

Primary germinoma of the medulla oblongata: illustrative case

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BACKGROUND Primary central nervous system germinomas of the medulla oblongata are extremely rare and usually have been found in young female Asian patients. The authors present an illustrative case of a patient who presented with severe medullary and posterior cord syndrome, the first South American case published to date, to the authors' knowledge.

OBSERVATIONS Initially, the radiological differential diagnosis did not include this entity. The lesion was located at the obex and exhibited a well-delineated contrast enhancement without hydrocephalus. An emergency decompressive partial resection following functional limits was performed. After histological confirmation, radiotherapy was indicated, with complete remission achieved at a 6-month follow-up. The patient, however, continued to have a severe proprioceptive disorder. The literature review identified 21 other such patients. The mean age for this location was 23 years, with a strong female and Asian origin predilection. All tumors exhibited contrast enhancement, and only one presented with hydrocephalus.

LESSONS In the absence of elevated tumor markers, radiological clues such as a well-delineated, contrast-enhanced lesion arising from the obex, without hydrocephalus, associated with demographic features such as young age, female sex, and Asian heritage, should evoke a high level of suspicion for this diagnosis. Gross total resection must not be attempted, because this tumor is potentially curable with high-dose radiotherapy.

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KEYWORDS germinoma; medulla oblongata; fourth ventricle; South America

Primary intracranial germinomas are unusual tumors formed by entrapment of migrating totipotent cells during the early period of rostral neural tube development and account for 0.5%–2% of primary intracranial neoplasms,¹ usually affecting young Asian patients, commonly in a suprasellar-infundibular or pineal location. Rarely, they may appear near the fourth ventricle, with only a handful of case reports published. Although they may be easily suspected after magnetic resonance imaging (MRI) in more typical locations, they are considered a diagnostic challenge when presenting near the brainstem. Current management is controversial; however, evidence suggests that treatment strategies based on radiotherapy (RT) can achieve over 90% 10-year disease-free and overall survival rates.²

The risks associated with extensive resection for other, more common diagnoses, such as posterior fossa ependymomas or dorsal exophytic brainstem gliomas, may be considerable. Thus, it is essential to recognize their clinicoradiological clues, considering that it is a potentially curable disease. This report is, to our knowledge, the first report of a case affecting the medulla oblongata without any known Asian heritage diagnosed in South America.

Illustrative Case

A previously healthy 33-year-old woman who was a native of Venezuela, without known Asian heritage, presented to the emergency

ABBREVIATIONS AFP = α -fetoprotein; β HCG = β -human chorionic gonadotropin; CH = chemotherapy only; CNS = central nervous system; CS = craniospinal; CSF = cerebrospinal fluid; CT = computed tomography; EKG = electrocardiogram; GCT = germ cell tumor; GTR = gross total resection; MEP = motor evoked potential; MRI = magnetic resonance imaging; PB = primary boost; RT = radiotherapy; SSEP = somatosensory evoked potential; T1WI = T1-weighted imaging; WB = whole-brain; WV = whole ventricular.

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department with a history of progressive cervical pain, left-side weakness, gait instability, hoarseness of voice, 72-hour history of choking, food intolerance, vomiting, and finally syncope. After the patient recovered her consciousness, she was able to recall frequent upper respiratory tract infections in the last two months. She exhibited a severe deglutition disorder, with an absent gag reflex, bitonal voice, multidirectional nystagmus, left facial palsy, spastic quadriparesis, signs of lower motor neuron involvement in the upper extremities, left-side loss of fine touch, and impairment of position sense and vibration. Aspiration pneumonia and electrocardiogram (EKG) rhythm abnormalities were also noted. Computed tomography (CT) scans showed an isodense mass without calcifications located at the lower end of the fourth ventricle and cisterna magna. MRI revealed a homogeneous mass, with slightly low intensity on T1-weighted imaging (T1WI), high-intensity on T2WI, and intense gadolinium enhancement. The lesion seemed to originate from the dorsal aspect of the medulla oblongata, extending from the cervicomedullary junction and obex up to the caudal aspect of the fourth ventricle, which caused severe compression of the medulla oblongata with significant edema extending from the pons to the sixth medullary segment. Cervical syringomyelia and posterior cord high-intensity changes on T2WI were also noted (Fig. 1). The differential diagnosis proposed by the radiology department consisted of dorsal exophytic glioma, ependymoma, and foramen magnum meningioma. The patient's critical clinical presentation was compatible with a severe medulla oblongata compression, and, for this reason, an emergency

neurosurgical decompression was considered mandatory, with a secondary gross total resection (GTR).

