Surgical Neurology International

SNI: Unique Case Observations, a supplement to Surgical Neurology International

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Editor: James I. Ausman, MD, PhD University of California, Los Angeles, CA, USA

Dyspnea and choking as presenting symptoms in primary medulla oblongata germinoma

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Received: 09 February 14 Accepted: 01 May 14 Published: 19 June 14

This article may be cited as:
Yip C, Tseng H, Hsu S, Liao W, Chen J, Chen C, *et al.* Dyspnea and choking as presenting symptoms in primary medulla oblongata germinoma. Surg Neurol Int 2014;5:S170-4.
Available FREE in open access from: http://www.surgicalneurologyint.com/text.asp?2014/5/5/170/134815

Abstract

Background: The medulla oblongata is the lower half of the brainstem. It contains the cardiac, respiratory, vomiting, and vasomotor centers and deals with autonomic functions such as breathing, heartbeat, and blood pressure. Primary medulla oblongata germinoma is very rare and less than 20 cases have been reported in the English literature.

Case Description: A 22-year-old female without any particular past medical history presented to us in October 2012 with the chief complaint of dyspnea and frequent choking for 1 month. Neurological examination revealed lower cranial nerve palsies and nystagmus. Her brain computed tomography (CT) and brain magnetic resonance imaging (MRI) demonstrated a mass lesion at the dorsal surface of medulla oblongata with extension into the inferior fourth ventricle and foramen magnum. She underwent bilateral suboccipital craniotomy and C1 laminoplasty with the grossly total resection of the tumor. The histological examination of the tumor proved germinoma. Postoperative adjuvant radiotherapy was arranged. The latest brain MRI and whole spine MRI done 1 year after surgery showed neither residual nor recurrent tumor in the whole axis. She is regularly followed-up at our outpatient department and is doing well except having left vocal cord palsy, which occurred before surgery.

Conclusion: Medulloblastoma, ependymoma, glioma, hemangioblastoma, and cavernous angioma are common intraaxial tumors in the medulla oblongata and fourth ventricle. Intracranial germ cell tumors originate from extragonadal seminal cells and have been found in 0.4-3.4% of patients with primary central nervous system (CNS) tumors in Western countries, while the incidence is reported to be 5-8 times greater in Japan and the Far East. Although germinoma of medulla oblongata is rare and difficult to diagnose preoperatively, it should be included in the differential diagnosis of medulla masses with fourth ventricle extension, especially in Asian population.

Key Words: Fourth ventricle, germinoma, medulla oblongata

Access this article online

Website: www.surgicalneurologyint.com

DOI: 10.4103/2152-7806.134815

Quick Response Code:

INTRODUCTION

Germ cell tumor is a neoplasm of germinal origin. It occurs in the gonads and extra-gonadal sites such as sacrococcygeum, retroperitoneum, mediastinum, intracranial, and rarely in nasopharynx and orbit.[4] In spite of site of origin, the histological features of germ-cell tumors are "identical" by light and electron microscopy.[2,4] Intracranial germ cell tumor has a significant geographic variation of its incidence. In Japan and Far East, it comprises 2.1-9.4% of primary intracranial neoplasms, which is much higher than the 0.4-3.4% reported in Western series.[4,10] Primary germinoma of medulla oblongata fourth ventricle is very rare. To the best of our knowledge, there are 17 cases of pure primary medulla oblongata germinoma reported in the English literature.[1,3,5,8,9,12-18] We would like to report a case of primary medulla oblongata fourth ventricle germinoma in a young female presented with dyspnea and frequent choking.

CASE REPORT

A 22-year-old female without any particular past medical history presented to us in October 2012 with the chief complaint of dyspnea and frequent choking for 1 month. Traced back her clinical course, she had suffered from suboccipital pain, dizziness, and blurred vision for 6 months; about 2 months prior to the visit, she experienced dysarthria and intermittent swallowing disturbance. On admission, she was clear and ill-looking. Her neurological examination revealed left vocal cord palsy, weak gag reflex, tongue fasciculation, and horizontal nystagmus in the right side gaze. She had neither motor nor sensory disorder of her extremities and her Babinski's sign was negative on both sides. Magnetic resonance imaging (MRI) of brain was performed, which demonstrated a mass lesion about 3.2 × 3 × 2.6 cm in size located in the inferior fourth ventricle with extension to foramen magnum, causing mild dilatation of fourth ventricle. This tumor showed heterogeneous enhancement with several foci of cystic change in postgadolinium enhancement study [Figure 1]. The tentative diagnosis was medulloblastoma with the differential diagnosis of ependymoma.

