Metastatic Peripheral Nerve Malignant Schwannoma of Lungs and Adrenal Gland: Case Report

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Schwanoma Maligno de Nervo Periférico Metastático para Pulmão e Glândula Adrenal: Relato de Caso

Schwannoma Maligno Metastásico de Nervio Periférico para Pulmones y Glándula Suprarrenal: Reporte de Caso

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ABSTRACT

Introduction: Schwannoma is a rare type of tumor which grows from Schwann cells that protect nerve extensions. The malignancy of these tumors is even rarer, corresponding to 5-10% of all sarcomas. The prognosis is dismal, even after complete surgical resection. **Case report**: A 79-year-old male patient presented with a crusted lesion in his left leg with two months of evolution. Initially, the biopsy of the lesion revealed pleomorphic sarcoma, but its immunohistochemical pattern was peripheral nerve sheath malignant tumor. The tumor developed lymph node, lung, and adrenal metastasis within a few years after the first diagnosis. Adrenal tumor resection was not possible. The patient developed paraneoplastic syndrome and his clinical status worsened, progressing to death. **Conclusion:** In view of the non-specific form of tumor appearance and its aggressiveness, it is important to highlight the role of wide surgical resection in its treatment. In addition, it is clear that new case reports of this type of neoplasia are necessary for better definition of more appropriate conducts, especially in recurrence or metastatic cases.

Key words: Peripheral Nervous System Neoplasms; Neurilemmoma; Neoplasm Metastasis; Adrenal Glands; Lung.

RESUMO

Introdução: O schwanoma é um tumor pouco frequente que se origina das células de Schwann que recobrem os prolongamentos nervosos. A malignidade desses tumores é ainda mais rara, correspondendo a 5-10% de todos os sarcomas. O prognóstico é reservado, mesmo após completa ressecção cirúrgica. **Relato do caso**: Paciente do sexo masculino, 79 anos, apresentou-se com lesão crostosa em perna esquerda com dois meses de evolução. A biópsia da lesão inicialmente revelou sarcoma pleomórfico, mas seu padrão imuno-histoquímico confirmou tumor maligno da bainha do nervo periférico. O tumor desenvolveu metástase linfonodal, pulmonar e adrenal dentro de poucos anos após o diagnóstico inicial. A ressecção do tumor adrenal não foi possível. O paciente desenvolveu síndrome paraneoplásica e teve piora do estado clínico, evoluindo a óbito. **Conclusão**: Tendo em vista a forma inespecífica do aparecimento do tumor e sua agressividade, é importante ressaltar o papel da ressecção cirúrgica ampla no seu tratamento. Além disso, fica evidente a necessidade de novos relatos desse tipo de neoplasia para melhor definição de uma conduta mais apropriada, principalmente em casos de recorrência ou disseminação metastática.

Palavras-chave: Neoplasias do Sistema Nervoso Periférico; Neurilemoma; Metástase Neoplásica; Glândulas Suprarrenais; Pulmão.

RESUMEN

Introducción: El schwannoma es un poco común, el cual se origina en las células de Schwann, que cubren las extensiones nerviosas. La malignidad de estos tumores es aún más rara, y representa 5-10% de todos los sarcomas. El pronóstico es reservado, incluso después de una resección quirúrgica completa. **Relato del caso:** Varón de 79 años que presenta una lesión costrosa en la pierna izquierda a los dos meses de evolución. La biopsia de la lesión reveló inicialmente un sarcoma pleomórfico, pero su patrón inmunohistoquímico era un tumor maligno de la vaina del nervio periférico. El tumor desarrolló metástasis en los ganglios linfáticos, pulmones y suprarrenales pocos años después del diagnóstico. La resección del tumor suprarrenal no fue posible. El paciente desarrolló síndrome paraneoplásico y empeoró el estado clínico, progresando hasta la muerte. **Conclusión:** Dada la forma inespecífica de aparición del tumor y su agresividad, es importante destacar el papel de la resección quirúrgica amplia en su tratamiento. Además, existe una clara necesidad de nuevos informes de este tipo de neoplasias para definir mejor un abordaje más adecuado, especialmente en casos de recurrencia o diseminación metastásica.