Debulking of the tumor was achieved under a midline suboccipital approach, removing the posterior arch of C1 under intraoperative neuromonitoring, including motor evoked potentials (MEPs) and somatosensory evoked potentials (SSEPs). The tumor was pinkish, without clear borders with the brainstem, and not highly vascular. An intraoperative pathological examination was requested, and a nonspecific malignant neoplasia was reported. Considering it was impossible to differentiate the tumor margins from the dorsolateral surface of the lower brainstem, after successful debulking and decompression of the tumor was achieved with only transitory intraoperative monitoring changes, our surgical team reconsidered a partial resection as the safest option (Fig. 2). Later histological examination revealed large polygonal tumor cells with abundant clear cytoplasm, a large vesicular nucleus, and prominent nucleoli. Infiltration of small lymphocytes was observed. The finding of immunohistochemistry for placental alkaline phosphatase, c-kit, and OCT 3/4 was positive, confirming the diagnosis of germinoma (Fig. 3). Serum and cerebrospinal fluid (CSF) α -fetoprotein (AFP) and β -human chorionic gonadotropin (β HCG) levels were unremarkable. Thoracic and abdominopelvic CT scans and pelvic MRI discarded any extracranial origin; therefore, the diagnosis of primary central nervous system (CNS) germinoma was made. The neuro-oncological committee decided to save chemotherapy for a potential relapse or in case of metastatic spreading of the disease.

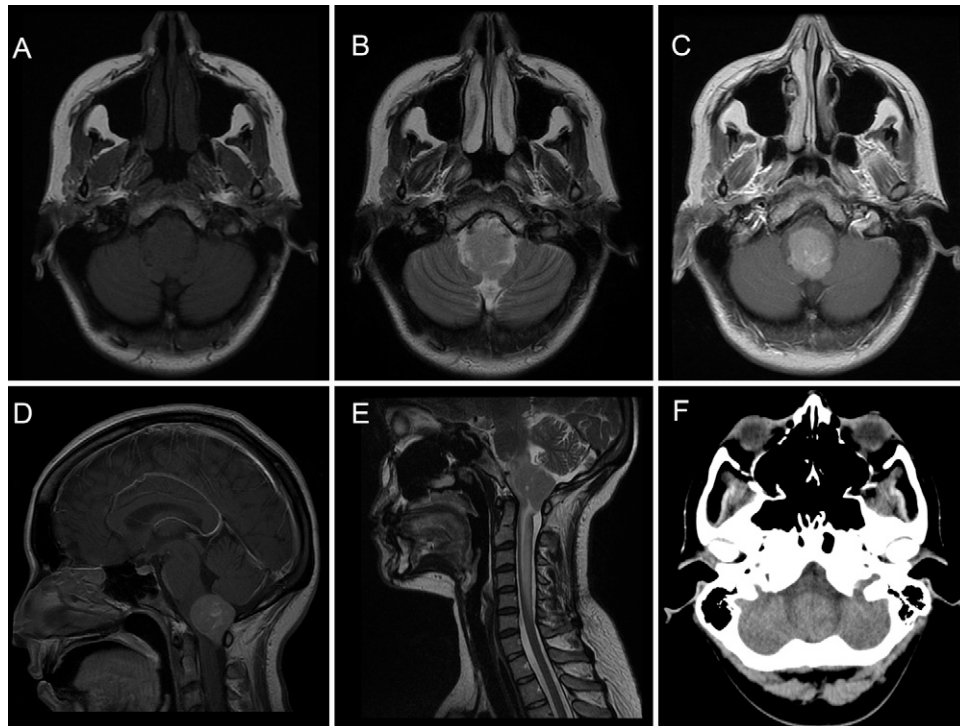


FIG. 1. Preoperative imaging. Axial MRI slices at the level of the medulla oblongata show a well-defined exophytic T1-isointense and T2-hyperintense dorsal medullary tumor in noncontrast T1WI (A), T2WI (B), and gadolinium-enhanced T1WI (C), on which homogeneous and intense enhancement was evident. Midsagittal gadolinium-enhanced T1WI (D) shows a large, 3.6 × 3 × 3-cm lesion with severe brainstem compression, arising from the obex, extending from the lower half of the fourth ventricle floor to C1. Midsagittal cervical T2WI (E) shows severe edema affecting the brainstem and cervical spinal cord, without hydrocephalus. Axial noncontrast CT (F) was without evidence of calcifications.

