

# Cervicomedullary Junction Ependymoma Associated with Neurofibromatosis Type II: Case Report and Literature Review

## *Ependimoma da junção cervicobulbar associado a Neurofibromatose tipo II: relato de caso e revisão de literatura*

Otávio Turolo da Silva<sup>1</sup> Carlos Eduardo Vasconcelos Miranda<sup>1</sup> Andrei Fernandes Joaquim<sup>2</sup>  
Luciano de Souza Queiroz<sup>3</sup> Enrico Ghizoni<sup>4</sup> Helder Tedeschi<sup>4</sup>

<sup>1</sup>Neurosurgery Resident, Neurology Department, Universidade Estadual de Campinas (Unicamp), Campinas, SP, Brazil

<sup>2</sup>Neurosurgery Assistant, Neurology Department, Unicamp, Campinas, SP, Brazil

<sup>3</sup>Professor of Pathology, Pathology Department, Unicamp, Campinas, SP, Brazil

<sup>4</sup>Professor of Neurosurgery, Neurology Department, Unicamp, Campinas, SP, Brazil

Address for correspondence Otávio Turolo da Silva, MD, Universidade Estadual de Campinas, R. Tessália Vieira de Camargo, 126, Dpto Neurologia, Cidade Universitária, Campinas, SP, Brazil 13083-887 (e-mail: turolo@gmail.com).

Arq Bras Neurocir 2017;36:54–57.

### Abstract

#### Keywords

- neurofibromatosis type II
- ependymoma
- surgery

### Resumo

#### Palavras-chave

- neurofibromatose tipo II
- ependimoma
- cirurgia

Neurofibromatosis type II (NF2) is a rare autosomal dominant inherited disease caused by a mutation in chromosome 22q12 and associated with multiple central nervous system tumors. In this paper, we describe a rare case of cervicomedullary junction ependymoma associated with NF2 in a 25-year-old man who underwent surgical treatment with total resection and had a good clinical outcome. We discussed the nuances of the surgical resection and the literature concerning this rare form of presentation of NF2.

Neurofibromatose tipo II (NF2) é uma doença autossômica dominante provocada por uma mutação no cromossomo 22q12, e que está relacionada ao surgimento de múltiplos tumores do sistema nervoso central. Neste artigo, é descrito um caso raro de um paciente com 25 anos de idade submetido ao tratamento cirúrgico de um ependimoma da junção cervicobulbar, com ressecção total “en bloc” e bom resultado clínico. Discutimos as nuances da ressecção cirúrgica, bem como a literatura sobre o tratamento destas lesões raras.

## Introduction

Neurofibromatosis type II (NF2), also known as multiple inherited schwannomas, meningiomas and ependymomas (MISME), is a genetic autosomal dominant disease characterized by a mutation in the 22q12 chromosome that causes

the inactivation of the moesin-ezrin-radixin-like-protein (merlin protein), a tumor suppression peptide.<sup>1,2</sup>

Despite the name, NF2 is less associated with neurofibromas than neurofibromatosis type I (NF1). Neurofibromatosis type II has two typical clinical presentations: 1) a

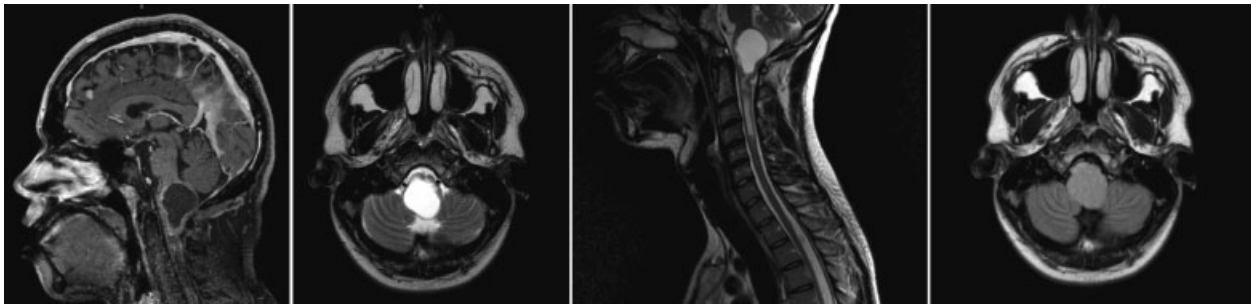
received  
October 10, 2016  
accepted  
November 9, 2016  
published online  
December 30, 2016

DOI <http://dx.doi.org/10.1055/s-0036-1597574>.  
ISSN 0103-5355.

