Case Report

Abdominal Tumor Requiring Surgical Resection in a Young Patient with Neurofibromatosis Type 1

Tumor Abdominal com Indicação de Ressecção Cirúrgica em Doente Jovem com Neurofibromatose Tipo 1

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ABSTRACT

Neurofibromatosis type 1 (NF1) is an autosomal dominant disorder that affects approximately 1 in 3000 births. Retroperitoneal tumors occur in 2%-5% of NF1 patients and pose diagnostic and therapeutic challenges. We report a 25-year-old male from Cape Verde with confirmed NF1 who presented with progressive abdominal pain and a 15 × 11 × 12 cm retroperitoneal mass in the left psoas muscle. He underwent a successful complete surgical resection. Histologically, it was a malignant peripheral nerve sheath tumor (MPNST), high-grade, with foci of heterologous rhabdomyosarcomatous differentiation (malignant triton tumor). Molecular testing confirmed a likely pathogenic variant (c.288+5G>A) in the *NF1* gene. This case highlights the importance of early diagnosis, appropriate surgical intervention, molecular confirmation for family genetic counseling, and the development of emerging systemic therapies, including targeted treatments for NF1-associated tumors.

Keywords: Neurofibromatosis 1/complications; Retroperitoneal Neoplasms/surgery

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RESUMO

A neurofibromatose tipo 1 (NF1) é uma doença autossómica dominante que afeta 1 em cada 3000 nascimentos. Os tumores retroperitoneais ocorrem em 2% a 5% dos doentes com NF1 e representam desafios diagnósticos e terapêuticos. Relata-se o caso de um homem de 25 anos, natural de Cabo Verde, com NF1 confirmada, que apresentava dor abdominal progressiva e uma massa retroperitoneal de 15 x 11 x 12 cm no músculo psoas esquerdo. Foi submetido a uma ressecção cirúrgica completa com sucesso. Histologicamente era um tumor das bainhas nervosas periféricas maligno (MPNST), de alto grau, com focos de diferenciação rabdomiossarcomatosa heteróloga (tumor de triton maligno). Os testes moleculares confirmaram uma provável variante patogénica (c. 288+5G>A) no gene *NF1*. Este caso enfatiza a importância do diagnóstico precoce, da intervenção cirúrgica adequada, da confirmação molecular para aconselhamento genético familiar e de terapias sistémicas emergentes, incluindo tratamentos direcionados para tumores associados à NF1.

Palavras-chave: Neoplasias Retroperitoneais/cirurgia; Neurofibromatose 1/complicações

INTRODUCTION

Neurofibromatosis type 1 (NF1) is an autosomal dominant neurocutaneous syndrome caused by mutations in the *NF1* gene on chromosome 17q11.2, which encodes neurofibromin, a tumor suppressor protein regulating the RAS-MAPK pathway.[1,2] The loss of neurofibromin function results in constitutive activation of RAS signaling, leading to increased cell proliferation, survival, and tumor formation.[3]

Retroperitoneal tumors represent a rare complication (2%-5% of NF1 patients), typically presenting between ages 20-40 years.[4,5] These tumors pose significant diagnostic challenges regarding malignant transformation and require aggressive surgical management. The lifetime risk of developing malignant peripheral nerve sheath tumors (MPNST) in NF1 patients is 8%-13%, with a particularly poor prognosis.[6]

CASE REPORT

1. PATIENT AND HISTORY

A 25-year-old male from Santiago Island, Cape Verde, with diagnosed NF1 presented in April 2025 with progressive left upper quadrant abdominal pain, significant weight loss, and asthenia. Family history was strongly positive for NF1 (father, aunt, uncle, and paternal grandfather affected).

2. PHYSICAL EXAMINATION

On admission (August 4, 2025) to Hospital Dr. Agostinho Neto, in Cape Verde, the patient was cachectic and dehydrated with:

- Vital signs: BP 117/86 mmHg, HR 148 bpm, temperature 36.5°C
- Skin: Multiple café-au-lait macules and cutaneous neurofibromas
- Abdomen: Large, non-mobile, tender mass in left upper and lower quadrants

3. LABORATORY FINDINGS

- Hemoglobin: 10.7 g/dL (anemia)
- Leukocytes: 17 200/mm^3 (leukocytosis)
- Platelets: 589 000/mm^3 (thrombocytosis)
- Glucose: 48 mg/dL (hypoglycemia)
- Total proteins: 3.81 g/dL (hypoproteinemia)
- Sodium: 131 mEq/L (hyponatremia)

4. IMAGING

CT scan (April 30, 2025, CIDIS Clinic, Dakar, Senegal) revealed (Fig. 1):

- Heterogeneous mass 15 × 11 × 12 cm in left psoas muscle
- Thickening of multiple nerve roots
- No pulmonary or hepatic metastases
- Radiological diagnosis: neurofibromas with probable sarcomatous degeneration

5. SURGICAL MANAGEMENT

After clinical optimization and correction of metabolic disturbances, the patient underwent exploratory laparotomy with complete tumor resection (Fig. 2).