Palabras clave: Neoplasias del Sistema Nervioso Periférico; Neurilemoma; Metástasis de la Neoplasia; Glándulas Suprarrenales; Pulmón.

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INTRODUCTION

Schwannoma is a rare type of tumor originated from the Schwann cells of the peripheral nerve sheath. Its malignant transformation corresponds only to 5 to 10% of all the sarcomas[1-3]. In 1935, the neoplasm was primarily interpreted as a fibrosarcoma and secondarily – in 1949 – the growth of the tumor from Schwann[4,5] cells was observed. Regardless of this, the histogenesis of the tumor is little known and other denominations were given: malignant peripheral nerve sheath tumor, neurogenic sarcomas and neurofibrosarcoma[2].

Solitary malignant sarcomas are rare tumors and affect mainly males. They can develop at any age, but the peak of the incidence occurs between 20 and 50 years, frequently in peripheral nerves of great diameter and can manifest symptoms of peripheral neuropathy[4-7]. The most common affected sites are neck, forearm, legs and buttocks. This tumor is frequently associated with neurofibromatosis type I and extremely rare in patients non-carriers of this condition. Diagnosis is influenced by the clinical presentation and must be confirmed by immunohistochemistry[6].

The treatment is surgical for failing to respond well to conventional chemotherapy or radiotherapy. Some studies demonstrated remission of the tumor, associating chemotherapeutics with adriamicin[8]. Its prognostic is dismal, even when completely resected. Metastasis occur mainly in the lungs, omentum, sigmoid colon and urinary bladder[1,2,5,6]. There are no recommendations in the literature about the adequate management in case of recurrence[6].

The objective of the present article is to report a case of malignant schwannoma of the peripheral nerve with metastasis to adrenal gland and lung. The Institutional Review Board of "*Liga Paranaense de Combate ao Câncer do Hospital Erasto Gaertner*", CAAE: 87548518.2.0000.0098 approved the study.

CASE REPORT

79 years old male patient with systemic arterial hypertension, moderate aortic insufficiency and depression. The onset occurred two months before the consultation with minor lesion of the anterior region of the lower third of the left leg, initially as a crust, evolving to extensive and hyperemic lesion. At the exam, crusty lesion of nearly 2 cm was detected with surrounding hyperemia of approximately 6 cm. Initially, the biopsy revealed pleomorphic sarcoma. The immunohistochemistry analysis is shown in Table 1A. The histological and the immunohistochemistry profiles revealed a malignant tumor of the peripheral sheath. The patient was not carrier of neurofibromatosis type I.

Two months after the diagnosis, an extensive resection of the tumor of the left leg was performed with grafting. The anatomopathological exam revealed: ulcerated, crusty, vegetating and ill-delimited 2.5 x 2 x 0.9 cm lesion with

Table 1. Immunohistochemistry panel of resected lesions. **A.** markers of the biopsy of the primary tumor. **B.** markers of the product of lymphadenectomy. **C.** markers of the product of resection of the pulmonary nodule. **D.** markers of the product of adrenalectomy

Marker	(A) Tumor biopsy	(B) Product of inguinal lymphadenectomy	(C) Pulmonary nodule	(D) Adrenal lesion
Alfa-AML	Positive multifocal in neoplastic cells	Negative	Negative	Negative
Vimentin	Positive strong and diffuse	Positive diffuse	Positive in the neoplastic cells	Positive
S-100	Positive in the neoplastic cells	Positive in pleomorphic cells	Positive in the neoplastic cells	-
CD-68	Positive multifocal in the neoplastic cells	Positive in histiocytes	-	Positive focal
Ki-67	Positive in 80% of the nuclei of the neoplastic cells	Positive in 60% of the nuclei of the neoplastic cells	Positive in 70% of the nuclei of the neoplastic cells	-
HMB-45	Negative	Negative	-	-
Desmin	Negative	-	-	-
CD-34	Negative	-	-	-
CKAE1/AE3	Negative	-	-	-
MYO D1	Negative	-	-	-
Melan A	Negative	-	-	-
PAX-8	-	-	-	Negative