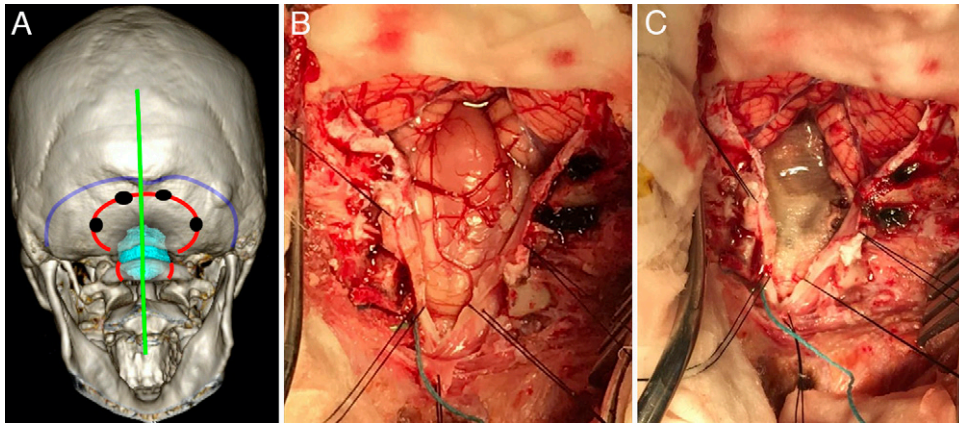


FIG. 2. Intraoperative images. **A:** Three-dimensional volumetric reconstruction of the lesion and surgical planning. **B:** Photograph showing the surgical field after a suboccipital approach with removal of the posterior arch of C1. The tumor was pinkish, without clear borders with the brainstem, and not highly vascular. **C:** Photograph showing the tumor remnant after partial debulking, following definition of functional limits under electrophysiological monitoring.

Consequently, the patient received whole-ventricular volumetric modulated arc therapy (23.4 Gy) with a tumor bed boost (45 Gy total). Six months after the surgery, the patient recovered from her lower cranial nerve impairment, facial palsy, and nystagmus. Her quadriplegia and upper extremity lower motor neuron involvement significantly improved. No more upper respiratory tract infections or EKG abnormalities were experienced. She maintained a severe proprioceptive disorder and a mild left-side loss of fine touch, consistent with a posterior cord spine syndrome or medial lemniscus injury, under rehabilitation at the time of manuscript writing. The patient did not experience any further neurological complications. MRI showed a complete remission (Fig. 4).

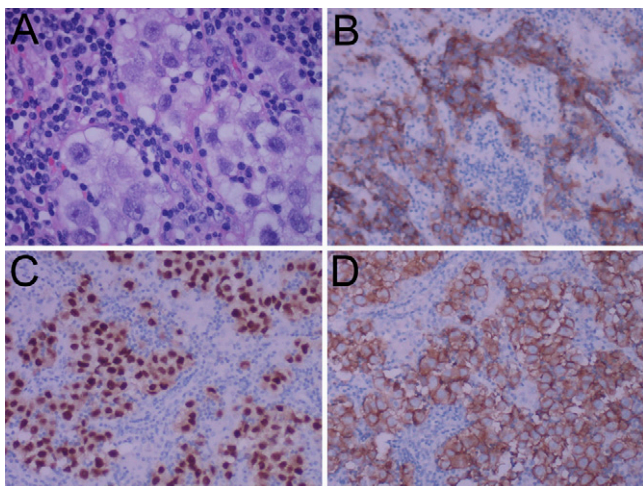


FIG. 3. Pathological examination. Hematoxylin and eosin–stained paraffin section (**A**) shows large polygonal tumor cells with abundant clear cytoplasm, large vesicular nucleus, and prominent nucleoli. Infiltration of small lymphocytes was also seen. Immunohistochemistry for placental alkaline phosphatase (**B**), OCT 3/4 (**C**), and c-kit (**D**) was positive, confirming the diagnosis of germinoma. Original magnification, $\times 40$.