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**Fig. 1** Pre-operative imaging (A) – Sagittal T1-weighted sequence, showing an intramedullary tumor, with marginal gadolinium enhancement. (B) – Axial T2-weighted sequence, suggesting a cystic lesion. (C) – Sagittal T2-weighted sequence, with a hyperintense lesion and a caudal syringomyelia. (D) – Axial T2-weighted fluid-attenuated inversion recovery imaging (FLAIR) with a hyperintense signal lesion in the medulla.

severe form, also known as Wishart type, which presents in younger adults and is characterized by rapid auditory impairment and multiple intracranial tumors (with different histologies); and 2) a less aggressive form, known as Gardner type, without a slow decrease in auditory function and more indolent tumor growth.<sup>3,4</sup>

Diagnosis is based on specific genetic evaluation,<sup>5</sup> but clinical criteria (the Manchester Criteria) have been proposed<sup>6</sup>

- 1) the presence of bilateral vestibular schwannoma on radiological exams;
- 2) unilateral vestibular schwannoma in a patient younger than 30 with a first-degree relative with NF2;
- 3) the presence of two of these conditions: meningioma, schwannoma, glioma or posterior lens opacity.

In this paper, we report the case of a 25-year-old patient with a severe clinical presentation of NF2, with multiple intracranial tumors. We discuss the nuances in the treatment and the surgical technique used for resecting an extensive cervicomedullary junction ependymoma.

## Presentation

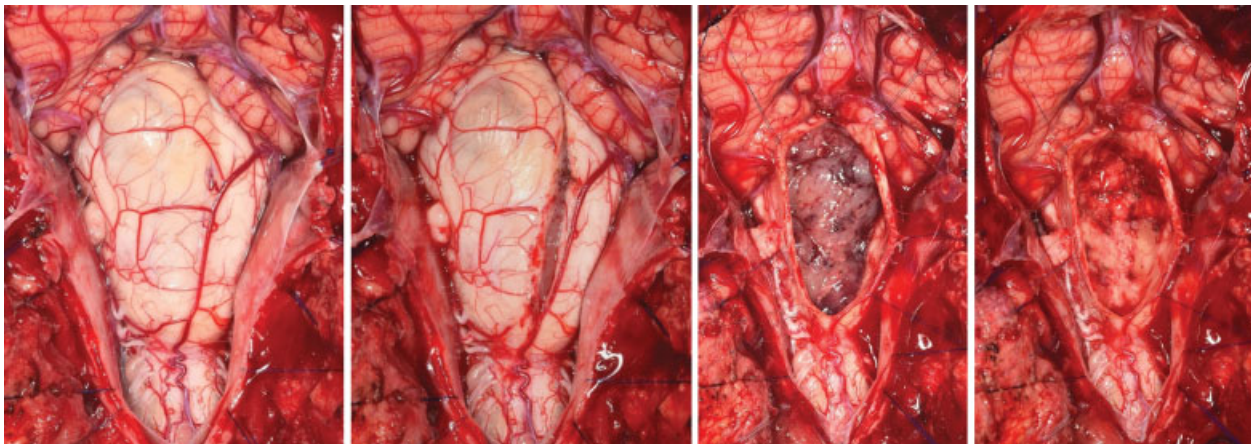
A 25-year-old man presented with a two-month history of progressive dysphagia and dysphonia, requiring a nasal tube

for feeding. He also had seizures controlled with anti-epileptic drugs that had started one year before, and complained of auditory loss on his left side.