characteristics of ulcerated fusocellular neoplasm in skin. The thoracic computed tomography (CT) and pelvis of control did not present abnormalities. Through abdominal CT, small 9 and 7 mm hypodense hepatic nodes and a 7 mm foci of calcification were encountered. The immunohistochemistry analysis of the material sent for anatomopathological exam revealed the same pattern seen in the biopsy (Figure 1) (Table 1A). Due to the absolute predominance of pleomorphic areas in tumor histology, areas Antoni A and Antoni B as well as Verocay bodies were not clearly found in the neoplasm sample.

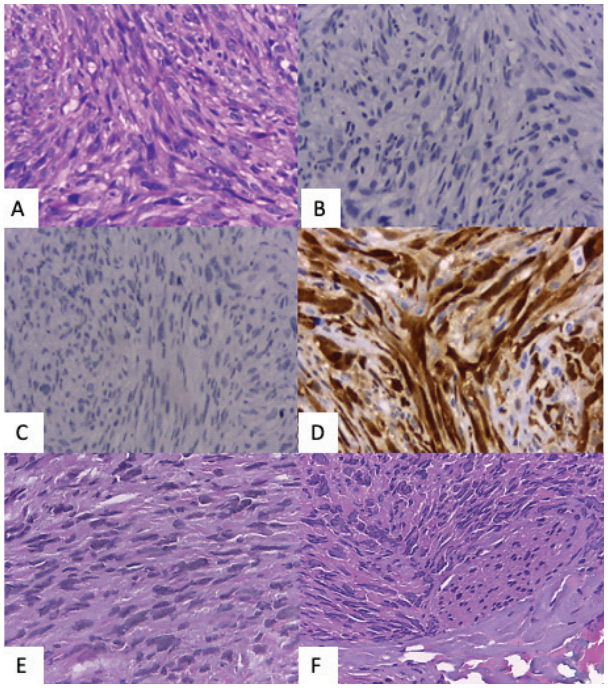

Figure 1. Histology and immunohistochemistry of the primary tumor. **A.** Histopathological cut with neoplasm with variably fusiform pleomorphic cells forming fascicles and storiforms patterns with myotic activity present. **B.** Absence of immunoreactivity for Melan-A. **C.** Absence of immunoreactivity for HMB-45. **D.** Presence of immunoreactivity for S-100. **E.** Histological cut with fusiform bundle arranged atypical cells, with indistinct cytoplasmatic contours and cytoplasm finally fibrillary and wavy following pattern of nervous fibers. **F.** Histopathological cut with neoplastic cells constituting sketches of neural fibers.

One year after resection, fine needle aspiration punction to investigate the lymphadenomegaly at the left inguinal region was performed. The histological analysis was positive for malignancy. Left inguinocrural lymph node emptying was suggested, whose anatomopathological exam revealed poorly differentiated, infiltrative neoplasm in one of the fifteen lymph nodes analyzed. The histological condition and the immunohistochemistry profile were consistent with malignant schwannoma. The immunohistochemical markers obtained are presented in Table 1B.

In the first thoracic CT (Figure 2A) performed one year and eight months after the diagnosis of neoplasm, a new 21 mm node appeared in the posterior segment of the lower lobe of the left lung without calcifications, the hypothesis was pulmonary metastasis. A new thoracic CT (Figure 2B), three months later, showed growth of the node to 31 mm. Left pulmonary segmentectomy with intraoperative freezing was performed, and confirmed metastasis (4 cm foci). The anatomopathological exam of the lesion showed poorly differentiated neoplasm with pleomorphic cells and extensive necrosis. Its immunohistochemistry pattern is shown in Table 1C.

