

Case Report

# Tumors Presenting as Multiple Cranial Nerve Palsies

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## Keywords

Cranial nerve palsies · Glomus jugulare tumor · B-cell lymphoma · Clivus tumor

## Abstract

Cranial nerve palsy could be one of the presenting features of underlying benign or malignant tumors of the head and neck. The tumor can involve the cranial nerves by local compression, direct infiltration or by paraneoplastic process. Cranial nerve involvement depends on the anatomical course of the cranial nerve and the site of the tumor. Patients may present with single or multiple cranial nerve palsies. Multiple cranial nerve involvement could be sequential or discrete, unilateral or bilateral, painless or painful. The presentation could be acute, subacute or recurrent. Anatomic localization is the first step in the evaluation of these patients. The lesion could be in the brain stem, meninges, base of skull, extracranial or systemic disease itself. We present 3 cases of underlying neoplasms presenting as cranial nerve palsies: a case of glomus tumor presenting as cochlear, glossopharyngeal, vagus and hypoglossal nerve palsies, clivus tumor presenting as abducens nerve palsy, and diffuse large B-cell lymphoma presenting as oculomotor, trochlear, trigeminal and abducens nerve palsies due to paraneoplastic involvement. History and physical examination, imaging, autoantibodies and biopsy if feasible are useful for the diagnosis. Management outcomes depend on the treatment of the underlying tumor.

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## Introduction

Cranial nerve palsy could be one of the presenting features of underlying benign or malignant tumors involving the head and neck. Various etiologies of cranial nerve palsies have been reported; however, tumor is one of the most common etiology [1]. Tumor can involve the cranial nerves by local compression, direct infiltration or by paraneoplastic process. We present 3 cases of cranial nerve palsy secondary to underlying malignancy. On further evaluation, these patients were diagnosed to have glomus jugulare tumor, clivus tumor and non-Hodgkin's lymphoma, respectively.

## Case Presentations

### *Case 1: Glomus Jugulare Tumor Presenting as Multiple Cranial Nerve Palsies*

A 65-year-old woman with a history of hypertension and autoimmune hepatitis presented with complaints of left-sided hearing loss for the past 2 years and hoarseness of voice for the past 2 months. She had had no surgeries in the past. She is a former smoker and quit smoking 25 years ago. There was no family history of cancer or autoimmune disorders. On examination, she had left-sided tongue deviation and left hemiglossal atrophy. The right side of the palate was higher compared to the left side. She was noted to have a normal gag reflex. Other cranial nerves were intact. Motor, sensory and cerebellar examinations were within normal limits. Ear, nose and throat examination was also normal. She underwent fiber-optic laryngoscopy which showed left vocal cord paralysis with no apparent mass lesion. Audiometry revealed sensorineural hearing loss and speech evaluation revealed speech discrimination and recognition on the left side. Laboratory tests were within normal limits including serum catecholamines. Magnetic resonance imaging (MRI) of the head showed a 1.8 × 1.8 × 3.1 cm enhancing mass centered in the left jugular foramen (Fig. 1a). A portion of the mass extends into the left cerebellomedullary cistern with the cisternal segment of the left glossopharyngeal nerve coursing into the anterior lateral aspect of the mass lesion. There was an extension inferior to the left hypoglossal canal. Radiological findings were suggestive of a glomus jugulare tumor. The diagnosis was further supported with carotid angiography, which revealed a characteristic tumor blush, with the main feeder to the vascular mass being the ascending pharyngeal branch of the external carotid artery. She underwent embolization of the feeding artery with subsequent excision of the tumor. Tumor resection was carried out through a left transmastoid/transjugular approach with no subsequent cranial nerve damage. Postoperative histopathological examination confirmed the diagnosis of glomus jugulare tumor (Fig. 1b).