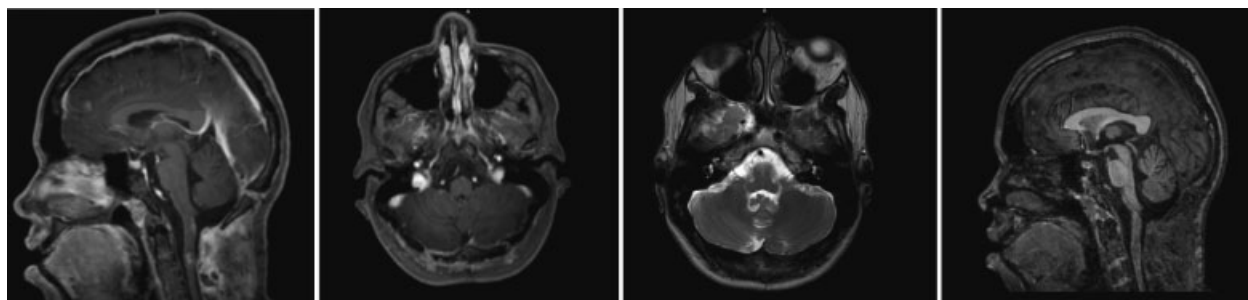
On clinical examination, he had proptosis in his left eye and severe tetraparesis (grade 4), unable to walk without assistance. There was also absence of vomiting reflex and left side dysmetria. An audiometry reported moderate to severe neuro-sensorial loss between 250 to 6k Hz in his left ear.

An MRI was performed and a tumor was visualized in his cervicomedullary junction – it was radiologically characterized by hyperintense signal changes in the T2 sequence and by hypointense signal changes in the T1 sequence, with evident gadolinium enhancement in its external portions (►Fig. 1). Additionally, other lesions suggestive of multiple tumors were diagnosed: an intradural extramedullary enhancement injury in the lumbar spine, bilateral acoustic schwannomas, a right III cranial nerve tumor and, finally, multiple meningiomas (related to the II cranial nerve, the temporal lobe, the anterior clinoid process, and the frontoparietal lobe), all on the left side.

We decided to operate the cervicomedullary tumor because of the severity of the dysphagia and the tetraparesis. Under general anesthesia, the patient was positioned on a “Concorde” position, under electrophysiological monitoring. A midline suboccipital craniotomy was performed, and the dura mater was opened in a standard fashion (►Fig. 2). A



**Fig. 2** (A) – Intra-operative view, after dural opening and neural exposure. (B) – Posterior myelotomy was performed in midline that was slightly displaced to the right side. (C) – A solid tumor could be clearly differentiated from the neural tissue. (D) – Final aspect of the surgical site inside the medulla after tumor removal.



**Fig. 3** Post-operative MRI. (A, B) – Sagittal and axial gadolinium-enhanced T1-weighted imaging, showing no gadolinium-enhanced areas in the surgical site. T2-weighted axial (C) and sagittal (D) imaging with no evidence of residual tumor.

posterior midline upper cervical myelotomy was performed, and we could observe a distinct surface from the tumor and the neural tissue. An “en bloc” resection was performed by the senior author (HT). During the resection of the anterior portion, motor potentials decreased by 80%. Warm saline irrigation was performed, in order to postpone the manipulation until recovery of the basal motor potential. The resection was then performed successfully. After surgery, the patient woke up well, and three days after the procedure he was able to eat and had partial recovery of his muscular strength. After six months, during his outpatient follow-up, he had full motor strength recovery. A post-operative MRI showed complete resection of the lesion. (→ **Fig. 3**)

Histological findings from the hematoxylin-eosin staining revealed a moderated cellular glioma with a regular round nucleus and imprecise cytoplasm edges. Perivascular pseudorosettes, characterizing an ependymoma, were also evident. There were also enucleated halos of longed cytoplasm surrounding radial vascular structures. These zones are rich in glial fibrillary acidic protein (GFAP) (→ **Fig. 4**).

