addition to that, these patients also had twelfth CN palsy due to retropharyngeal lymph node involvement near the hypoglossal canal. The clinical syndrome of sixth CN and twelfth CN palsy described by Godtfredsen was due to pathology in 2 different anatomical location caused by malignant nasopharyngeal tumours.

Years after, similar cases of sixth CN and twelfth CN palsy were occasionally detected, however not all of these patients were diagnosed with malignant nasopharyngeal tumour. Keane reviewed a series of 1262 patients seen with sixth CN lesion and 116 patients with twelfth CN palsy from Los Angeles County/University of Southern California Medical Centre for a 29.5-year period, he found that 21 patients had both nerves involved, and only 5 out of them had no other cranial neuropathies [2]. He found that tumours at the mid and lower clivus are ideally located to cause the presentation of a combined sixth CN and twelfth CN palsy, and therefore he termed it "Clival Syndrome" [2]. Up to date, there is no case report on clival metastasis from thymoma, hence, we are reporting the first case of such presentation.

2. Case Report

A 34-year-old lady with no known medical illness presented with 1-month history of diplopia and a progressively worsening headache. She denied history of trauma, orbital pain, or symptoms of increased intracranial pressure. Detailed clinical examination revealed right abducens nerve palsy (**Figure 1(a)**) and right hypoglossal nerve palsy (**Figure 1(b)**). Other neurological examinations revealed no abnormalities. An initial non-contrasted CT scan of the head was performed and revealed a subtle extra-axial hyperdense mass over the base of skull adjacent to clivus measuring approximately 0.9 cm × 0.8 cm (AP × W) with focus of calcification within. In view of this finding, we proceeded with contrasted CT brain which then showed enhancing extra-axial base of skull lesion adjacent to clivus (**Figure 2**). Differential diagnosis includes meningioma and metastasis. MRI Brain was not done during that time as this facility was not available in our centre and patient was not keen to be transferred to another hospital with this facility available. During the same admission as well, a mediastinal mass was revealed during routine chest x-ray imaging (**Figure 3**). We further investigated the lesion with a contrast-enhanced CT of Thorax, Abdomen and Pelvis (CT TAP) which showed

presence of a heterogenous mixed solid cystic mass seen located at right anterior mediastinum, measuring approximately 6.3 cm × 7.1 cm × 7.5 cm (A × P × W) causing compression of the right brachiocephalic vein with bony metastasis and multiple lung nodules (Figure 4). In addition, ultrasonography scan of the hepatobiliary system also revealed an ill-defined hypoechoic lesion suspicious of liver metastasis. For further evaluation, Video-Assisted Thoracoscopic Surgery (VATS) guided biopsy of the mediastinal mass was done, and the histopathological examination reported as Thymoma type B2 (Figure 5). Hence, the final diagnosis for her was thymoma with bone, lung, liver and brain metastasis.

