

## Two Cases of Granular Cell Tumors that Clinically Mimicked Hypertrophic Scars and Keloids

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We report two cases of granular cell tumors (GCTs) arising on rare sites, namely, the nape and umbilicus. While GCTs have a very characteristic histology, their clinical signs and symptoms are non-specific. Therefore, it is extremely difficult to make a diagnosis of GCT on the basis of clinical findings only. The two cases reported here were clinically similar to hypertrophic scars and keloids, respectively. Skin surgeons should remember that GCTs are an important differential diagnosis from hypertrophic scars and keloids. (J Nippon Med Sch 2018; 85: 279–282)

**Key words:** granular cell tumor, subcutaneous tumors, soft tissue

### Introduction

Granular cell tumors (GCTs) are rare soft tissue tumors that were first reported by Abrikossoff<sup>1</sup> in 1926. While the differentiation of neoplastic cells has been disputed, it is now believed that GCTs differentiate towards Schwann cells<sup>2</sup>. GCTs frequently occur on the oral cavity, the skin, and subcutaneous tissue. Although GCTs are basically benign, cases with distant metastases have been reported<sup>2</sup>. Thus, it is desirable to be able to diagnose GCTs preoperatively. However, it is extremely difficult to diagnose GCTs because although they have very characteristic histopathological features, their clinical findings are generally non-specific and the incidence of GCTs is very small<sup>2</sup>. We report here two cases of GCTs that occurred in rare sites and clinically mimicked hypertrophic scars and keloids, respectively.

### Cases

#### Case 1

An 84-year-old woman presented with an intradermal tumor on her nape. The lesion had gradually grown over the preceding 2 years and was slightly painful. An examination revealed an intradermal tumor that was 3×2 cm in diameter. The skin surface of the tumor was partially and slightly red. The lesion itself was elastic and hard, and did not adhere to the underlying tissue (Fig.

1). Palpable cervical lymph nodes were not detected. The patient did not have any notable prior medical problems and her laboratory results were normal. The clinical findings suggested that the lesion could be a hypertrophic scar but it was not possible to establish a definitive clinical diagnosis. The patient underwent excision of the tumor under local anesthesia.

Histopathology of the resected specimen showed that it was a well-circumscribed intradermal nodular lesion (Fig. 2a). The tumor was composed of the cells that characterize GCTs, namely, cells with large eosinophilic granular cytoplasm and fascicles that are separated by dermal collagen bundles. Nuclear atypia was not noted (Fig. 2b). The tumor cells were positive for S-100 protein (Fig. 2c). Slight epidermal hyperplasia due to elongation of the rete ridges was noted. GCT was diagnosed on the basis of these findings.

The tumor was removed completely, and recurrence was not observed during the two follow-up years after surgery.

#### Case 2

A 54-year-old woman presented with an umbilical tumor that appeared 6 months prior to her presentation. It had grown gradually and was painful. An examination showed that the tumor was located in the skin and subcutis. It was elastic, hard, and red, and 2×2 cm in size

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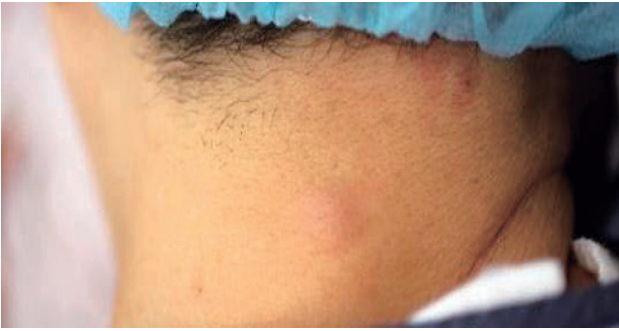


Fig. 1 Clinical findings of Case 1. The tumor was firm, partially and slightly red, and mobile. It was 3×2 cm in size and located in the dermis and subcutaneous tissue in the nape. Its margins were unclear.