Intraoperative findings:

- Well-delimited tumor adherent to the left psoas muscle
- No invasion of adjacent structures
- Complete resection with preservation of neurovascular structures

Specimen: 16 × 15 × 10 cm encapsulated mass with firm consistency and lobulated surface

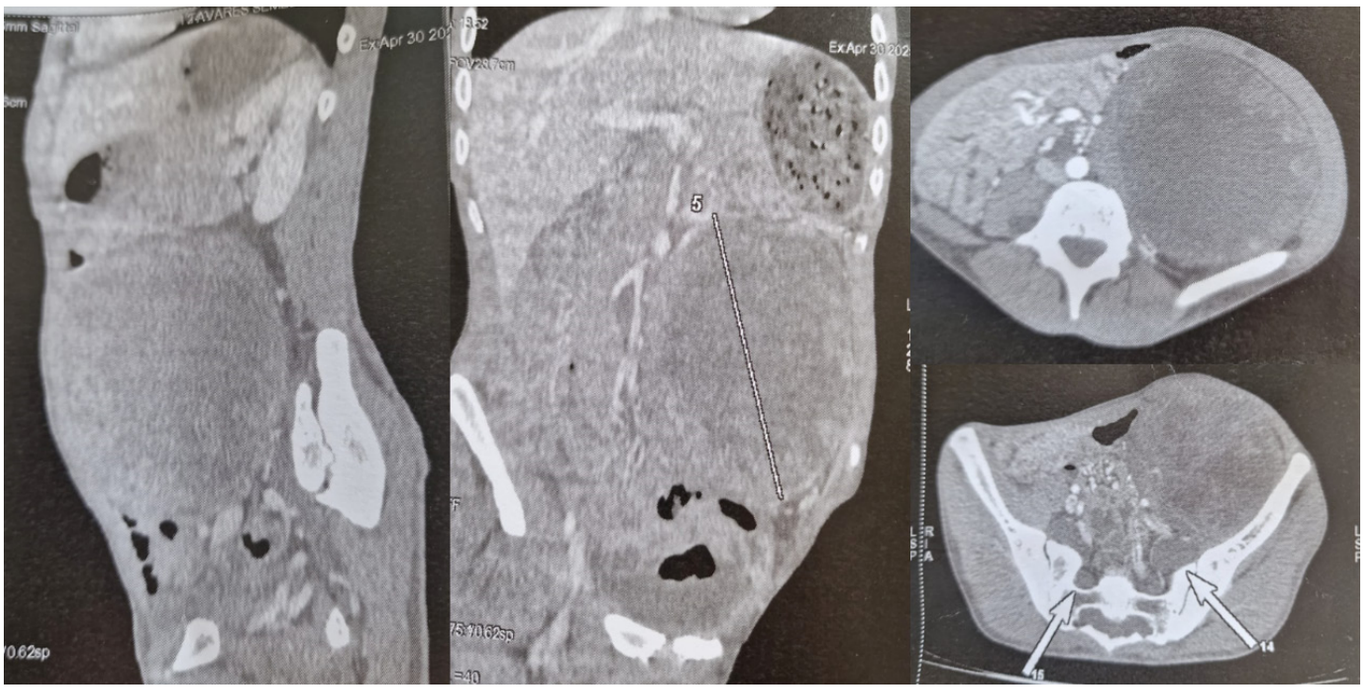

Figure 1 – CT scan reveals a heterogeneous mass 15 × 11 × 12 cm in the left psoas muscle, with thickening of multiple nerve roots. Radiological diagnosis: neurofibromas with probable sarcomatous degeneration.