Literature Review

We conducted a search in PubMed for all articles containing the terms “medulla oblongata/medullary,” “germinoma,” “brainstem,” and “fourth ventricle/ventricular” in the title or abstract. The search yielded 26 results, which were assessed for inclusion. References for each article were checked for additional publications that were of potential relevance to our review. Two investigators independently screened each article. Eighteen studies totaling 21 patients, including single-patient information for primary CNS germinoma of the medulla oblongata, were included in the review. Details are summarized in Table 1.

Discussion

Observations

Primary CNS germinomas are tumors derived from totipotent germ cells and amount to up to two-thirds of CNS germ cell tumors (GCTs).³ They are usually found in children and young adults and represent between 0.5% and 2% of primary intracranial neoplasms.¹ As a group, they present between 10 and 12 years of age, with a higher incidence in East Asian populations, and are more commonly diagnosed in males, with a male-to-female ratio of 1.88:1.⁴ Germinomas arise predominantly from midline structures, and the vast majority have a suprasellar-infundibular (49%) or pineal location (37%).⁵ Less frequently, they may appear in the third ventricle, basal ganglia, thalamus, lateral ventricle, or the medulla oblongata. An association between location and sex has been described; 75% of females are more likely to have suprasellar tumors, and 67% of males present with tumors in pineal locations.⁴ An entrapment of migrating totipotent cells during the early period of rostral neural tube development has been proposed as the presumed primary pathological mechanism. The delayed closure of the anterior neuropore in females in comparison with males may explain their sex-specific differences.⁶

Clinical presentation will depend on the location and size of the lesion. Suprasellar tumors usually present with a long history of polydipsia, polyuria, pituitary dysfunction, and visual impairment, whereas pineal lesions usually have a short history of progressive headache, vomiting, and Parinaud syndrome, secondary to hydrocephalus after mesencephalic aqueduct blockage. Basal ganglia

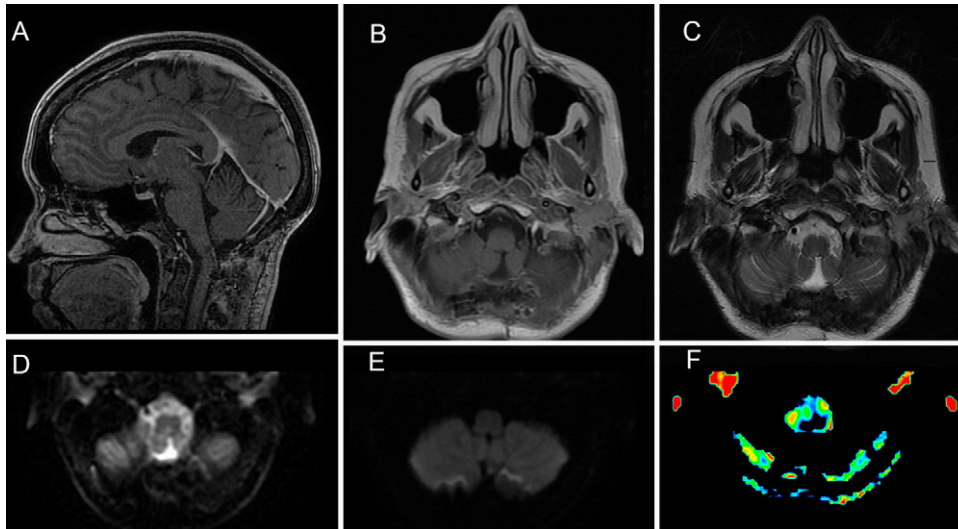


FIG. 4. Postoperative imaging. **A:** Sagittal gadolinium-enhanced T1WI. **B:** Axial image. **C:** Axial T2WI. No signs of a tumor remnant were observed. The cisterna magna reappeared, and no hydrocephalus was noted. Significant regression of the previously seen edema was also noted. **D:** Axial apparent diffusion coefficient map. **E:** Axial diffusion-weighted imaging. **F:** Arterial spin labeling MRI perfusion. Cerebral blood flow on an axial cut at the level of the lower brainstem. No signs of brainstem ischemia were noted.

and thalamic locations, although rare, often manifest with hemiparesis, dyskinesia, and involuntary movement disorders.⁷

Primary germinomas of the medulla oblongata were first described by Hashimoto in a young Japanese male with Klinefelter syndrome in 1992.⁸ Since then, only 22 cases, including the present case, have been published (Table 1).^{6,9–24} According to our review, the mean age of presentation was 23 years, older than in patients with germinomas arising from more common locations.⁴ Like suprasellar lesions, a strong sex bias appears with a female-to-male ratio of 2.14:1. Most cases (77.3%) originated in East Asia or were reported by East Asian authors, also following the trend observed in germinoma patients in general. Only two cases have been described previously on the American continent,¹⁶ and, to our knowledge, ours represents the first from South America. The clinical presentation of this group usually includes headaches, lower cranial nerve dysfunction, and motor or cerebellar signs. As expected for medullary lesions, impairment of the cardiovascular and respiratory centers could manifest as sleep apnea, EKG rhythm abnormalities, and syncope.

