Malignant Schwannoma of the Vagus Nerve

Bernardes Correia *, L. Carriço*, Lélita Santos**, T. Veríssimo**, F. Santos***, M. H. Saldanha de Oliveira****

Abstract

Von Recklinghausen neurofibromatosis (neurofibromatosis type I) is an autosomal dominant disorder that occurs in 1 in 3,000 live births. Malignant degeneration of subcutaneous neurofibroma occurs in about 5 to 10 percent of patients; however, manifestations in the vagus nerve are rare. There are five reported cases of malignant schwannoma of the intrathoracic vagus nerve, only one of which was associated with von Recklinghausen neurofibromatosis. We believe that we present the second reported case of a malignant peripheral nerve sheath tumor involving the vagus nerve in a patient with von Recklinghausen neurofibromatosis.

Key words: neurofibroma, neurofibromatosis type I, von Recklinghausen's disease, vagus nerve, malignant schwannoma.

Introduction

Intrathoracic neurogenic tumors are relatively common, making up 10% to 34% of all mediastinal tumors. They are usually located in the posterior mediastinum, constituting the majority of neoplasms in this location. Normally, they originate from an intercostal nerve or sympathetic chain.[1] However, neurogenic tumors may arise from the vagus nerve or the phrenic nerve in the middle mediastinum, those of the vagus nerve being the most common. Tumors of the vagus that arise from the nerve sheath are called neurofibromas and schwannomas.[1,2] The latter come from the Schwann cells.

With the exception of the first and second pair of cranial nerves, all peripheral nerves have Schwann cells, and are a potential site of schwannomas.[1,3,4]

In 1935, Stout and Carson gave the name "neurilemmoma" to tumors from Schwann cells (schwannomas), and this term is still quite common in the literature.[3,4,5]

Vagal schwannomas are usually benign; they produce few symptoms; they are slow growing, and they rarely cause significant neurological alterations in patients with type 1 neurofibromatosis (NF1), classically known as Von Recklinghausen's disease.[1]

Malignant schwannoma should be suspected when these tumors are symptomatic or when associated with Von Recklinghausen's disease.[6,7,8,9] Malignant schwannomas, together with neurofibrosarcomas, are soft tissue sarcomas and form malignant tumors along the peripheral nerve sheath.[6,7,8,10,12,13]

The diagnosis of these tumors is based on Stout and D'Agostino's criteria, i.e., previous existence of benign schwannoma or neurofibroma, associated with Von Recklinghausen's disease and histological confirmation.[3,12,13,14]

The risk of developing malignant tumors along the peripheral nerve sheath is 4,600 times higher in patients with Von Recklinghausen's disease than in the general population,[5,6] given that 50% to 10% of subcutaneous neurofibromas suffer malignant generescence.[6,7,8,13,14] However, malignant schwannomas originating in the intrathoracic vagus nerve are extremely rare. The location of the tumor, its size, and association with Von Recklinghausen's disease are the most important prognostic factors.[8,10,12,13]

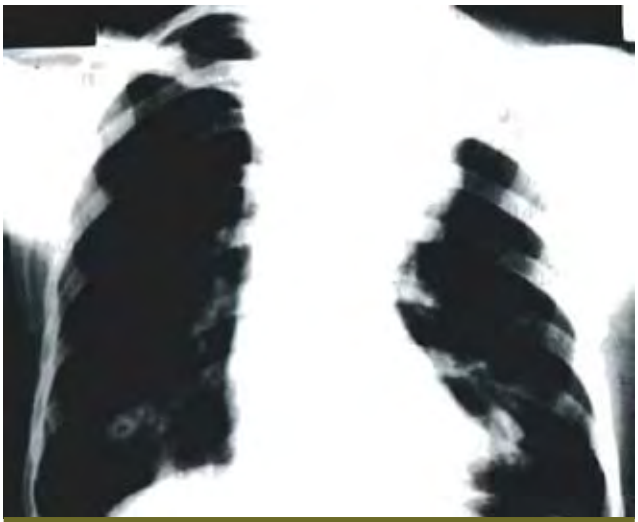
In a literature review using the MEDLINE (Medical Literature Analysis and Retrieval System Online) database of the National Library of Medicine of the USA, searching on works since 1983, we found five reported cases of malignant schwannoma of the vagus, of which only one patient had NF1.[18]

The authors present a rare case of malignant schwannoma of the vagus in a patient with type 1 neurofibromatosis, supported by a literature review.