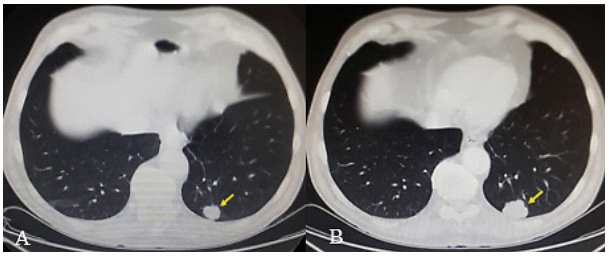

Figure 2. Pulmonary node primarily portrayed in **A** and its evolution in **B**

One year after resection the magnetic resonance imaging (MRI) showed the appearance of adrenal mass at left (Figure 3) characterized as expansile lesion of irregular contours and predominantly peripheral enhancement with restricted diffusion in its peripheral portion, measuring 65 x 35 mm. In its central portions, necrotic content was identified. At this moment, the patient was admitted due to episodes of diarrhea, vomits, fever and important worsening of the renal function.

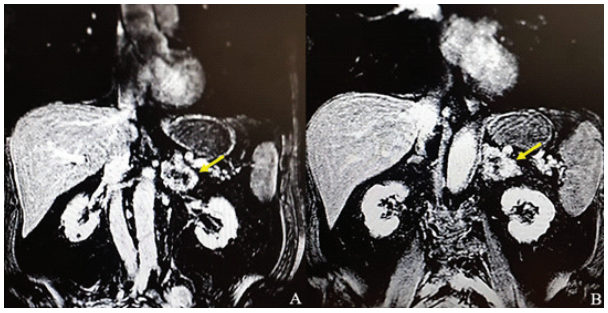

Figure 3. Left adrenal mass

A new thoracic CT revealed infracarinal lymphadenomegaly, elongated nodule associated with bands of atelectasis in posterior basal segment of the left lower lobe and nodules with medial lobulated contours in the right lower lobe. Exenteration of the upper adrenal quadrant was performed due to the absence of cleavage plane with aorta, left renal vein and splenic hilum. By video laparoscopy, a lesion of the splenic parenchyma with ineffectual hemostasis was detected requiring

splenectomy. The patient did not develop infection while at the Intensive Care Unit (ICU).

The anatomopathological exam of the adrenal lesion revealed poorly differentiated neoplasm and immunohistochemistry consistent with high degree pleomorphic sarcoma (Table 1D) (Figure 4). Evolved in post-operation with hyporexia, nausea and ponderal loss of nearly 10 kg. New thoracic CT revealed sparse metastatic nodes in both lungs (the largest with 21 mm) and increase of the mediastinal lymphadenomegaly. The abdominal CT showed solid mass in left adrenal gland measuring 86 x 69 x 67 mm, involving the left renal vein and artery in contact with the aorta, pancreas and left kidney.

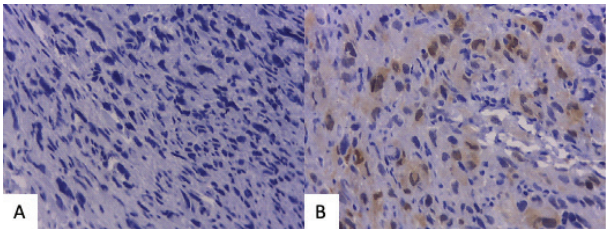

Figure 4. Immunohistochemistry of the metastasis to adrenal. **A**. Absence of immunoreactivity for Melan-A in metastatic neoplasm formed by variable pleomorphic fusiform cells. **B**. Presence of immunoreactivity for S-100

Based in the clinical conditions of the patient, no indication of chemotherapy was made and was referred to exclusive palliative care. Few months later, was admitted for hyperkalemia control by paraneoplastic syndrome (treatment with zoledronic acid). Presented limited ability of ambulation, dyspnea, anorexia and important decline of the clinical condition and evolved to death.