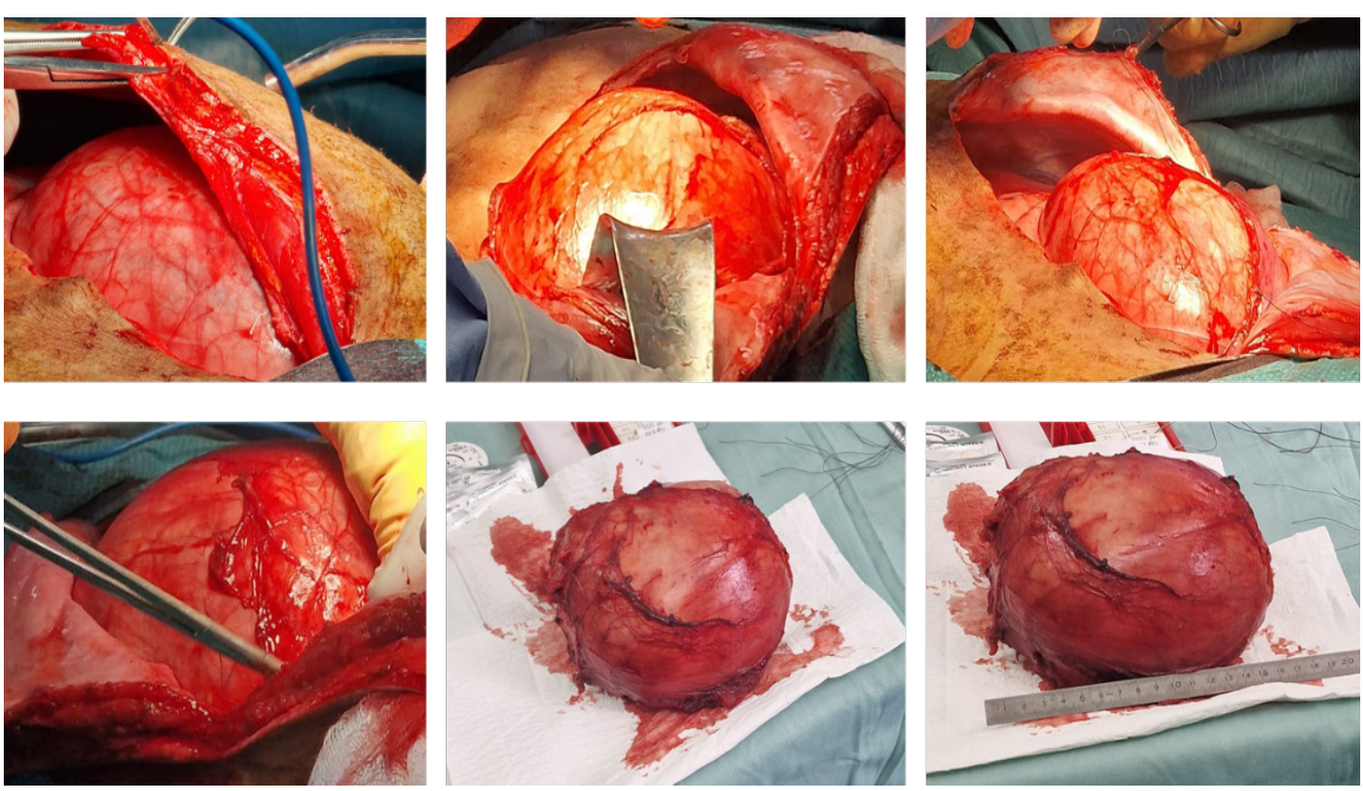

Figure 2 – Surgical specimen.

Postoperative course: Uneventful recovery without complications

6. HISTOPATHOLOGY

Surgical specimen corresponding to an abdominal tumor fixed in formalin measuring 16x15x10 cm. Upon sectioning, several cavitated areas with necrosis and hemorrhagic regions are observed. Histological examination reveals a densely cellular malignant mesenchymal neoplasm, composed of cells with oval and vesicular nuclei, inconspicuous nucleoli, and scant cytoplasm. The cells are arranged in long bundles, in a "fishbone" pattern, within a richly vascularized stroma, partly fibrillar and partly dense.

In the observed material, nuclear pleomorphism is discreet to moderate, the mitotic index is greater than 20 mitoses/10HPF, and no foci of necrosis are identified.

Immunohistochemical study shows:
- Multifocal positivity for PS100 and CD34
- Focal positivity (rare cells) for desmin
- Loss of expression of H3K27me3 and p16 is observed.

In conclusion it was a malignant peripheral nerve sheath tumor (MPNST), high-grade, with foci of heterologous rhabdomyosarcomatous differentiation (Malignant Triton tumor) (Fig. 3).

