

## CASE REPORT

# Malignant granular cell tumor of the ulnar nerve: A case report of long-term follow-up and literature review

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## ABSTRACT

**Background:** The incidence of malignant granular cell tumors, representing an extremely rare Schwann cell-derived tumors with a poor prognosis, is reported to be approximately 0.2% of all malignant soft tissue tumors. We report a case of a malignant granular cell tumor originating from the ulnar nerve.

**Case presentation:** A 71-year-old woman presented with a mass in her right forearm. Magnetic resonance imaging showed a tumor with homogenous intensity of T1 and heterogeneous hyperintensity of T2, continuous with the ulnar nerve. An incisional biopsy revealed a malignant granular cell tumor, and a marginal excision of the tumor was performed. Histologically, the tumor size was 9.2 cm and consisted of eosinophilic, granular polygonal to round and spindle-shaped cells, with vesicular and prominent nucleoli, and increased mitosis. Immunohistochemically, the tumor cells were positive for S-100 protein, CD68, H3K27me3, TFE3, and SOX10 and negative for smooth muscle alpha-actin, desmin, cytokeratin AE1/3, epithelial membrane antigen, and synaptophysin. The Ki-67 positivity rate was 12%. These findings were consistent with those of other malignant granular cell tumors. In addition, no metastases or recurrence could be observed 15 years after the excision.

**Conclusion:** Surgical resection represents the standard treatment option, whereby in our case the diagnostic criteria for malignant granular cell tumors were histologically met. Patients with malignant granular cell tumors have a poor prognosis. However, no metastases or recurrence was observed in this case 15 years after surgery.

**Key Words:** Granular cell tumor, Long-term follow-up, Malignant, Ulnar nerve

## 1. INTRODUCTION

Granular cell tumors are rare and account for approximately 0.5% of all soft tissue tumors.<sup>[1]</sup> Malignant granular cell tumors are soft tissue tumors derived from Schwann cells, with a frequency of occurrence reported to be approximately 0.2% of malignant soft tissue tumors and 2% of all granu-

lar cell tumors, which is extremely rare and has metastatic capacity.<sup>[2,3]</sup> The gold standard of treatment is surgical resection, as the tumor is resistant to chemotherapy and radiation therapy.<sup>[4,5]</sup> To the best of our knowledge, 17 cases of malignant granular cell tumors arising from various peripheral nerves have been reported so far.<sup>[4,6-21]</sup> We report a case of

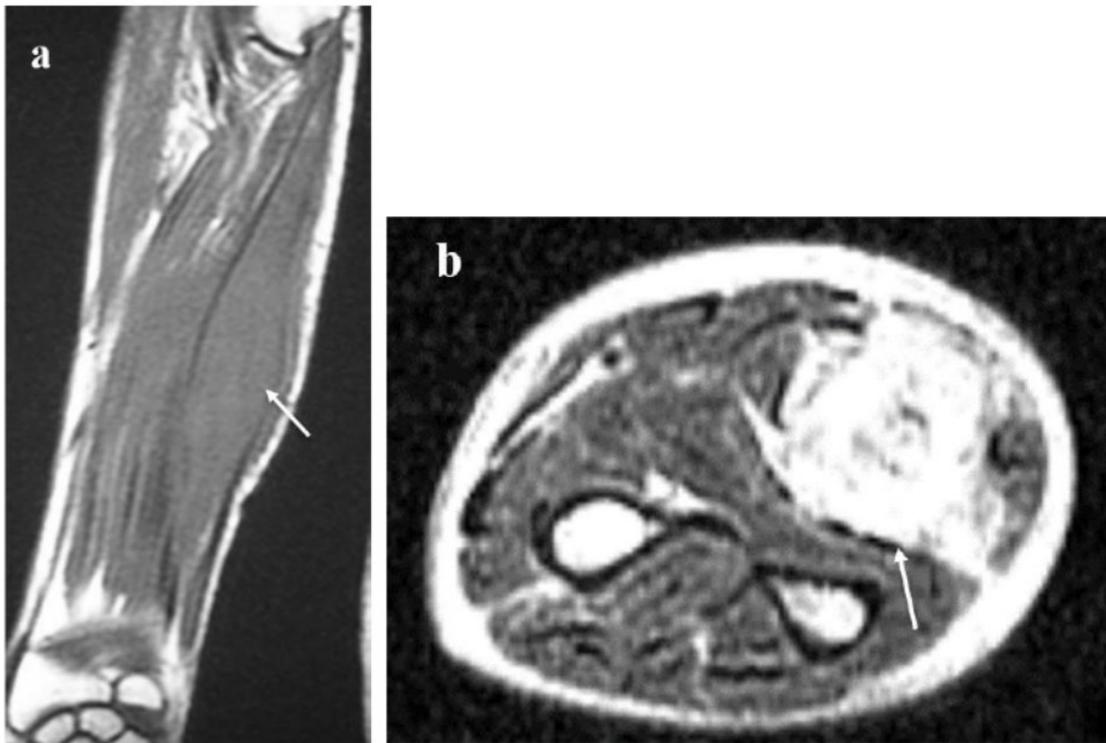
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a malignant granular cell tumor originating from the ulnar nerve with a good clinical outcome.