Clinical case study

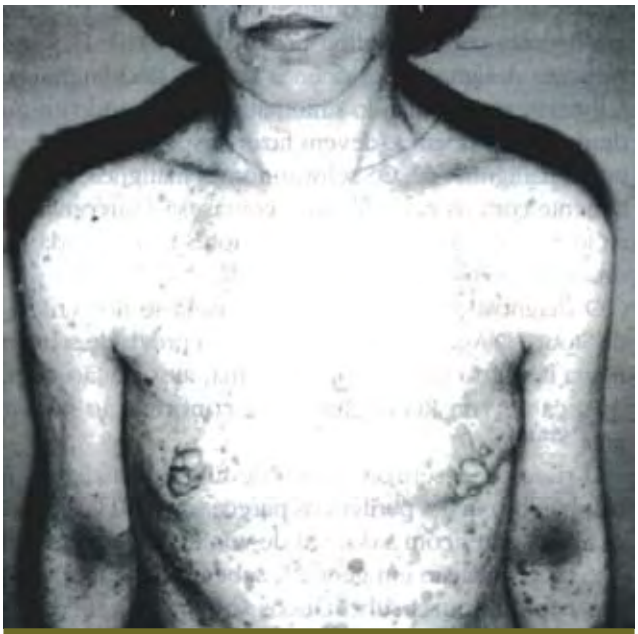
A woman aged 33 years, Caucasian, with type 1 neurofibromatosis, was admitted to the University Hospitals of Coimbra with evolution of the clinical

*Resident to the Internal Medicine Supplementary Internship
**Hospital Assistant in Internal Medicine
***Senior Hospital Assistant in Internal Medicine
****Full Professor of the Faculty of Medicine, University of Coimbra
Medicine Service 1, of the Hospitals of the University of Coimbra (HUC)



Voluminous expansive formation starting in the mediastinum.

FIG. 1



Multiple neurofibromas.

FIG. 2

condition of around two months, characterized by chronic back pain on the left with no irradiation, dry cough, mild fever in the evening and unquantified weight loss.

On admittance, the chest radiograph showed a voluminous expansive formation located in the mediastinum (*Fig. 1*).

The patient did not smoke, had worked as a legal secretary for twelve years, and was active and healthy.

The personal history recorded an excision, at eighteen years of age, of two neurofibromas from the sternal region due to increased size, and also, at twenty-two years of age, the removal of a neurofibroma mass from the left thigh.

There were no cases of neurofibromatosis in the patient's family history.

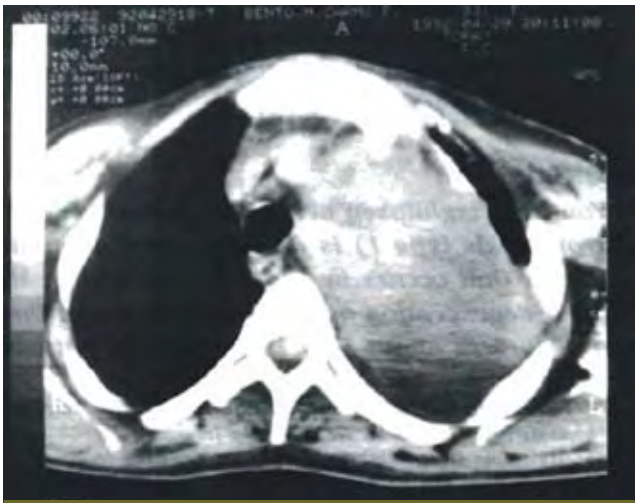
On physical examination, we observed that the patient was slightly malnourished, with a body mass index (BMI) of 18 kg/m^2, presenting multiple neurofibromas on the skin and some coffee-with-milk colored blemishes (*Fig. 2*). She presented no peripheral adenopathies, carotid sounds, or cervical vein distension, and her voice was normal. Cardiopulmonary auscultation was normal, systolic blood pressure was 125 and diastolic pressure was 80 mm Hg. The results of the neurological examination showed no changes.