Under general anesthesia, she was put in prone position and underwent a bilateral suboccipital craniotomy and C1 laminoplasty with the removal of the tumor. A midline longitudinal incision was made from external occipital proturbance to the spinal process of C2, then a Y shape incision was made on the exposed dura of cerebellum and upper cervical spinal cord. Reflected the dural flaps to expose the cerebellar hemisphere and upper cervical cord. After the arachnoid membrane was opened and the cerebrospinal fluid (CSF) was drained, bilateral tonsils and the superficial part of the tumor was exposed. Grossly, the tumor was soft and gray-red [Figure 2], quite circumscribed but the margin between the tumor and the dorsal side of medulla was not very clear. Internal decompression of the tumor was done first to gain more working space, then dissected the tumor from the neighboring structures with extreme caution and finally this tumor was removed in piece-meal fashion with the aid of Cavitron Ultrasonic Surgical Aspirator (CUSA). Intraoperative frozen section of the specimen reported "malignant tumor", therefore, we tried to achieve maximum tumor resection. Histology examination showed that the specimen composed of sheets of large anaplastic cells divided by delicate fibrovascular septa with small lymphocytes [Figure 3a]. Mitosis and necrosis were present. The immunohistochemistry results of neoplastic cells revealed positive for CD117 and placenta alkaline phosphatase [Figure 3b], but negative for CD3, CD20, and synaptophysin immunostains. Germinoma was diagnosed based on the morphology of the tumor cells and the result of immunohistochemical stains. Based on the histological diagnosis of the tumor, whole spine MRI was checked, which disclosed no evidence of abnormal enhancing mass lesion. Although her immediate postoperative brain MRI showed no evidence

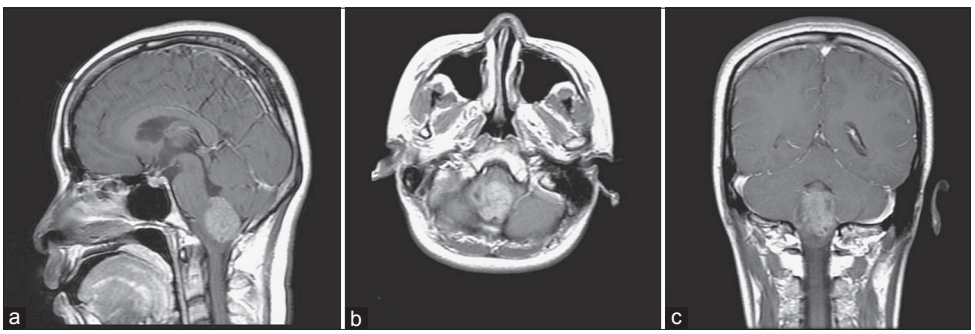

Figure 1: Preoperative brain MRI. T1-weighted postcontrast image, sagittal (a), axial (b), coronal (c) views revealed a heterogeneous enhancing mass lesion with several foci of cystic change over inferior fourth ventricle, about 3.2 × 3 × 2.6 cm, and extension to foramen magnum, causing mild dilatation of fourth ventricle

of abnormal enhancing mass lesion, or abnormal leptomeningeal enhancement in the brain [Figure 4], we administered postoperative adjuvant radiotherapy as following dosage: Total 45 Gy on the tumor bed and total 30.6 Gy on the ventricle system. Chemotherapy was not recommended by the oncologist because the patient's α-fetoprotein (AFP) and human chorionic gonadotropin (β-HCG) levels were within normal limits, and there was no dissemination of the tumor cells.

She is doing well except having left vocal cord palsy, which occurred before surgery. Her dyspnea and choking were much resolved after the operation. The latest brain and whole spine MRI done 12 months after the surgery showed no abnormal enhancing tumor in the whole axis [Figure 5] and is on regular follow-up at our out-patient department.

DISCUSSION

The medulla oblongata is the lower half of the brainstem. It contains the cardiac, respiratory, vomiting, and vasomotor centers and deals with autonomic functions such as breathing, heartbeat, and blood pressure. Surgery on this vital area remains a challenge to most neurosurgeons. Medulloblastoma, ependymoma, glioma, hemangioblastoma, and cavernous angioma are common intraaxial tumors in the medulla oblongata and fourth ventricle.[15] There are no significant differences in the clinical presentation among all medulla oblongata fourth ventricle lesions. Lower cranial nerves dysfunction, disturbance of breathing and cerebellar function, headache, nystagmus, sensory and motor disturbance, visual disturbance, and hiccups are the key symptoms reported.[3,9] From preoperative brain MRI of our patient, the tumor was located at the dorsal side of medulla oblongata with extension into the fourth ventricle and foramen magnum. This tumor was large and could compress the vagal trigone, hypoglossal trigone as well as the respiratory center in the medulla oblongata: Nucleus ambiguous and nucleus tractus solitarii. Respiratory center is divided into four major cliques: Inspiratory centre (dorsal respiratory group), expiratory centre (ventral respiratory group), pneumotaxic centre, and apneustic centre [Figure 6]. Pneumotaxic centre and apneustic centre are located in the upper part of pons and lower part of pons, respectively, which are not closed to the tumor location of our patient. However, inspiratory centre and expiratory centre locate at the dorsal portion and anterolateral part of medulla respectively and their corresponding nuclei are nucleus tractus solitarii and nucleus ambiguous. Before operation, our patient's neurological examination revealed left vocal cord palsy, weak gag reflex, tongue fasciculation, which reflected the dysfunction of