7. MOLECULAR GENETIC TESTING

Testing at Instituto Português de Oncologia at Porto, Portugal, identified a likely pathogenic variant in the *NF1* gene: c.288+5G>A (heterozygous).

Clinical Significance:
- Confirms molecular diagnosis of NF1
- Suspected to cause aberrant splicing (ClinVar ID 642764)
- First-degree relatives have 50% carrier risk
- Enables family cascade screening

DISCUSSION

1. CLINICAL PRESENTATION

Retroperitoneal tumors in NF1 typically grow silently to large dimensions before diagnosis.[7] This patient presented with classic features: a large tumor (15 cm), pain, cachexia, and constitutional symptoms. The metabolic derangements (anemia, hypoproteinemia, hypoglycemia) reflected a significant tumor burden.

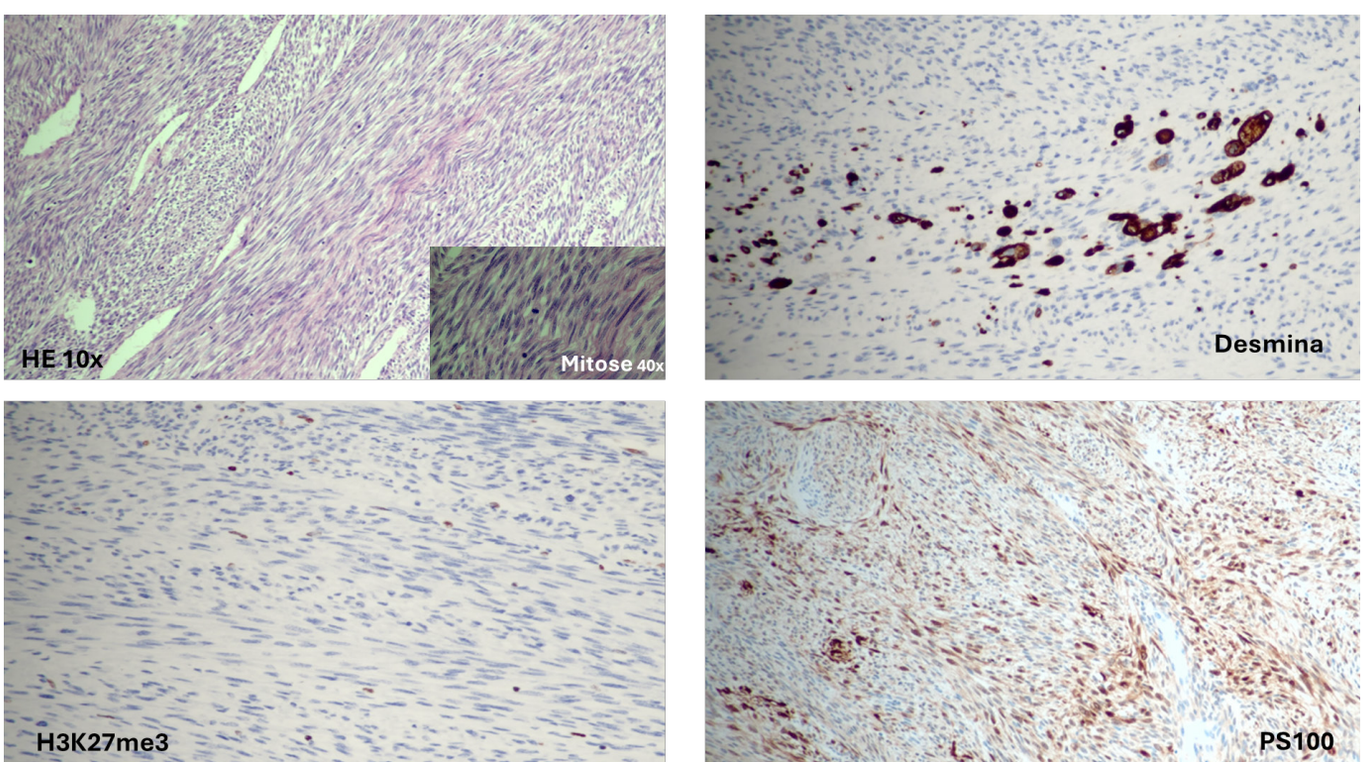

Figure 3 – Malignant peripheral nerve sheath tumor (MPNST), high-grade, with foci of heterologous rhabdomyosarcomatous differentiation (malignant triton tumor).