## 2. CASE PRESENTATION

The patient was a 71-year-old woman who noticed swelling in her right forearm and numbness in her right 4th and 5th fingers in September 2003. As the swelling gradually progressed, she consulted a doctor in May 2004. She was referred to our department because a soft tissue tumor was identified on magnetic resonance imaging (MRI). The patient's medical history included appendicitis. The mass on

the ulnar side of the right forearm was firm. There was numbness in her right 4th and 5th fingers of the ulnar nerve distribution, tenderness at the mass, and Tinel-like sign. There was no warmth or erythema, and the mass was immobile. Radiographs showed a swelling of the soft tissue on the ulnar side of the right forearm, whereby no calcifications were observed. MRI showed a tumor with homogenous intensity of T1 and heterogeneous hyperintensity of T2, continuous with the ulnar nerve. There was gradual enhancement of the mass on MRI with contrast and moderate accumulation on thallium scintigram(see Figure 1).

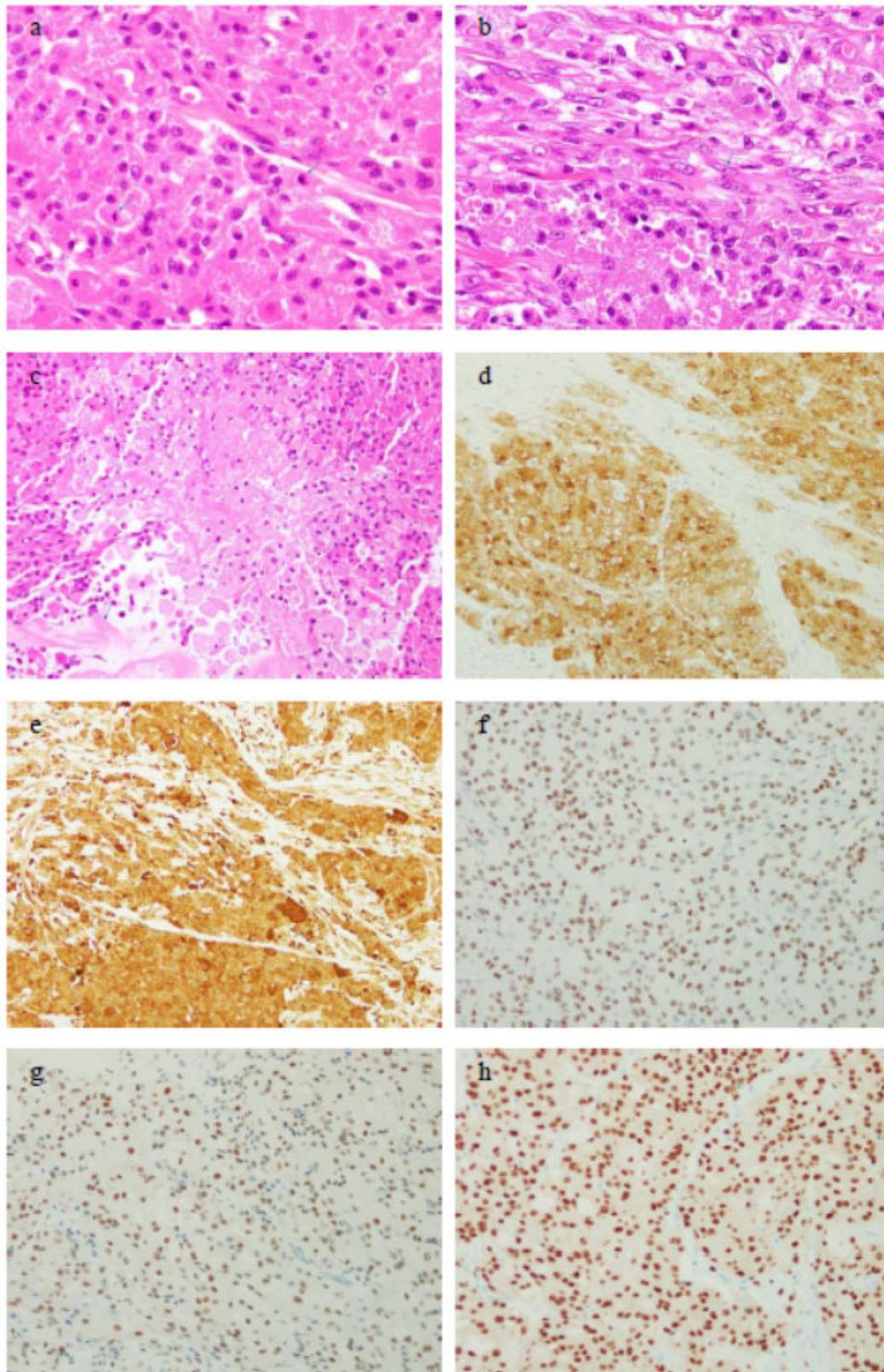


**Figure 1.** MRI from previous hospital. a. Coronal T1-weighted and b. Axial T2-weighted images. The lesion displays intermediate intensity on T1-weighted images (arrow) and high intensity on T2-weighted images (arrow).

Considering the possibility of malignant soft tissue tumors, such as a malignant peripheral nerve sheath tumor (MPNST), an incisional biopsy was performed. A malignant mesenchymal tumor, such as MPNST, as well as a malignant granular cell tumor were initially considered as a possibility upon examination of the frozen sections. The final pathology result was a malignant granular cell tumor, and tumor excision was planned. During surgery, there was a continuous tumor in the ulnar nerve. Marginal excision of the tumor was performed with a biopsy tract included in the excised tissue(see Figure 2).



**Figure 2.** Intraoperative image during marginal excision. Note that the tumor is continuous with the ulnar nerve (arrow).



**Figure 3.** a: Hematoxylin and eosin staining (HE) showing mitosis; b: HE with spindling of the tumor cells; c: HE with necrosis; d: S-100; e: CD68; f: H3K27me3; g: TFE3; h: SOX10

The tumor size was 9.2 cm in diameter and histologically consisted of eosinophilic, granular, polygonal to round, and spindle-shaped cells, with vesicular and large nucleoli, and increased mitosis (2-3/10 high-power fields) with a small necrosis area. Immunohistochemically, the tumor cells were positive for S-100 protein, CD68, H3K27me3, TFE3, and SOX10 and negative for smooth muscle alpha-actin, desmin,