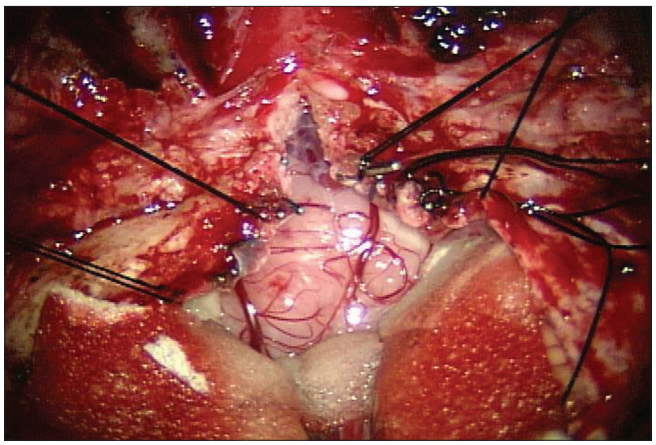

Figure 2: Intraoperative picture showed a mass lesion arising from the dorsal side of medulla oblongata with extension into inferior fourth ventricle

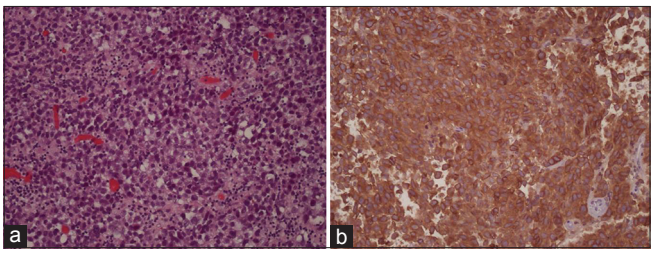

Figure 3: Histology of the tumor. H and E, ×200 (a) shows the specimen composed of sheets of large anaplastic cells divided by delicate fibrovascular septae with small lymphocytes, mitosis and necrosis. CD117 stain (b) shows the positive staining

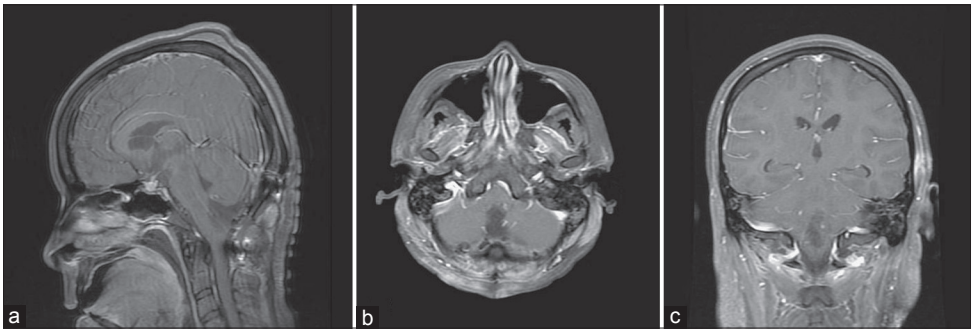

Figure 4: Immediate postoperative brain MRI. T1-weighted postcontrast image, sagittal (a), axial (b), coronal (c) views showed the completed removal of the tumor in the inferior portion of fourth ventricle and foramen magnum

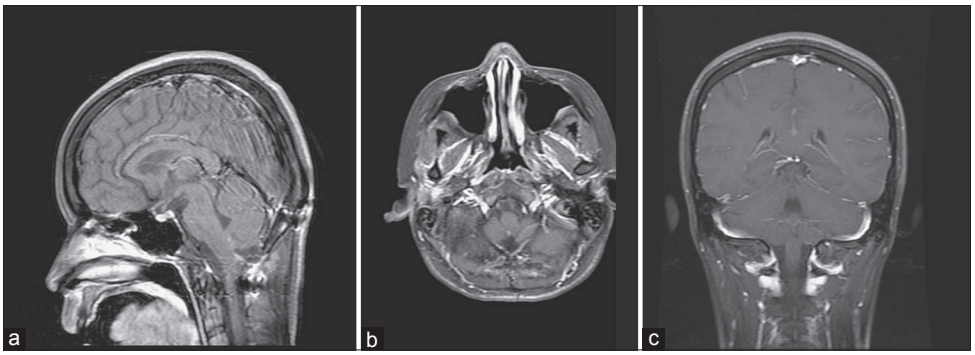

Figure 5: 1-year postoperative brain MRI.T1-weighted postcontrast image, sagittal (a), axial (b), coronal (c) views demonstrated neither residual nor recurrent tumor