On MRI, a well-delineated ovoid or lobulated soft tissue mass was observed arising from the obex, extending cranially to the fourth ventricle floor. A heterogeneous lesion with a cystic component was observed in 52.4% of the cases. Their usual appearance included a low or isointense signal on T1WI and high intensity on T2WI. All cases exhibited vivid and well-delineated gadolinium enhancement. Interestingly, even though these tumors may appear to compress the Luschka and Magendie foramina, the presence of hydrocephalus was exceptional, only observed in one case (5%).

Except for Asian heritage, our case followed the same characteristics of the cohort. A young female presenting with signs of brainstem involvement, with a well-delineated, contrast-enhanced tumor located at the obex, causing severe compression of the medulla oblongata and cisterna magna, without hydrocephalus, may well be considered as a clinical vignette representative of this entity.

Infratentorial ependymomas and dorsal medullary exophytic gliomas represent the most recognized differential diagnoses of posterior midline intraaxial tumors at this location. Ependymomas are among the most common CNS neoplasms affecting children, 70% of the cases appearing in the posterior fossa (mean age, 6 years).²⁵ Although rare in adults, accounting for only 3%–5% of all intracranial tumors, 50% of those will be located at the posterior fossa.²⁶ Some authors have proposed that ependymomas arising near the obex that displace the brainstem anteriorly can be classified as midfloor-type tumors, whereas those displacing the brainstem laterally and sparing the obex can be considered lateral-type tumors.²⁷ This classification may be associated with prognostic and treatment factors currently under study.²⁸ Their appearance varies, ranging from solid masses to cystic components, usually enhancing heterogeneously after gadolinium injection, with calcifications being common. A highly suggestive finding is the extension through the Luschka, Magendie, or magnum foramina, such as a plaster cast, despite the fact that this can also be seen in medulloblastomas.²⁹ Reduced diffusion may be present, reflecting higher cellularity, as seen in other types of neoplasms.³⁰ This aspect, however, was not described for any of the medullary germinomas analyzed in Table 1. Also, unlike for germinomas, hydrocephalus is common with posterior fossa ependymomas.²⁹

Dorsal exophytic medullary gliomas are an uncommon group of brainstem gliomas that also frequently affect children, although they can appear at any age. Their most common histology includes pilocytic astrocytoma; fibrillary diffuse astrocytoma;³¹ and, less likely and usually in older patients, anaplastic astrocytoma and glioblastoma. On MRI, they generally present as heterogeneous masses, and, unlike primary germinomas, they are not well defined from normal parenchyma having a dorsal exophytic component protruding into the fourth ventricle. Thickening and cystic changes of the brainstem can be observed.³² For posterior fossa ependymomas and dorsal exophytic medullary gliomas, surgery aiming to achieve GTR or subtotal resection under functional limits (in the case of