cytokeratin AE1/3, epithelial membrane antigen, and synaptophysin. The Ki-67 positivity rate was 12%. These findings were consistent with those of malignant granular cell tumors. Clawing of the hand persisted after the surgery, but the patient was still able to farm. No recurrence or metastases were observed 15 years postoperatively (see Figure 3).

**Table 1.** Literature review of malignant granular cell tumor of the named peripheral nerve DOD, died of disease; NED, no evidence of disease; NA, not available; AWD, alive with disease

Case	Age, sex	Nerve, location	Size (cm)	Follow up (months)	Outcome	References
No.1	60, female	Suboccipital nerve	4	1	NED	Meling et al. [4]
No.2	34, male	Radial nerve in the upper arm	10	19	DOD	Usui et al. [6]
No.3	33, female	Laryngeal nerve in the neck	2	24	NED	Weisman et al. [7]
No.4	43, female	Sciatic nerve in the buttock	9	13	DOD	Shimamura et al. [8]
No.5	51, female	Sciatic and tibial nerve in the popliteal fossa	12	12	DOD	Saperstein et al. [9]
No.6	30, male	Fifth cranial nerve in the infratemporal fossa	10	12	AWD	Simsir et al. [10]
No.7	54, male	Radial nerve in the forearm	3	60	AWD	Sonobe et al. [11]
No.8	64, female	Tibial nerve in the leg	2.5	16	AWD	Wieczorek et al. [12]
No.9	48, female	Cervical sympathetic nerve trunk	8.6	36	NED	Hyodo et al. [13]
No.10	42, male	Lateral femoral cutaneous nerve	6	7	AWD	Tommaso et al. [14]
No.11	74, male	Ulnar nerve in the forearm	4.5	NA	NA	Papachristou et al. [15]
No.12	46, female	Brachial plexus	7.8	41	NA	Go et al. [16]
No.13	64, female	Sympathetic nerve in the posterior mediastinum	15	NA	NA	De Luca et al. [17]
No.14	14, female	Radial nerve in the forearm	1.5	10	NED	Aviles et al. [18]
No.15	51, female	C5 root	5	52	DOD	Imao et al. [20]
No.16	67, female	Median nerve in the palm	5.2	6	AWD	Tsukamoto et al. [21]
No.17	81, male	Sciatic nerve in the thigh	3.5	NA	NA	Hurrell et al. [28]
No.18	71, female	Ulnar nerve in the forearm	9.2	180	NED	Current case