DISCUSSION

Malignant schwannoma with metastasis to adrenal gland has not been reported in the literature yet. The patient of this case presented a malignant, aggressive tumor but was not carrier of neurofibromatosis type I. The presence of adrenal metastases is, on its own, a factor of poor prognosis with 5-years survival of 20%[9].

The tumors that most frequently cause adrenal metastasis are lung and breast. Due to the paucity of studies, surgery is the treatment of choice. It must be indicated when control or plan of extra-adrenal disease control are in place, presence of isolated and encapsulated metastasis in one or both glands, highly suggestive imaging or proof by pathological exam and functioning condition that are able to allow surgery[9].

This type of tumor does not present specific symptoms or well-defined diagnostic criteria (except if tumor is clearly connected to a nerve or associated with neurofibromatosis type I)[10]. Usually it presents as low growth fixed nodule and its investigation can reveal the nervous origin of the tumor[4].

Typically, malignant schwannoma produce hematologic metastasis and the most common sites are lungs, omentum, sigmoid colon and urinary bladder[1,2,5,6]. Lymph node metastases are rare. Two of the cases studied by White[1] presented lymph nodes metastasis but none was encountered in 31 patients with malignant schwannoma investigated by Vieta and Pack[11]. Das Gupta and Brasfield[12] did not report lymph node metastasis in 232 cases of solitary malignant schwannoma.

Angiography contributed for better therapeutic approach while validating the vascularization of the tumor, origins of the supply and its anatomic relations[5]. The radiologic characteristics of tumor are not well-defined[2] yet. Surgery is the treatment of choice for offering better possibility of cure or long-term palliative care. Radiotherapy or chemotherapy were unsuccessful, except for patients in use of combinations with adriamicine[1,5,10].

Complete resection is essential, it is also recommended, in addition to adjacent tissues, the resection of a long segment of the proximal nerve to the tumor and its analysis by intraoperative freezing based in case-reports with local spread of the tumor. Some authors advocate amputation as the treatment of choice for tumors with nodule growth in peripheral nerve, affirming that local excision[1,5,6,10] increases survival. In a study of 1952, it was estimated that 30% of the cases submitted to surgery had survival higher or equal to five years[1]. In a study of 1981, it was reported that survival of patients with malignant schwannoma and neurofibromatosis type I was significantly lower (23% in five years) than patients with isolated malignant schwannoma (47% in five years). Most of the carriers of the disease died in the first two years of the tumor[8] onset .

The prognosis of paravertebral tumors is worse than in other sites because typically they present at advanced stages involving adjacent viscera[4]. Another factor of worst prognosis is the association of the tumor with neurofibromatosis type I since the lesions are more pleomorphic and less frequently encountered in lower extremities[4,5,8]. It is worst still in patients with lung metastasis: only three of 71 patients investigated by Yamakami et al.[2] survived for more than two years after spread was detected. Better prognosis[2,5] for tumors with less than 5 cm located in the extremities far from the axillary and inguinal regions are anticipated when submitted to proper treatment.

Osteoid and cartilaginous formations were already detected in this pathology[4]. The development of this tumor is characterized by hypocellularity, cellular/nuclear pleomorphism, presence of mitosis and proliferation of

small vessels, similar to fibrosarcoma[3]. The presence of findings of neural morphology contributes strongly for the hypothesis. The negativeness of the marker HMB 45 also corroborates the diagnosis of schwannoma, as occurred in the current case-report and the positiveness of the protein S100 confirms the diagnosis[13].

CONCLUSION

Malignant schwannoma are rare neoplasms of unspecified clinical condition and dismal prognosis, generally associated with neurofibromatosis type I. The current report holds no relation with this disease and is the first in the literature to present adrenal metastasis. Also, it brings up the necessity of describing more cases on that theme to elucidate the characteristics of the tumor and to determine proper management.

CONTRIBUTIONS

The authors contributed equally for all the stages of the article and approved the final version to be published.

DECLARATION OF CONFLICT OF INTEREST

There is no conflict of interests to declare.

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None.

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