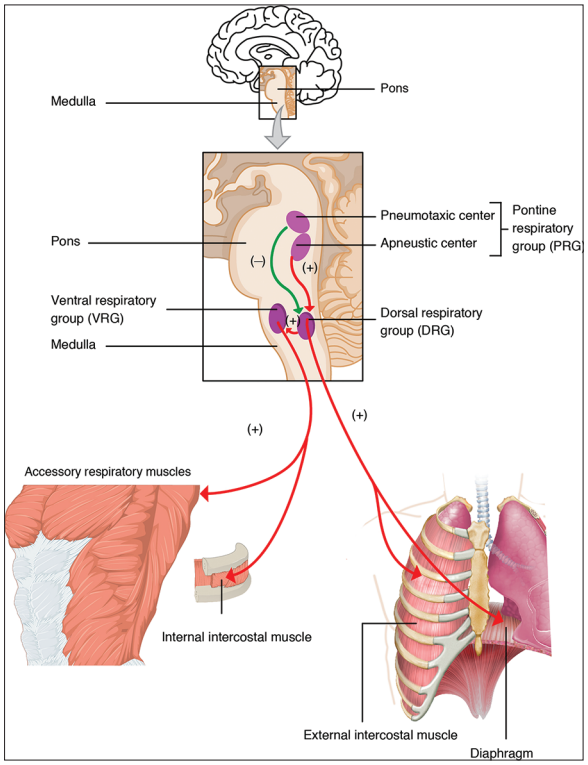

Figure 6: Schematic diagram of respiratory centers. (+): stimulate. (-): inhibit. (Source of the diagram: from Anatomy and Physiology, OpenStax College resource Unit 5 Chapter 22)

glossopharyngeal nerve, vagus nerve, and hypoglossal nerve. Due to the dysfunction of her low cranial nerves, she suffered from swallowing disturbance and choking with resultant aspiration pneumonia. Respiratory center compression and aspiration pneumonia contributed to her dyspnea.

Intracranial germ cell tumors originate from extragonadal seminal cells and frequently arise in the midline brain structures, such as pineal and suprasellar regions, floor of the third ventricle; they also happen in the basal ganglia and thalamus.[2,4] In 2007, the World Health Organization classified central nervous system germ cell tumors into the following histological types: Germinoma, embryonal carcinoma, yolk-sac tumor, choriocarcinoma, mature teratoma, immature teratoma, teratoma with malignant transformation and mixed germ cell tumors.[6] Germinoma is the most common subtype accounting for 50% or even more of the germ cell tumors.[4] The clinical presentation of intracranial germinomas varies according to anatomical location.[2] Suprasellar lesions are often present with a visual field defect, hypothalamic, and pituitary abnormalities. Pineal lesions often present with headaches, associated hydrocephalus, and Parinaud's syndrome. Germinoma at basal ganglia and thalamus often present with hemiparesis, mental disturbance, and movement disorders.[3,4,10]

To the best of our knowledge, from 1991 to 2013, there were 17 cases of pure primary medulla oblongata fourth ventricle germinoma, which have been reported in the English literature.[1,3,5,8,9,12-18] Most of them were from Asian countries, and female was predominant. Imaging with computed tomography (CT) and MRI are important for diagnosis but are often unable to differentiate germinomas from other neoplastic pathologies in the brainstem. Although germinoma of medulla oblongata is rare and difficult to diagnose preoperatively, it should be included in the differential diagnosis of medulla masses with fourth ventricle extension, especially in Asian population. There is no established management guidelines to medulla oblongata fourth ventricle germinoma.[5,9,12] From the reported cases, as well as our patient, surgery, for both tissue diagnosis and tumor debulking, often constitutes initial management. Postsurgical adjuvant therapy, either radiotherapy or chemotherapy or both, was applied after the tissue diagnosis. Most of them have favorable outcome except in two patients who died due to pneumonia, which was related to the dysfunction of the medulla oblongata. Pure germinoma is sensitive to radiotherapy and chemotherapy and indicates a good prognosis.[7,11] Thus, treatment of primary medulla oblongata fourth ventricle germinoma may follow the guidelines for other intracranial germinomas, however, long-term follow-up is necessary.

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