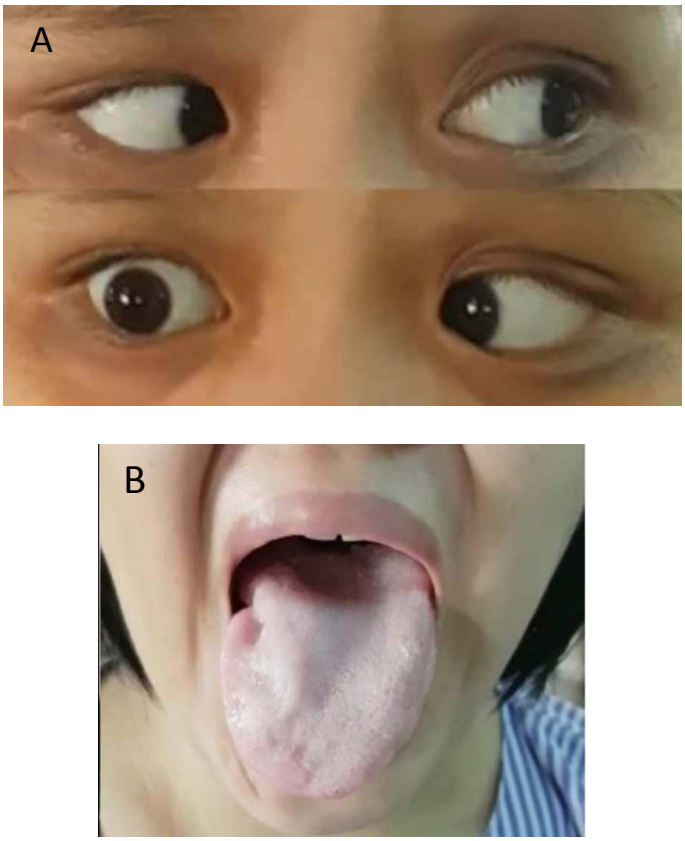


Figure 1. (A) (Top): Normal left gaze of bilateral eyes. (Bottom): Right eye 6th cranial nerve palsy; (B): Right 12th cranial nerve palsy evidence bye the of deviated tongue to the right.

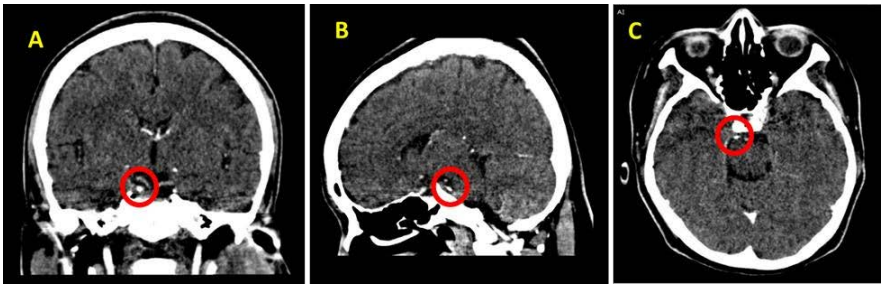


Figure 2. CECT brain which shows enhancing lesion over the base of skull adjacent to clivus in coronal (A), sagittal (B) and axial (C) views.

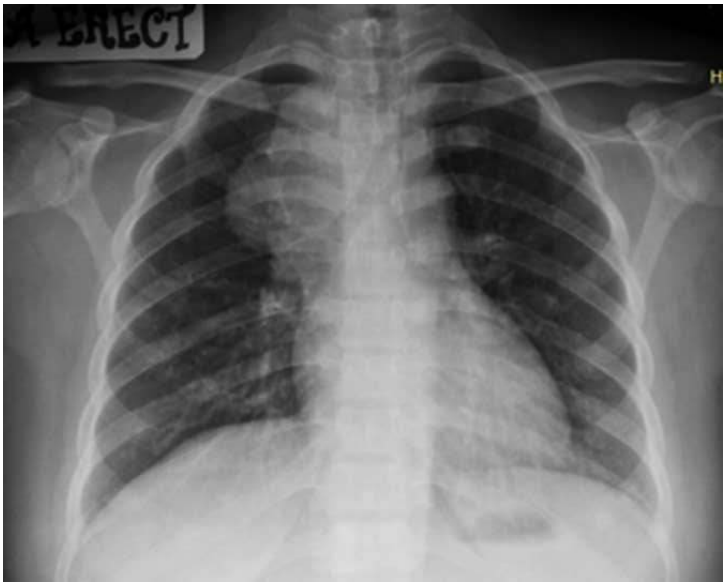


Figure 3. CXR showing prominent right mediastinal mass.