### *Case 2: Clivus Tumor Presenting as Sixth Nerve Palsy*

A 58-year-old Haitian man with a history of hypertension and type 2 diabetes mellitus presented with complaints of double vision and clear nasal discharge for 6 months. The patient had diplopia on seeing objects towards his right side. He also had clear nasal discharge on leaning forward. He denied photophobia, nausea or vomiting. He had mild intermittent headache in the vertex and the frontal region. He had quit smoking 23 years ago and denied alcohol or recreational drug use. His parents had gastric cancer and his sister had pancreatic cancer. Examination was significant for medial deviation of the right eye. The patient had difficulty abducting the right eye. Other cranial nerves were intact. Motor, sensory and cerebellar examinations were normal. Laboratory tests were within normal limits. Nasal endos-

copy showed septum deviation to the right, posteriorly with spur and no visible intranasal masses or cerebrospinal fluid leak. Computed tomogram (CT) of the head and sinuses showed a large soft tissue mass centered on the clivus and involvement of the sphenoid sinus, right posterior nasal cavity, right carotid canal, left pterygopalatine fossa, and orbital apex with intracranial extension into the prepontine cistern. MRI of the head showed an extensive abnormal marrow signal involving the clivus, dorsum sellae, occipital condyles, and medial petrous temporal bones with extension into the nasopharynx, prevertebral space, sphenoid sinuses, left pterygopalatine fossa, inferior orbital fissure, orbital apex, and prepontine cistern (Fig. 2a, b). The patient underwent transnasal endoscopic sphenoidotomy and biopsy of clival mass. Pathology showed invasive poorly differentiated carcinoma, favoring nonkeratinizing squamous cell carcinoma (Fig. 2c). The patient underwent further imaging but no primary tumor was found. He has been followed by an oncologist and recommended chemoradiation.

### *Case 3: Multiple Cranial Nerve Palsies in a Patient with Large B-Cell Lymphoma*

A 75-year-old Hispanic man with a history of hypertension presented with complaints of left eyelid droop and double vision for 1 day. He admitted to have had a blunt trauma to the left eye 5 days prior to presentation. He denied any eye pain, difficulty in eye movements or decreased vision. He had had cataract surgery and laser procedure for corneal ectasia a year ago. He denied any exposure to tobacco, alcohol or any recreational drugs. He also admitted to have had weight loss of more than 20 pounds over the past 2 months and had had decreased appetite for the past 3 months. On physical examination, he had ptosis of the left eye with limited abduction, depression, and decreased facial sensation of the left side. Optometry revealed visual acuity of 20/30 and 20/150 in the left and right eyes, respectively. Slit lamp examination of the left eye confirmed ptosis with an interpalpebral distance of 3.5 mm. Other cranial nerves were intact. Motor and cerebellar examination was normal. Fundoscopy showed hypertensive changes. On neck examination, a 3 × 2 cm nontender, mobile left supraclavicular lymph node was palpable. Abdominal examination revealed splenomegaly and ascites. Initial laboratory findings were significant for mild microcytic anemia and hypercalcemia. In view of multiple cranial nerve palsies (third, fourth, fifth and sixth), he underwent MRI and magnetic resonance venogram of the brain which were normal. Magnetic resonance angiogram showed a 2-mm saccular aneurysm in the left internal carotid artery that did not explain the patient's symptoms. A CT scan of the chest, abdomen and pelvis revealed splenomegaly with splenic masses, ascites, and mediastinal and retroperitoneal lymphadenopathy (Fig. 3). He underwent endoscopic evaluation for his anemia and weight loss that revealed benign polyps in the stomach, duodenum, descending colon, and sigmoid colon. Further workup with fine needle aspiration of the supraclavicular lymph node revealed a high-grade, diffuse large B-cell malignant lymphoma. Immunohistological staining showed CD20(+), CD79s(+), CD43(+), and BCL-6(+). The patient developed resistant hypercalcemia and tumor lysis syndrome. The family opted for comfort measures and hospice care, hence further workup including onconeural antibodies were not pursued. He continued to deteriorate and subsequently expired.

### **Discussion**

Evaluation of patients presenting with cranial nerve palsies is challenging as the etiology is very extensive. A patient may present with single or multiple cranial nerve palsies. Mul-

tiple cranial nerve involvement could be sequential or discrete, unilateral or bilateral, painless or painful. The presentation could be acute, subacute or recurrent. Anatomic localization is the first step in the evaluation. The lesion could be in the brain stem, meninges, base of skull, extracranial or systemic disease itself [1, 2].