2. DIFFERENTIAL DIAGNOSIS

Distinguishing benign neurofibromas from malignant peripheral nerve sheath tumors (MPNST) is challenging. Features suggesting malignancy include[8]:

- Size >5 cm (present)
- Rapid growth
- Persistent pain (present)
- Radiological heterogeneity (present)

However, the well-delimited, encapsulated nature and absence of invasion suggest possible benign pathology. Final histopathology will be determinant.

3. MOLECULAR DIAGNOSIS

The c.288+5G>A splice-site variant confirms NF1 diagnosis and enables:

- Family genetic counseling
- Predictive testing for at-risk relatives
- Implementation of appropriate surveillance protocols
- Reproductive planning guidance

Loss of neurofibromin function results in hyperactivation of the RAS-MAPK and mTOR pathways, providing rational targets for systemic therapy.[9]

4. SURGICAL MANAGEMENT

Complete surgical resection with negative margins remains the gold standard for localized retroperitoneal tumors in NF1.[10] Bloc resection with negative intraoperative margins represents optimal management, though long-term outcomes depend on final histopathology.

The systemic treatment options are condensed in Table 1.

Table 1 – The systemic treatment options

Category	Treatment/Topic	Key Information	Bibliography
Conventional Chemotherapy	Overview	Remains the backbone of systemic treatment, though outcomes are generally poor	11
	Doxorubicin-based regimens	Doxorubicin + ifosfamide is the standard first-line regimen	12
		Response rates: 15-25% for MPNST	
		Median progression-free survival: 4-6 months	13
	Alternative regimens	Gemcitabine + docetaxel: demonstrated activity with better tolerability	14
		Eribulin: approved for liposarcoma and leiomyosarcoma	15
		Trabectedin: active in certain sarcoma subtypes	16
Targeted Therapy: MEK Inhibitors	Rationale	Constitutive activation of RAS-MAPK pathway in NF1	17
	Selumetinib	FDA approved (April 2020) for pediatric patients ≥2 years with NF1	18
		Phase II trial (SPRINT Stratum 1): 71% achieved partial response	19
		Clinical trials ongoing for MPNST	20
	Trametinib	Potent MEK1/2 inhibitor approved for BRAF-mutant melanoma	21
		Phase II trial: 40% achieved ≥20% volume reduction	22
	Cobimetinib	Under investigation in combination strategies	23
mTOR Inhibitors	Pathway	mTOR pathway dysregulated in NF1-deficient tumors	24
	Sirolimus	Phase II trial: clinical benefit in 82% of patients	25
		Combination with MEK inhibitors under investigation	26
	Everolimus	Limited single-agent activity, combination strategies being explored	27
Immunotherapy	Checkpoint inhibitors	Limited activity in soft tissue sarcomas including MPNST	28
		SARC028 trial: Pembrolizumab showed 18% response rate	29
		Combination strategies under investigation	30
	Adoptive cell therapy	CAR-T cell therapy targeting GD2 in early clinical development	31
Novel Targeted Approaches	HDAC inhibitors	Vorinostat showed preclinical activity	32
	FGFR inhibitors	Preclinical evidence suggests FGFR signaling contribution	33
	Combination strategies	MEK inhibitor + CDK4/6 inhibitor: promising preclinical synergy	34
		MEK inhibitor + HSP90 inhibitor: under investigation	35
		Vertical pathway inhibition (MEK + mTOR): rational combination	26

Treatment based on Histopathology is condensed in Table 2.

5. SURVEILLANCE RECOMMENDATIONS

Following current guidelines[41], NF1 patients require:

- Clinical examination every 3-6 months for 5 years, then annually
- Imaging (CT or MRI) every 6-12 months for 5 years
- Annual whole-body MRI for new tumor detection (particularly plexiform neurofibromas)
- Monitoring for additional NF1-associated malignancies:
  - Breast cancer screening starting age 30 (annual MRI + mammography)[42]
  - Annual blood pressure monitoring (pheochromocytoma)
  - Annual ophthalmologic examination (optic pathway gliomas)
- Family cascade screening with genetic counseling

6. CANCER RISKS IN NF1

NF1 patients face significantly increased lifetime risks[43]:

- MPNST: 8%-13%
- Breast cancer: 20%-40% (females)
- Optic pathway gliomas: 15%-20%
- Gastrointestinal stromal tumors (GIST): 7%
- Pheochromocytoma: 1%-5%
- Rhabdomyosarcoma: increased risk (especially pediatric)
- Various CNS tumors: increased risk

CONCLUSION

This case illustrates a typical retroperitoneal tumor presentation in a young NF1 patient. Key management elements include:

1. Complete surgical resection as the primary curative treatment
2. Molecular confirmation enabling family genetic counseling and cascade screening

Table 2 – Treatment based on Histopathology and prognostic factors.