### 3. DISCUSSION

To the best of our knowledge, 17 cases of malignant granular cell tumors arising from the peripheral nerve have been reported in the English literature (see Table 1).<sup>[4, 6-18, 20, 21]</sup> Only one case of an ulnar nerve-derived malignant granular cell tumors has been described.<sup>[16]</sup> The diagnostic criteria of Fanburg et al.<sup>[3]</sup> were used to distinguish between benign and malignant granular cell tumors: (1) necrosis, (2) spindling of the tumor cells, (3) vesicular nuclei with large nucleoli, (4) increased mitotic rate (>2 mitoses/10 high-power fields), (5) a high nuclear-to-cytoplasmic ratio, and (6) polymorphism.

Tumors with three or more of these features were classified as malignant granular cell tumors. Tumors with only one or two features were classified as atypical, whereas tumors with none of these features or with only focal nuclear pleomorphism were considered benign. The specimens of this case were reviewed in 2020 by a pathologist from our institution using the World Health Organization classification and the diagnostic criteria by Fanburg-Smith et al. Items (2) through (4) were applicable for this case, and which met the histological diagnostic criteria for malignant granular cell tumors. Fanburg et al.<sup>[3]</sup> reported a Ki-67 index <5% in be-

nign granular cell tumors, 5%–10% in atypical tumors, and 10%–50% in malignant granular cell tumors. Kapur et al.<sup>[22]</sup> reported similar correlations and suggested that the Ki-67 index may be useful in distinguishing malignant or atypical granular cell tumors from benign ones. The Ki-67 index rate in this case was 12%, which also indicated a malignant granular cell tumor. The differential diagnoses of malignant granular cell tumors include rhabdomyosarcoma, MPNST, and spindle cell carcinoma. Immunohistochemical staining is important for the diagnosis. Myogenic tumors show SMA positivity; MPNST shows weaker and focal expression of S100 and H3K27me3 in comparison to malignant granular cell tumors; and carcinomas more often express cytokeratins. Granular cell tumors express higher levels of TFE3.<sup>[23,24]</sup> Patients with malignant granular cell tumors have a poor prognosis with a 5-year survival rate of 60%–65%, local recurrences in about 30%, and distant metastases in about 50%.<sup>[3,25]</sup> Metastasis at the first visit, local recurrence, and tumor size > 5 cm have been reported as poor prognostic factors.<sup>[3,26,27]</sup> Moten et al.<sup>[27]</sup> reported that undergoing surgery to excise malignant granular cell tumors was associated with a significantly better 5-year survival rate than not undergoing surgery (81.9% vs. 30.7%, respectively;  $P < 0.001$ ). Chemotherapy has largely been used for locally recurrent disease or metastasis, and radiotherapy has also been used as both an adjuvant and palliative therapy.<sup>[25,26]</sup> In contrast, our patient demonstrated a prolonged survival

without signs of a recurrence or metastatic disease, although the tumor size was significantly > 5 cm in diameter.

In summary, the authors report an interesting and rare case of 71-year-old woman presenting with a mass in her right forearm, which turned out to represent a malignant granular cell tumor originating from the ulnar nerve. After surgical removal of this mass, a detailed histological, as well as immunohistological examination was performed. In contrast to most of the published reports, the respective patient demonstrated a prolonged long-term survival without signs of a recurrence or metastatic disease, although the tumor size was large. Moreover, because of the rarity of malignant granular cell tumors, this case report adds interesting information to the field of this tumor entity.

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### CONFLICTS OF INTEREST DISCLOSURE

The authors declare that they have no conflicts of interest.

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