The largest case series of 979 cases of multiple cranial neuropathies was reported by Kaene [1]. As per the case series, the tumors constituted 30% of multiple cranial neuropathies, followed by vascular diseases like infarctions (12%), trauma (12%), infection (10%), Guillain-Barré syndrome (6%), Fisher syndrome (3%), idiopathic cavernous sinusitis (5%), surgery (5%), multiple sclerosis and autoimmune demyelinating encephalomyelitis (5%), functional disease (3%), diabetes mellitus (2%), benign and miscellaneous causes. The most common tumor was schwannoma (17%) followed by metastases (16%), meningioma (13%), lymphoma (10%), pontine glioma (9%), nasopharyngeal carcinoma (9%), pituitary adenoma (5%), chordoma (5%), leukemia (3%), epidermoid tumor (2%), glomus jugulare tumor (2%), miscellaneous and unknown cases. The most common site was cavernous sinus (25%), nonlocalized neuropathy (18%), clivus and skull base (13%), subarachnoid space (10%), cerebellopontine angle (8%), neck (2%), unknown and functional causes. The most common cranial nerve involved is the sixth nerve followed by the seventh, fifth, third, and tenth nerve. The most common recurrent cranial nerve involvement includes the seventh nerve followed by the third and the sixth nerve. The most common combinations of cranial nerves include the third and sixth nerves, the fifth and sixth nerves, and the fifth and seventh nerves [1, 2].

The glomus jugulare is a collection of paraganglionic cells derived from the neural crest [3]. Glomus jugulare consists of one or more bodies lying in the adventitia of the dome of the jugular bulb [4]. Paraganglionic cells are widely distributed within the autonomic system and are divided into 2 groups based on their endocrine activity. The paraganglia of the adrenal medulla secrete adrenaline and noradrenaline and on histological examination stain chromaffin positive. Nonphysiologically active paraganglia have a negative chromaffin reaction, and the glomus jugulare falls into this group. Only very small proportions (2%) of glomus tumors have any endocrine activity, which can be diagnosed by measurement of 24-h urinary vanillylmandelic acid levels. The glomus jugulare receives its innervation from the tympanic branch of the glossopharyngeal nerve and its blood supply from the ascending pharyngeal artery. Malignant transformation and metastatic spread are rare. Most glomus tumors arise sporadically, but there are case reports of familial glomus tumors, with an autosomal dominant pattern of inheritance and variable penetrance [3–6].

Classic presenting features of glomus jugulare tumors include hearing loss (69%) and pulsatile tinnitus (55%). Examination may reveal a middle-ear mass, the so-called “rising sun sign” (75%). Cranial nerve deficits most commonly affect the vagus, glossopharyngeal, facial and hypoglossal nerves [3]. Cranial nerve involvement produces hoarseness and dysphagia. The presence of jugular foramen syndrome (paresis of cranial nerves IX–XI) is pathognomonic of this tumor, but it usually follows the initial symptoms of hearing loss and pulsatile tinnitus. Less commonly, glomus tumors produce facial nerve palsy, hypoglossal nerve palsy, or Horner syndrome [5]. In about 2–4% of cases, the first or leading symptoms are hypertension and tachycardia (pheochromocytoma-like symptoms) produced by catecholamines, norepinephrine, or dopamine excreted by the tumor. These tumors are locally destructive and invasive of surrounding bone and neural tissue. Also, vasoactive intestinal polypeptide, somatostatin, calcitonin, and neuron-specific enolase may be produced by the tumor. Other related symptoms include headache, perspiration, pallor, and nausea. The cause of hearing loss could be due to several reasons which include large tumor size causing com-

pression of the vestibulocochlear nerve at the cerebellopontine angle, direct invasion of the labyrinth or hemodynamic alteration of the cochlear nerve blood supply. Symptoms of pulsatile tinnitus, conductive hearing loss, lower cranial nerve deficits and radiographic evidence of a vascular lesion of the jugular foramen have been considered diagnostic of a glomus jugulare tumor. Angiographic evidence of a blood supply from the external carotid artery system, especially the ascending pharyngeal artery, substantiates this diagnosis. A pre-treatment biopsy of lesions of the jugular foramen by exploratory tympanotomy or postauricular mastoidectomy has been advocated by some surgeons as it provides a pathological diagnosis on which to base treatment; however, it is not routinely done nor recommended widely in the literature [4].

It has been suggested that surgical management is the treatment of choice in younger patients with glomus jugulare, with complete resection and conservation of cranial nerves. Radiosurgery proves to be a safe treatment for glomus tumors with no acute morbidity; however, due to the tumor's slow growth rate, up to 10 years of follow-up will be necessary to establish effectiveness of radiosurgery for glomus tumor [4]. Stereotactic radiosurgery is useful to control symptoms and is safe in patients with primary or recurrent glomus tumors who are poor surgical candidates. Megavoltage radiotherapy has been recommended for primary treatment of all glomus tumors that present with evidence of bone invasion or nerve involvement; however, the presence of viable tumor cells after radiotherapy has been associated with unpredictable long-term outcome. The side effects of radiotherapy include radiation-induced secondary malignancy and temporal bone osteoradionecrosis. However, radiotherapy may be advantageous over surgical resection in elderly patients, poor surgical candidates, very large tumors with intracranial extensions and for recurrent lesions [3–6].