TABLE 1. Literature review and presented case

Case No.	Authors & Year	Age (yrs)/ Sex	Origin/ Ethnicity*	Clinical Presentation	Hydrocephalus	MRI Features	MRI Contrast Enhancement	Histology	Treatment	Outcome	FU
1	Hashimoto et al., 1992 ⁸	19/M	Japan	Klinefelter syndrome, CN IX, X paresis, apnea	No	Low T1WI	Y	Germinoma	Biopsy, CS RT	CR	2 mos
2	Tashiro et al., 1993 ⁹	30/F	Japan	Amenorrhea, galactorrhea, CN V, VI, IX, XII paresis	No	High T1WI	Y	Germinoma	Biopsy, CH, FB RT	CR	14 mos
3	Sugiyama et al., 1994 ¹⁰	32/F	Japan	CN VII, IX, XI, XII paresis, ataxia	No	No MRI	n.d.	Germinoma w/ STGC	Partial resection, CS RT	CR	9 yrs
4	Nakajima et al., 2000 ⁶	18/F	Japan	Hiccups, nystagmus	No	n.d.	Y	Germinoma	Partial resection, CH, GKS	CR	8 mos
5	Yoshida et al., 2003 ¹¹	33/F	Japan	CN V, VI, VII paresis	No	Iso T1WI, high T2WI	Y	Germinoma	STR, CH	CR	7 mos
6	Yen et al., 2003 ¹²	16/F	Taiwan	HA, ataxia	Yes	Iso T1WI, high T2WI, cystic	Y	Germinoma	STR, CS RT	CR	7 yrs
7	Kakani et al., 2006 ¹³	16/F	India	Tuberculosis, CN IX, XII, ataxia	No	Low T1WI, high T2WI, cystic	Y	Germinoma	STR	Died (cardiac arrest)	12 days
8	Yang et al., 2009 ¹⁴	12/M	Australia	CN IX, X, XII paresis, lethargy	No	Cystic	Y	Germinoma	Partial resection, CH, RT(?)	CR	6 mos
9	Akimoto et al., 2009 ¹²	30/F	Japan	CN VI, IX, X, XII paresis	No	Low T1WI, high T2WI, cystic	Y	Germinoma	STR, CH, FB RT	CR	15 mos
10	Akimoto et al., 2009 ¹⁵	24/M	Japan	HA	No	Iso T1WI, high T2WI	Y	Germinoma	Partial resection, CH	CR	10 mos
11	Madden et al., 2009 ¹⁶	12/M	USA	Pneumonia, apnea	No	n.d.	Y	Germinoma	STR, CH, FB + CS RT	CR, ventilator dependent	12 mos
12	Madden et al., 2009 ¹⁶	21/M	USA	Pneumonia, apnea, vomiting, headaches	No	n.d.	Y	Teratoma w/ germinoma & embryonal carcinoma elements	GTR, CH, WB + PB RT	CR (died: respiratory failure)	3.5 yrs
13	Neelima et al., 2010 ¹⁷	24/F	India	HA, CN VII, IX, XII paresis, bilat papilledema, cerebellar signs, ataxia	No	Low T1WI, cystic	Y	Germinoma	GTR	n.d.	n.d.
14	Yasuhara et al., 2011 ¹⁸	27/F	Japan	CN VIII, IX, X, XII paresis, ataxia, apnea, sensory deficit	No	Iso T1WI, high T2WI, cystic	Y	Germinoma	Biopsy, CH, WV + PB RT	CR	6 mos
15	Shuto et al., 2012 ¹⁹	28/M	Japan	Ataxia	No	Low T1WI, high T2WI, cystic	Y	Germinoma	STR, CH, FB + CS RT	CR	3 yrs

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TABLE 1. Literature review and presented case

Case No.	Authors & Year	Age (yrs)/ Sex	Origin/ Ethnicity*	Clinical Presentation	Hydrocephalus	MRI Features	MRI Contrast Enhancement	Histology	Treatment	Outcome	FU
16	Nakatsuka et al., 2012 ²⁰	31/F	Japan	Hiccups, CN IX, X, XII paresis	No	Iso T1WI, iso T2WI	Y	Germinoma	STR, CH, WV + PB RT	CR	6 mos
17	Hao et al., 2013 ²¹	14/M	China	CN VII, VIII, IX paresis, nystagmus	No	Low T1WI, high T2WI, cystic	Y	Germinoma	STR, GKS, CH	CR	4.5 yrs
18	Hao et al., 2013 ²¹	22/F	China	CN IX, XI paresis, nystagmus, sensory deficit	No	Low T1WI, cystic	Y	Germinoma	GKS, STR	Died (pneumonia)	8 mos
19	Khan et al., 2013 ²²	25/F	UK (Afro-Caribbean)	HA, ataxia, EKG rhythm abnormalities	No	n.d.	Y	Germinoma	Partial resection, FB + CS RT	CR	10 mos
20	Yip et al., 2014 ²³	22/F	Taiwan	HA, CN IX, XI, XII paresis, nystagmus	No	Cystic	Y	Germinoma	GTR, WV + PB + CS RT	CR	12 mos
21	Budohoski et al., 2015 ²⁴	23/F	UK	CN IX, XI, XII paresis, ataxia, hemiparesis	No	High T2WI, cystic	Y	Germinoma	GTR, WB + WS RT	CR	12 mos
22	Present study, 2022	33/F	Chile	Pneumonia, EKG rhythm abnormalities, CN VII, IX, X, XII paresis, nystagmus, quadraparesis, sensory deficit	No	Low T1WI, high T2WI	Y	Germinoma	Partial resection, WV + PB RT	CR	6 mos