Category	Condition/Scenario	Management Approach/Details	Bibliography
Treatment Algorithm Based on Histopathology	**Benign neurofibroma**	Surveillance with clinical examination and imaging every 6-12 months	
		No systemic therapy indicated	
		Consider MEK inhibitor only if symptomatic progression or inoperability	
	ANNUBP	Close surveillance every 3-6 months	
		Consider MEK inhibitor for progressive disease	36
	Localized MPNST with positive margins	Adjuvant radiotherapy (50-60 Gy)	37
		Consider adjuvant chemotherapy (controversial, no clear survival benefit)	38
		Clinical trial enrollment preferred	
	Unresectable or metastatic MPNST	First-line: Doxorubicin + ifosfamide	12
		Second-line: Gemcitabine + docetaxel or clinical trial with MEK inhibitor	20
		Consider immunotherapy in checkpoint inhibitor combinations	30
		Palliative radiotherapy for symptomatic sites	
Prognosis	**Benign tumors**	Excellent prognosis with complete resection	
	MPNST - Overall	Poor prognosis with 5-year survival 20%-50%	6,39
	MPNST - Localized resectable	50%-60% 5-year survival	
	MPNST - Unresectable or metastatic	<20% 5-year survival	
	NF1-associated vs sporadic	NF1-associated MPNSTs have worse prognosis than sporadic MPNST	40
Prognostic Factors	Tumor size	>5 cm: worse prognosis	
	Surgical margin status	R0 resection critical	
	Tumor grade	Affects prognosis	
	Presence of metastases	Affects prognosis	
	NF1 status	NF1-associated worse than sporadic	

3. Histopathological diagnosis determining prognosis and treatment strategy
4. Emerging targeted therapies, particularly MEK inhibitors like selumetinib, offer new hope for patients with inoperable or progressive disease
5. Multidisciplinary approach essential for optimal outcomes
6. Lifelong surveillance is mandatory due to multiple cancer risks

The integration of surgical expertise, molecular genetics, and novel targeted therapies exemplifies modern management of NF1-associated tumors. For this patient, awaiting final histopathology is critical: if benign, surveillance alone is appropriate; if MPNST is confirmed, consideration of adjuvant therapy and clinical trial enrollment should be discussed. The established efficacy of selumetinib in NF1-associated plexiform neurofibromas[19] and ongoing trials in MPNST[20] represent significant therapeutic advances.

Standardized screening protocols, specialized center referral, and participation in clinical trials investigating novel targeted therapies are essential to improve outcomes in this high-risk population.

Malignant triton tumor is a rare and aggressive variant of malignant peripheral nerve sheath tumor (MPNST) characterized by rhabdomyosarcomatous differentiation, accounting for only 5%-10% of all MPNSTs and occurring sporadically or in association with neurofibromatosis type 1 (NF1).[44] The prognosis is poor, with 5-year survival rates of 10%-15%, high local recurrence rates (40%-60%), and distant metastases developing in 40%-65% of cases, most commonly affecting the lungs and bone.[44,45] The most critical prognostic factor is achieving negative surgical margins, followed by tumor size (>5 cm portends worse outcomes) and NF1 association.[46] Treatment centers on wide surgical excision with clear margins as the cornerstone of therapy, typically followed by adjuvant radiation therapy to improve local control. At the same time, the role of chemotherapy remains controversial though it may be considered using sarcoma or rhabdomyosarcoma-based regimens.[45,47] Intensive post-treatment surveillance is essential due to the high risk of recurrence and metastatic disease, making complete surgical resection the patient's best chance for long-term survival.[44,45]

ETHICAL DISCLOSURES

Conflicts of Interest: The authors have no conflicts of interest to declare.
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Confidentiality of Data: The authors declare that they have followed the protocols of their work center regarding the publication of patient data.
Patient Consent: Consent for publication was obtained.
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CONTRIBUTORSHIP STATEMENT:

The authors: VC, HS, PB, MA, MT, CB, and LLS designed the study and reviewed and edited the manuscript.
All authors approved the final version to be published.

DECLARAÇÃO DE CONTRIBUIÇÃO

Os autores: VC, HS, PB, MA, MT, CB e LLS conceberam o estudo e reviram e editaram o manuscrito.
Todos os autores aprovaram a versão final a ser publicada.

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