Clivus is a posterior structure on the base of skull. Clivus tumors are rare tumors. The tumors affecting the clivus are chordoma, chondrosarcoma, metastatic tumors, plasmacytoma (myeloma), meningioma, monostatic fibrous dysplasia, lymphoma, giant cell tumors, Langerhans histiocytosis, and intraosseous hemangiomas [7, 8]. Clival chordomas and chondrosarcomas are the most common of these tumors [7]. Diseases from adjacent structures like invasive pituitary macroadenoma, nasopharyngeal carcinoma, cholesteatoma, and sphenoid mucocele can also affect the clivus [8]. Most metastatic lesions involving the clival region arise from the lung, prostate, breast, thyroid, and lymphoma [9, 10]. Clivus disease usually presents as cranial nerve palsies or headache [7]. Diplopia usually results from the sixth nerve involvement [11]. Combination of the sixth and twelfth nerve can also occur [9]. The sixth cranial nerve is extremely vulnerable to injury from clival tumors because of its long tortuous path from the brain stem to the superior orbital fissure [7]. The transsphenoidal approach is the preferred approach for histopathological diagnosis [11]. MRI can be used for diagnosis. Fluorodeoxyglucose-positron emission tomography and radionuclide bone scan can be used for staging and surveillance of other malignancies. Management of clivus tumors depends on the specific diagnosis [10, 12].

Paraneoplastic syndromes (PNS) are a group of heterogeneous disorders with a wide array of presentation caused by an immune response to substances secreted by occult or known malignant tumors [13]. PNS are rarely associated with Hodgkin's and non-Hodgkin's lymphoma. PNS in lymphoma often develop in the advanced stage of the disease. PNS associated with lymphomas are limbic encephalitis, granulomatous angiitis, cerebellar degeneration, paraneoplastic chorea, opsoclonus-myoclonus, stiff-person syndrome, paraneoplastic myelopathy, motor neuronopathy, sensory neuronopathy, autonomic ganglionopathy, sensorimotor neuropathy, vasculitic neuropathy, neuromyotonia, Lambert-Eaton myasthenic syndrome, myasthenia, and dermatomyositis. Among these, cerebellar degeneration, opso-

clonus-myoclonus, sensory neuronopathy, Lambert-Eaton myasthenic syndrome, and dermatomyositis are considered as classical syndromes. They are called classical because they almost always indicate the presence of an underlying tumor. Diagnosis of PNS depends on the type of neurological syndrome (classical or nonclassical), detection of well-characterized onconeural antibodies, and the presence of cancer [14]. Onconeural antibodies are absent in most PNS except for anti-Tr antibodies in paraneoplastic cerebellar degeneration and anti-mGluR5 antibodies in limbic encephalitis. Management depends on the clinical presentation. Even though steroids, intravenous immunoglobulins, plasma exchange and immunomodulatory therapies have been tried, the best treatment is early detection and immediate treatment of the underlying tumor [13–15].

## Conclusion

Cranial nerve palsies could be a presentation of head and neck tumors as well as tumors at other sites causing PNS. Cranial nerve involvement depends on the anatomical course of the cranial nerve and the site of the tumor. The differential diagnosis is very extensive. Imaging and autoimmune antibodies are helpful in the diagnosis. The localization of the cranial nerve lesion and histopathological diagnosis of the tumor are key factors in the management.

## Statement of Ethics

The authors have no ethical conflicts to disclose.