## Discussion

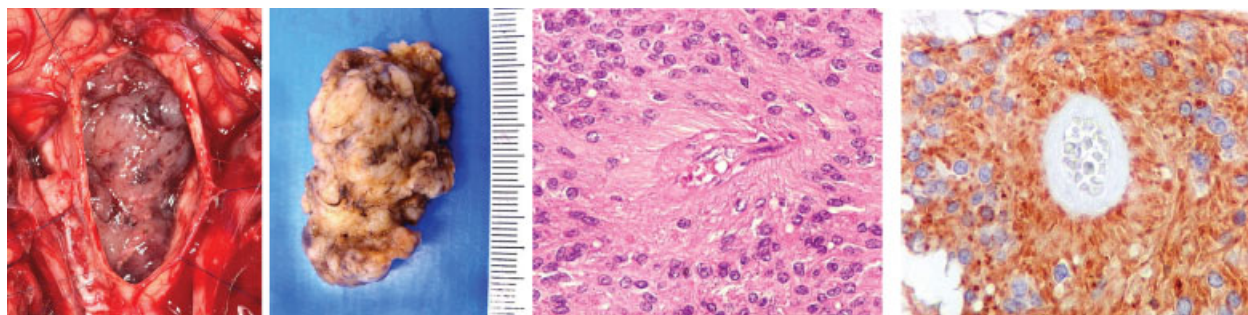
Bilateral vestibular schwannomas were first reported more than 200 years ago by Wishart, but only in 1986 a genetic source was proposed that differentiated NF2 from NF1.<sup>3</sup> Neurofibromatosis type II is a rare genetic syndrome that occurs in 1 to 40 thousand newborns. Schwannomas and meningiomas are the most common tumors found in patients with NF2, followed by gliomas, which are less common

and generally found in the spinal canal. In NF2, ~ 65% of gliomas correspond to ependymomas, and only 10% are in the medullary region.<sup>7,8</sup>

The treatment for gliomas associated with NF2 has been debated, because of the rarity of these lesions and their weak response to chemotherapy/radiation. Therefore, an individualized approach is recommended. There are few reports of ependymomas associated with NF2, and most of them suggest low-grade (I and II) tumors, generally the presentation trend is multiple tumors.<sup>9</sup>

One of the major literature series was published by Plotkin et al,<sup>10</sup> who reported 55 cases of ependymomas associated with NF2. In their series, 58.2% of cases had multiple ependymomas, with predilection to cervicomedullary junction and cervical spine in 85.7%. Surgical treatment was proposed for 13 patients who had symptomatic lesions, and, out of those patients, 7 had cystic changes observed on the MRI. They only achieved complete resection in 4 patients. In the final follow-up, they did not report any recurrence or progression of the operated tumors.

Aguilera et al<sup>9</sup> reported two cases of ependymomas in the cervicomedullary junction associated with NF2: one patient underwent a gross total resection of the lesion (a grade II ependymoma) and showed no signs of recurrence during follow-up. As for the other patient, because of the configuration of multiple and small lesions, suggesting a subependymoma, the case was conducted with straight imaging follow-up, and showed no progression during the study period. In their review, the most common sites of NF2-associated ependymomas were the cervicomedullary



**Fig. 4** (A, B) – Comparative intra-operative finding and macroscopic lesion rubber-like. (C) – Presence of perivascular pseudorosettes, which suggest ependymoma. (D) – Glial fibrillary acidic protein (GFAP) area.

junction (43%) and the cervical spine (52%). Gross total resection was performed only in 30% of patients, and, without the association of adjuvant treatments, the overall 5-year survival rate was 100%.

Nowak et al<sup>11</sup> also reported two cases of patients with spinal ependymomas who underwent surgical treatment, with complete resection and histopathological diagnosis of grade II ependymomas. In their study's follow-up period, one patient developed recurrence after three years. Capeda et al<sup>12</sup> reported one case of a patient with spinal tanycytic ependymoma who underwent gross total resection. They also emphasized the rarity of these lesions in NF2, suggesting that the treatment of choice in symptomatic cases was gross total resection, because the ependymomas showed no recurrence even after 9 years of follow-up.

## Conclusion

Symptomatic ependymomas associated with NF2 should be treated surgically. When gross total resection is achieved, only radiological follow-up is recommended.

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