CH = chemotherapy; CN = cranial nerve; CR = complete response; CS = craniospinal; EKG = electrocardiogram; FB = focal brain; FU = follow-up; GKS = Gamma Knife surgery; GTR = gross total resection; HA = headache; iso = isointense; n.d. = not disclosed; PB = primary boost; RT = radiotherapy; STGC = syncytiotrophoblastic giant cells; STR = subtotal resection; T1WI = T1-weighted imaging; T2WI = T2-weighted imaging; WB = whole brain; WV = whole ventricular.

* Origin of the study and ethnicity of the patient.

medullary gliomas) is considered the treatment of choice; nevertheless, this is usually not feasible when the tumor infiltrates inside the brainstem. Unlike germinomas, the extent of resection plays a significant role in these patients' survival.²⁹

Germinomas, unlike other GCTs, do not necessarily elevate any blood or CSF tumor markers. Pure germinomas should always have normal AFP levels in serum and CSF, although they may have low levels of β HCG. In the absence of oncoprotein elevations, the standard of care when primary germinomas are suspected is surgical confirmation of tumor histology, with perhaps the only exception being patients with bifocal or multifocal lesions, in whom radiological findings are considered pathognomonic.⁵

Theoretically, these tumors have the potential for malignant behavior and can infiltrate brain tissue and metastasize through the ventricular system. Yet, they usually have a great response to RT and systemic chemotherapy. To date, there is no accepted standard treatment algorithm for these patients. According to their rarity, only a few prospective randomized trials have been published, none for this particular location. Several different strategies have been tried, including RT-only, chemotherapy-only (CH), and multimodality regimens, as the various case reports gathered here illustrate (Table 1), leaving optimal treatment often to be decided by professional consensus.²

RT is considered the primary treatment and, as a single strategy, can achieve overall survival rates of more than 90% at 10 years.³³ According to the theoretical risk of CSF spreading, whole ventricular (WV), whole-brain (WB), and craniospinal (CS) RT have shown superior 5- and 10-year progression-free survival rates when compared with patients treated with local field RT.^{34,35} It was proposed that for localized lesions, the risk of spinal relapse did not differ significantly between WVRT + primary boost (PB) or WBRT + PB and those treated with CSRT.³⁶ For this reason, some experts suggest that WVRT + PB should be the treatment of choice for nonmetastatic localized germinomas, such as our case. CH regimens were introduced in the 1990s but by themselves were unable to cure the disease, despite their marked initial responses. CH followed by low-dose focal RT was introduced in the early 2000s, following the rationale that a reduced RT volume and dose could reduce unwanted side effects of radiation, a particular concern in younger patients. Initially, this approach achieved results similar to those for higher doses of RT,³⁷ still, longer follow-up eventually showed higher recurrence rates along the ventricles, suggesting that CH could not eradicate microscopic disease outside the RT field.² Chemoradiotherapy combinations, with or without autologous stem cell rescue, can also be used after relapse or initially in metastatic or disseminated disease³⁸ and, in patients with a bifocal disease without evidence of dissemination, as an alternative to CSRT.³⁹

The most extensive single-institution study to date, aiming to find the optimal management for this disease, included 213 patients treated with all the modalities mentioned before, between 1971 and 2017.² After a median follow-up of 141 months, the 10-year disease-free and overall survival rates were 91.6% and 95.6%, respectively, confirming the excellent prognosis overall presumed in earlier studies. Notably, all patients treated with a CH-only regimen had recurrences, and, in contrast, recurrence rates were similar for patients treated with RT only and RT + CH: 6.6% and 5.5%, respectively. In the subgroup treated with WV/WB RT, rates were lower, reaching 5.9%, making the authors question the alleged additional benefit of CH. CH has its own set of adverse effects, some related to toxicity, longer treatment duration, and higher expense.⁴⁰ New trends such as de-escalation RT doses are being tested, although this topic is still controversial.