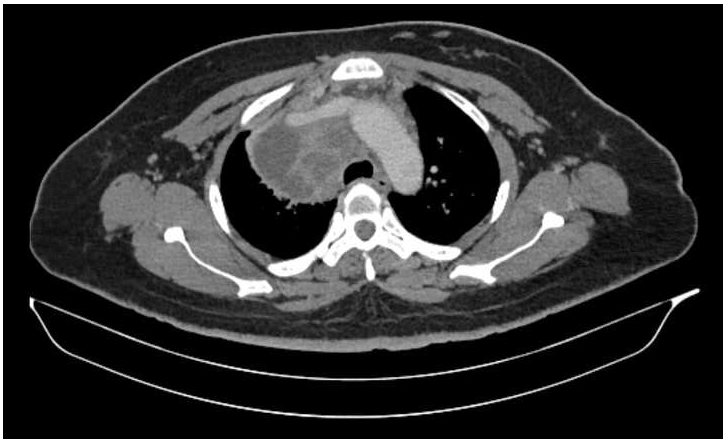
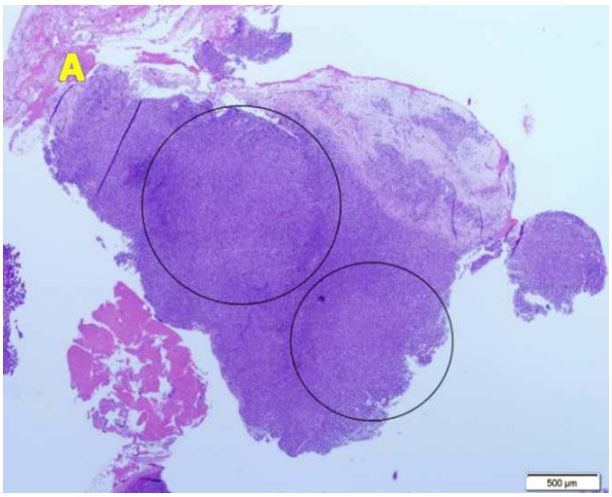


Figure 4. CECT noted a heterogenous mixed solid cystic mass seen located at the right anterior mediastinum causing compression of the right brachiocephalic vein.



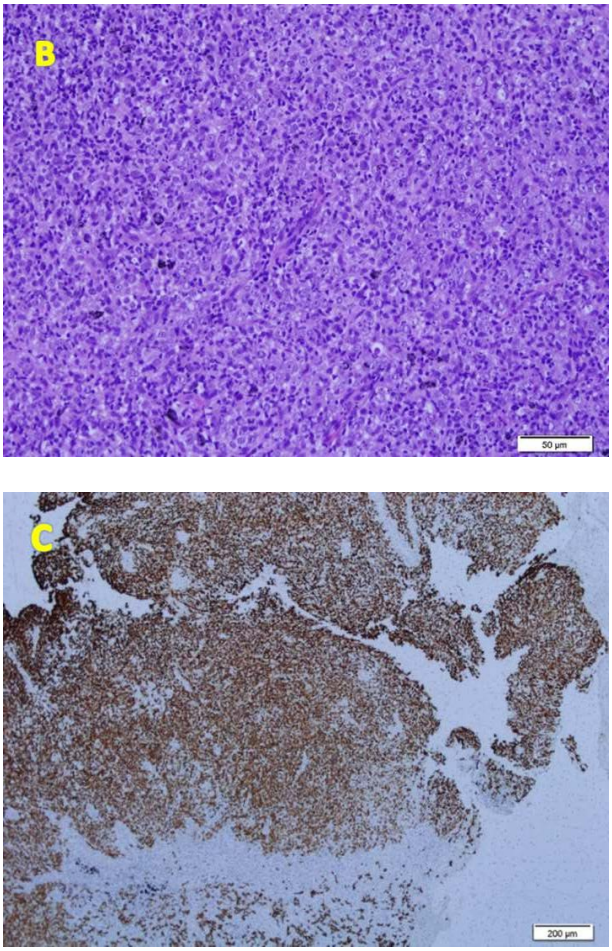


Figure 5. Thymic tissue composed of neoplastic epithelial cells.