## Disclosure Statement

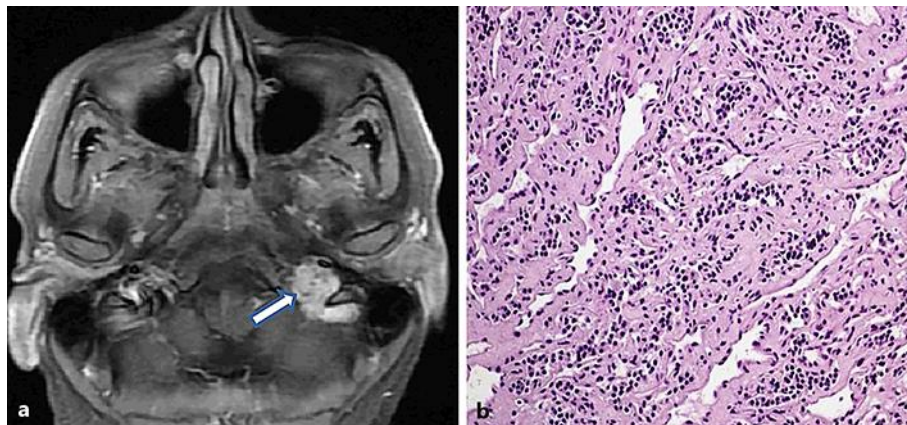
The authors have no conflicts of interest to disclose.

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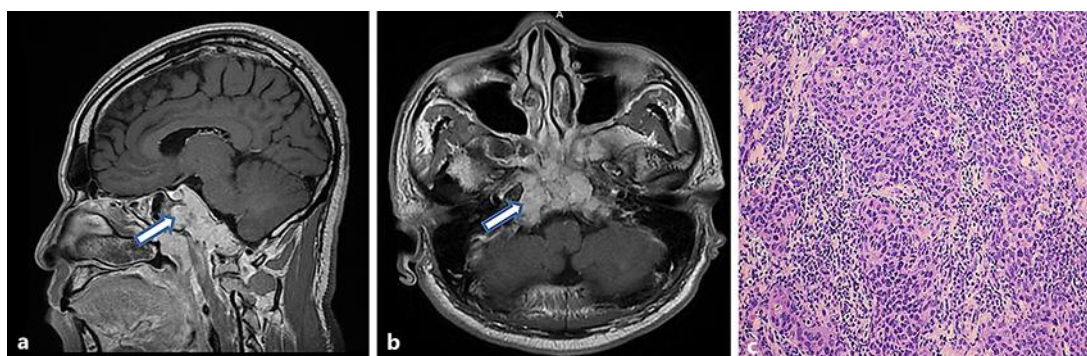
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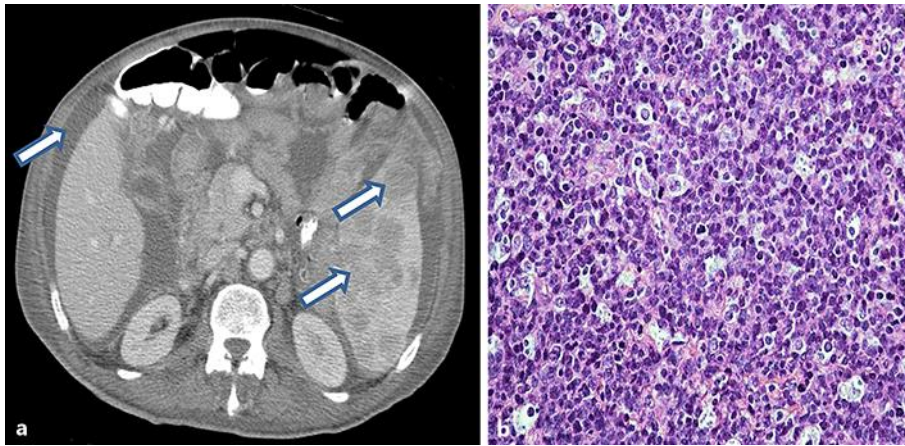
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**Fig. 1.** a MRI of the head showing a mass involving the left jugular foramen. b Surgical specimen showing glomus tumor with rich vascular plexus-associated nests of tumor cells. H&E, magnification  $\times 200$ .



**Fig. 2.** a Sagittal section of MRI of the brain showing destruction of the clivus by the clivus tumor. b Coronal section of the MRI of the brain showing destruction of the clivus by the clivus tumor. c Poorly differentiated squamous cell carcinoma of the neoplastic cells are arranged in groups surrounded by nonneoplastic lymphoid cell component. H&E, magnification  $\times 200$ .



**Fig. 3.** **a** CT of the abdomen showing splenomegaly, splenic masses, and ascites. **b** Diffuse large B-cell lymphoma involving lymph nodes. The neoplastic cells are large with prominent nucleoli and mitotic figure. H&E, magnification  $\times 400$ .