From the point of view of the laboratory and imaging, sediment velocity of 60 mm/hour and CT scan of the chest and abdomen showing a mass measuring approximately 6.9 x 10.6 cm in the anterosuperior mediastinum (*Fig. 3*) are emphasized. The patient underwent left posterolateral thoracotomy at the level of the 4th intercostal space, followed by excision of a tumor with an elastic consistency, measuring approximately 10 x 10 cm, surrounding the vagus nerve at a location above the recurrent laryngeal nerve. The dissection of the mass of adjacent tissues was relatively straightforward; however, it was not possible to save the vagus nerve. There were no postoperative complications, although the patient had paralysis of the left vocal cord, evidenced by hoarseness and confirmed by laryngoscopy.

The histopathological exam revealed that it was a malignant schwannoma (*Fig. 4*). The patient was subsequently submitted to local radiotherapy, and due to local recurrence and thoracic and abdominal metastases after six months, chemotherapy was started, which proved ineffective. The patient died two months later.

Comments

In the case presented here, the patient was a carrier of von Recklinghausen neurofibromatosis, also



Mediastinal mass - 6.9 x 10.6 cm.

FIG. 3

Malignant Schwannoma: (A) spindle cell lesion with high cellularity, showing areas with lattice pattern. (H.E. x100). (B) Cellular pleomorphism and nuclear hyperchromasia. Some vessels showed hyalinization in their walls (H.E. 320x).

FIG. 4

called "sporadic neurofibromatosis", with no family history of this disease.[17,21,22,23]

Schwannomas tend to occur in younger individuals, and are most often located centrally, particularly in the middle mediastinum.[5,18,19,24] Patients usually show few symptoms, and in the majority of cases, Schwannomas constitute an occasional finding of chest teleradiography. In some cases, patients become hoarse, suggesting tumor involvement in the recurrent laryngeal nerve or vagus nerve in the proximal portion, in relation to its emergence. Chest pain and cough occur in tumors which compress the trachea or major bronchus.[21] These symptoms can develop over months or years until there is a diagnosis, especially in patients with Von Recklinghausen's disease, which is consistent with the slow growth typical of schwannomas.[7,8] In the case described here, the patient reported these symptoms with onset two months earlier. The hoarseness was a post-surgical sequelae, given the close relationship between the tumor and the vagus nerve, in the proximal portion relative to the emergence of the recurrent laryngeal nerve, which meant the nerve could not be saved at the time of surgery.

Neurofibrosarcomas, lymphoma, bronchogenic cyst, aneurysm of a large blood vessel containing intraluminal thrombus, paraganglioma, neuroblastoma, and phaeochromocytoma should be included in the differential diagnosis.[6,22]

Malignant schwannomas generally spread contiguously, distant metastases being uncommon. They tend to be radio-resistant and respond poorly to chemotherapy.[8,24,25,26]

Most authors recommend surgical exploration and excision of the tumor, not only to confirm the nature of the lesion, but also to prevent progressive habitual growth leading to the invasion and compression of adjacent structures.[4,8,8,20,24,25,25]

Aspiration puncture aimed at reaching a conclusive diagnosis is not indicated, due to the usual shortage of material that can be obtained.[8,7,8,20]

The role of adjuvant radiotherapy and chemotherapy remains inconclusive. In the present case, faced with a T4 NO MO staging in the TNM system, the increased dimensions of the mass threatening adjacent structures therefore being relevant, an excision was performed. While in the case of benign schwannomas excision is a curative process, the same thing cannot be said when it is malignant.[8,7,8,,25]

Also in the presence of NF 1 and a tumor larger

than 5 cm, the prognosis becomes significantly worse, and recurrence and metastatization are very common, as demonstrated by the fatal outcome seen in our patient.[7,8,21]

Acknowledgements

The authors acknowledge the ongoing commitment to the histological diagnosis demonstrated by Dr. Helena Garcia, Pathological Anatomy Assistant with the Pathological Anatomy Service of the HUC.