She was subsequently referred to Oncology and Cardiothoracic team for further management. In view of extensive bone metastasis, Oncology team suggested for chemotherapy followed by restaging CT prior to mediastinal mass resection surgery. Patient agreed for chemotherapy and eventually underwent chemotherapy with CAP regime for total of 6 cycles. Despite the chemotherapy, repeated imaging study post-chemotherapy showed disease progression with worsening liver, lung and bone metastases. Her illness was also unfortunately complicated with severe hospital-acquired pneumonia. Due to no clinical improvement, the patient herself and her family wished for palliative care. She eventually succumbed to her illness and passed away in peace.

3. Discussion

The causes for the 5 cases of "Clival Syndromes" were a case of local chordoma, 3 cases of distant metastases from prostate, pancreas and ?ovary, and a case of ?self-limited cranial polyneuropathy. Thapa *et al.* [3] described a case with similar presentation secondary to metastasis from rectal adenocarcinoma. Amalnath [4] described a similar case due to retro-clival subdural hematoma. Wai Y.Z. *et al.* [5] also described a similar case presentation due to clival Chondrosarcoma.

Clival tumours are very rare, 46 patients with clival bone tumour was operated between January 1995 and December 2007 at the Institute of Neurosurgery, Catholic University School of Medicine, Rome, out of which 38 patients were found to be due to primary chordomas and chondrosarcomas, seven were found to be metastatic in origin, and 1 patient had ectopic pituitary adenoma [6]. Chordomas, which are the commonest primary tumour at this anatomical location represent only 0.1% - 0.2% of all intracranial tumour [7]. In a study by Roberto *et al.* the incidence of clivus chordomas is 1.32% of intracranial tumours at Institute of Neurosurgery, Catholic University School of Medicine, Rome, and the metastases of the clivus bone at the same institution represents 0.18% of all intracranial tumours and 0.42% of skull base tumours. This figure is likely an overestimation of the actual incidence as the reported incidence of the clivus chordoma in the same institution was 10 folds higher than commonly reported [7]. They also did literature review on 27 single case reports of metastatic clival bone tumour and found that the most common primary tumour originated from prostate cancer, thyroid carcinoma and hepatocarcinoma [6]. A summary of all the cases of clivus syndrome are listed in **Table 1**.

Our case report is the first to describe clival metastases from thymoma. Cranial nerves VI and XII only the only two CN that lies on the medial portion of the clivus compared to other CN (V, VII, VIII, IX and X), thus midline lesion located at clivus can disrupt cranial nerve VI and XII without involving other cranial nerves (**Figure 6**). Shortfall that we have in this case is that we do not have an MRI brain to better visualize the clival mass. However, given that histopathological examination reported the tumor as Thymoma B2, Thymoma B2 has a moderate aggressive nature as compared to other subtypes, it may cause distant metastases. Hence, this patient came with combined right 6th and 12th CN nerve palsy, CT brain showing clival mass, has underlying Thymoma with bone, liver and lungs metastases, the clival mass is most likely to be metastases from thymoma. In summary, the clinical findings of combined 6th and 12th nerves should alert clinician to look for clival mass via imaging preferably with MRI Brain as it provide better accuracy of the anatomy of the area. Subsequent workup and treatment could be instituted accordingly.

Table 1. Repoted cases of clivus syndrome.