Surgery inside or around the brainstem is among the most challenging procedures for neurosurgeons, requiring an unconditional understanding of the microsurgical and functional neuroanatomy. The systematic use of intraoperative neuromonitoring during brainstem surgery is expected to reduce iatrogenic damage to critical neural structures and to increase the likelihood of successful surgical outcomes. SSEPs and brainstem auditory evoked potentials were classically used in the past, despite being able to functionally evaluate less than 20% of brainstem areas.⁴¹ The addition of MEPs, cranial nerve motor nuclei mapping, and intraoperative testing of brainstem reflexes further facilitates safer tumor resections, particularly when surface landmark anatomy is distorted. Real-time assessment of the integrity of the corticospinal and corticobulbar tract recording MEPs from limb and cranial innervated muscles elicited by transcranial electrical stimulation is considered a must according to the modern surgical standard. Monitoring medial lemniscus integrity can be achieved through upper limb SSEPs because the ascending arm and leg fibers are packed together in the medial lemniscus. Regardless, this technique may be more helpful in documenting but not preventing surgically induced neurological injury.⁴² On the one hand, conscious proprioceptive information travels along the spine's posterior column up through the medial lemniscus in the medulla oblongata, making it possible to test using SSEPs. On the other hand, unconscious proprioception, which travels along the different ascending spinocerebellar tracts, has no specific test.

Even under current standards, the iatrogenic risk associated with surgical procedures of the brainstem remains. Attempting a complete resection of a midline dorsal cervicomedullary tumor, rather than a more conservative approach, such as intraoperative and/or definitive biopsy first, may put these young patients at unnecessary risk. Germinomas should probably be discarded in some instances before assuming that a more common diagnosis, such as a dorsal exophytic medullary glioma or ependymoma, is indeed the definitive histology. For our case, neither the radiology team nor the neurosurgical team suspected this diagnosis before histological confirmation. Moreover, the patient presented severe brainstem compression symptoms, which determined that surgical decompression was needed. Because (to our knowledge) no such cases were previously described in South America, our team was unfamiliar with this entity; besides, the intraoperative biopsy was unable to convey the specific diagnosis, only reporting the presence of a nonspecific malignant neoplasia. In this regard, intraoperative pathological consultation for this context usually consists of frozen section and crush smear analysis, which, in broader terms, yield a high level of accuracy in CNS tumors. However, both techniques have limitations with errors and pitfalls that physicians should be aware of.⁴³ For CNS germinomas, intraoperative diagnosis is usually straightforward. However, their classic morphology may not be present, and cases mimicking carcinoma, gliosis, and granulomatous reaction have been published.^{44,45} Furthermore, the biopsy sample from this location could be small, making immunohistochemistry necessary.

After current evidence and patient preference were taken into account, our neuro-oncological committee chose a WVRT + PB without CH approach. At the time of preparing the manuscript, a complete response had been obtained, as expected, without adverse radiation side effects. It is unclear if the remaining proprioceptive deficit was caused by tumor compression of the medial lemniscus, by the syringomyelia and edema of the posterior cervical

spinal cord, or by surgical manipulation at the level of the obex and inferior cerebellar peduncles. The latter seems unlikely, especially because no persistent SSEP abnormalities were noted, and no ischemic changes were observed in postoperative MRI (Fig. 4). Diagnostic efforts should be made to ensure that this rare but noticeable clinicoradiological pattern is not ignored. Neurosurgeons and radiologists should incorporate this entity as part of their differential diagnosis, regardless of their country of origin, limiting the extent of unnecessary resection to histological confirmation only and increasing the likelihood of a successful recovery in a potentially curable disease.

Lessons

We report the first South American patient with a primary CNS germinoma arising from the medulla oblongata. Our patient is the 22nd case reported to date. In the absence of elevated tumor markers, radiological clues such as the presence of a well-delineated, contrast-enhanced, exophytic lesion arising from the obex, without hydrocephalus, in association with demographic features such as young age, female sex, and Asian heritage, should evoke a high level of suspicion. GTR must not be attempted, because this tumor is potentially curable with high-dose RT or chemoradiotherapy.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Albiña, Solis, Lorenzoni. Acquisition of data: Albiña, Solis. Analysis and interpretation of data: Lorenzoni, Henny, Manriquez. Drafting the article: Albiña, Solis. Critically revising the article: Albiña, Lorenzoni, Henny. Reviewed submitted version of manuscript: Albiña, Lorenzoni, Henny, Manriquez. Approved the final version of the manuscript on behalf of all authors: Albiña. Administrative/technical/material support: Manriquez. Study supervision: Albiña, Lorenzoni. Photographs and pathologic diagnosis: Manriquez.

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