References

1. Holliday AL, Sobel RA, Martuza RL. Martuza RL. Benign spinal nerve sheath tumors: their occurrence sporadically and in neurofibromatosis types 1 and 2. J Neurosurg 1991; 74:248-253.
2. Howard T, Chen T, Weiss MH. Sixth nerve schwannomas. J Neurosurg 1991; 75:638-641.
3. Stout AP, Carson W. The peripheral manifestation of the specific nerve sheath tumor (neurilemoma). Am J Cancer 1935; 24:751-796.
4. Das Grupta TK, Brasfield RD, Strong EW, Hajdu SI. Benign solitary schwannomas (neurilemomas). Cancer 1979;24:355-366.
5. Heitmiller RF, Labs JD, Lipsetl PA. Vagal Schwannoma. Ann Thorac Surg 1990; 50:811-813.
6. Dabir RR, Piccione W, Kittle CF. Intrathoracic Tumors of the Vagus Nerve. Ann Thorac Surg 1990; 50:494-497
7. Ducatman BS, Scheithauer BW, Piepgras DG, Reiman HM, Ilstrup AD. Malignant Peripheral Nerve Sheath Tumors. Cancer 1986;57:2006-2015.
8. Sordillo PP, Helson L, Hadju Sl et al. Malignant Schwannoma – Clinical Characteristics, Survival and Response to Therapy. Cancer 1981; 47:2503-2506.
9. Cavstens H, Schrodt G. Malignant transformation of a benign encapsulated neurilemoma. Ann J Clin Pathol 1969; 51:144-149.
10. Lodding P, Kinngdblom LG, Angervall L et al. Cellular schwannoma. A Clinicopathologic study of 29 cases. Virchows Arch Pathol Anat. 1990; 416:237-248.
11. Brasfield RD, Das Grupta TK. Von Recklinghausen's disease, a clinical pathologic study. Ann Surg 1972:175:86-114.
12. White HR. Survival in malignant schwannoma: an 18-year study. Cancer 1971; 27:720-729.
13. Currier AR, Gale JW. Mediastinal tumors. Arch Surg 1949; 58:797-818.
14. D'Agostino NA, Walsh WS, Clarke TH. Primary malignant neoplasms of nerves (malignant neurilemomas) 9n patients without manifestations of multiple neurofibromatosis (von Recklinghausen disease). Cancer 1963;16:1003-1011.
15. Preston FW, Walsh WS, Clark TH. Cutaneous neurofibromatosis (von Recklinghausen's disease): Clinical manifestations and incidence of sarcoma in 61 male patients. Arch Surg 1952;64:813-824.
16. Maebeya S, Miyoshi, Fugiwara K, Sekii H, Susuma T, Yosimaso T, Naiato Y, Nishino E. Malignant schwannoma in the intrathoracic vagus nerve, report of a case. Surg. Today 1993;23(12):1078-1080.`
17. Chields TW, Reynolds M. Neurogenic tumors of the thorax. Surg Cli North Am 1988:68:645-668.
18. DeVault KR, Miller ES et al. Acute esophageal hemorrhage from a vagal neurilemoma. Gastrenterology 1992;102:1059-1061.
19. D'Angelo V, Casadei G, Bizzozero L, Cerebral Metastasis from an Epithelioid Malignant Schwannoma: Case Report 1991:29:906-909.
20. D'Agostino AN, Walsh WS, Clarke TH. Primary malignant neoplasms of nerves (malignant neurilemomas) in patients without manifestations of multiple neurofibromatosis (von Recklinghausen disease). Cancer 1963; 16:1003-1011.
21. Vaghei R, Yost Nl. Vagal Schwannoma Involving Esophagus. Ann Thorac Surg 1991: 52:1334-1336.
22. Dabir RR, Piccione W Jr, Kittle CF. Intrathoracic tumors of the vagus nerve. Ann Thorac Surg 1990;50:494-497.
23. Maillet-Vioud M, Narod S et al. Génétique des neurofibromatoses: progrès récents et perspectives. Rev Neurol 1991 ; 147 :644-648.
24. Halliday AL, Sobel AR, Martuza RL. Benign spinal nerve sheath tumors: their occurrence sporadically and in neurofibromatosis types 1 and 2. J Neurocirurg. 1991; 74:248-245.
25. White HR, Survival in malignant schwannoma: an 18 year study. Cancer 1971;27:720-729.
26. Pinedo HM, Kenis Y. Chemotherapy of advanced soft-tissue sarcomas in adults. Cancer Treat Rev 1977;4:67-69.
27. Rober PE, Smith JB, Sakr W, Pierce JM. Malignant peripheral nerve sheath tumor (malignant schwannoma) of urinary bladder in von Recklinghausen neurofibromatosis. Urology 1991;5:473-476.