Author, year	Etiology
Godtfredsen, 1947	Nasopharyngeal tumour with cavernous sinus and retropharyngeal lymph node metastasis
Keane, 2000	• Clival chordoma • Clival metastasis from prostate cancer • Clival metastasis from pancreatic cancer • Clival metastasis from ovarian Cancer • ? Self-limited cranial polyneuropathy
Thapa, 2011	Clival metastasis from rectal adenocarcinoma
Amalnath, 2018	Retroclival subdural hematoma
Wai, 2022	Clival chondrosarcoma

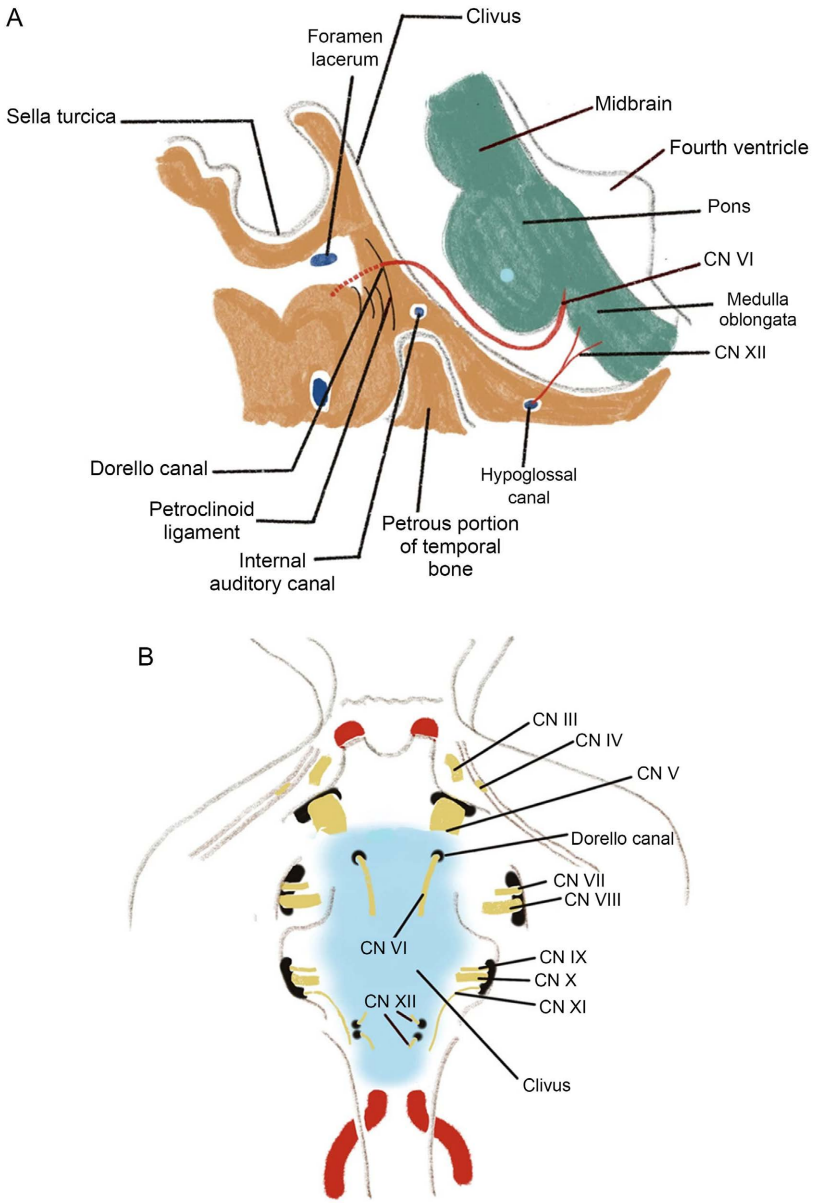


Figure 6. (A) Illustration of the sagittal section of the clivus, shows CN VI and XII in relation to the clivus. (B) Posterior view of the clivus shows CN VI and XII are located more medially compared to other cranial nerves on the clivus.

4. Conclusion

The finding of ipsilateral 6th and 12th nerve palsy with tumours or mass localizing at the clivus is an uncommon manifestation. It will be helpful to keep this in mind when one encounters this combination of cranial nerve palsy, so it would raise suspicion of clival mass or tumour and help to narrow down our investigation to that area of interest.

Consent

Consent has been taken from the patient.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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