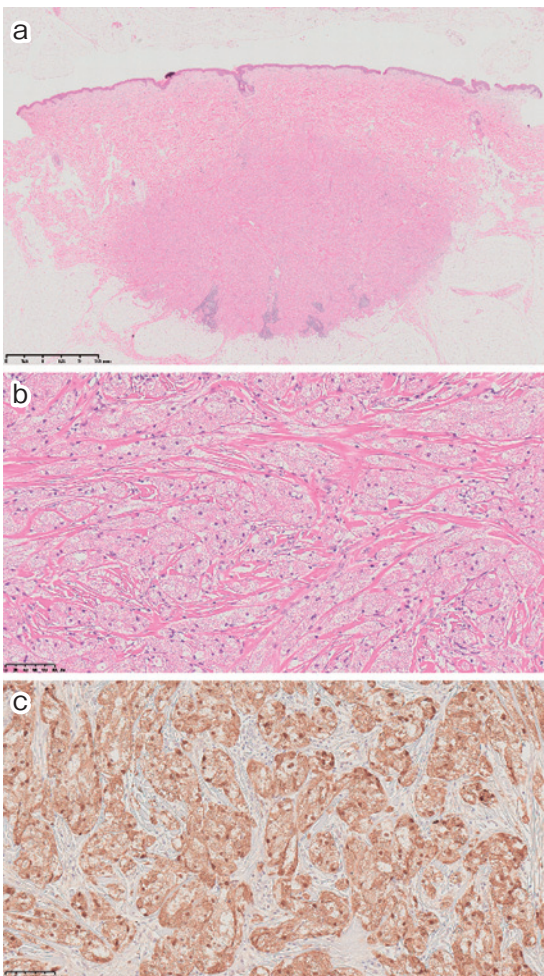


Fig. 2 Histopathological findings of Case 1. (a) The tumor was a well-circumscribed intradermal nodular lesion. (b) The tumor was composed of cells that are characteristic for granular cell tumors, namely, they had a large eosinophilic granular cytoplasm and their fascicles were separated by dermal collagen bundles. Nuclear atypia was not noted. (c) The tumor cells were positive for S-100 protein.

(Fig. 3). The patient did not have any notable medical problems. Her laboratory results were normal. The clinical findings were suggestive of a keloid. However, a definitive clinical diagnosis could not be made. The lesion was excised under local anesthesia.

Histopathology of the resected specimen showed that the tumor closely resembled the tumor in Case 1. Thus, the lesion was located in the dermis and subcutis, and it was a well-circumscribed nodular lesion (Fig. 4a) that was composed of characteristic granular cells (Fig. 4b) that expressed S-100 protein (Fig. 4c). These findings led to the diagnosis of GCT. The tumor was removed completely and recurrence over the 5 years after surgery was not observed.

### Discussion

GCTs were first reported by Abrikossoff<sup>1</sup> in 1926, who called them myoblastomas. Thereafter, various theories about the cellular differentiation of GCTs were reported: some proposed GCTs were derived from myocytes, histiocytes, or fibroblasts, while others suggested they originated from undifferentiated mesenchymal cells or epidermal keratinocytes<sup>3</sup>. Others proposed that GCTs could derive from multiple different cells<sup>4</sup>. However, GCT cells are immunohistochemically positive for S-100 protein and neuron-specific enolase. Moreover, ultrastructural observations show that they have the myelin structure and basement membrane-like structure that are also seen in neurinomas. Therefore, GCTs are now thought to differentiate towards Schwann cells<sup>3,4</sup>.

GCTs tend to be more common in females: the female to male incidence ratio ranges from 1.8:1 to 2.9:1<sup>3,5,6</sup>. Over the past 5 years, 92 cases of GCTs in Japanese patients, including ours, were newly reported<sup>2</sup>. Whereas GCT lesions are most often seen in the skin, subcutis, gastrointestinal tract, and oral cavity, they can occur anywhere in the body. Of the 92 Japanese cases of GCTs, 44 occurred in the dermis and subcutis. Of those, the majority were on the trunk (63%), followed by the limbs (21%), head and neck area (9%), and vulva (5%). None occurred on the nape or umbilicus. Similarly, a large case series in the English literature<sup>7,8</sup> reported only one case of a GCT on the umbilicus and no cases of GCTs on the nape<sup>2</sup>.

Generally, GCTs are elastic, hard, and solitary dermal and/or subcutaneous nodules that are several centimeters in diameter. The skin surface of the lesions is brown or pinkish. They are sometimes associated with spontaneous pain, tenderness, and/or itching. Their clinical appearance often resembles that of dermatofibromas,





Fig. 3 Clinical findings of Case 2. The tumor was firm, raised, pink, and mobile. It was 2×2 cm in size and located in the dermis and subcutaneous tissue of the umbilicus.

atheromas (epidermal cysts), and pilomatricomas. In our two cases, the clinical appearances were similar to those of hypertrophic scars and keloids, respectively. This is because at the histopathological level, GCTs often exhibit increased numbers of collagen fibers and epidermal hyperplasia with basal pigmentation; these findings are also often seen in hypertrophic scars and keloids. Skin surgeons should be aware that the clinical findings of GCTs can resemble those of hypertrophic scars and keloids.

Generally, the diagnosis of a GCT is only made after surgery, when the resected specimen is subjected to histopathology. This can be problematic because although GCTs are basically benign, insufficient resection can lead to local recurrence<sup>8</sup>. Moreover, there are extremely rare cases (about 2%) of GCT metastasis<sup>7</sup>. Fanburg-Smith *et al.*<sup>9</sup> proposed the following histopathological criteria for malignant GCTs: (1) many areas of necrosis, (2) prominent spindling of the tumor cells, (3) easily identifiable mitotic figures, (4) nucleolar prominence, (5) striking atypia with a marked increase in cellularity and nuclear/cytoplasmic ratio, and (6) substantial pleomorphism of nuclei. If a GCT has none or only one of these six items, it is considered to be benign, whereas GCTs with three or more items are considered to be malignant. GCTs with one or two items are considered to be heterogeneous but not malignant.

In summary, we report two cases of GCTs that occurred on rare sites and clinically mimicked hypertrophic scars and keloids, respectively. Skin surgeons should be aware that GCTs are an important differential diagnosis from keloids and hypertrophic scars.

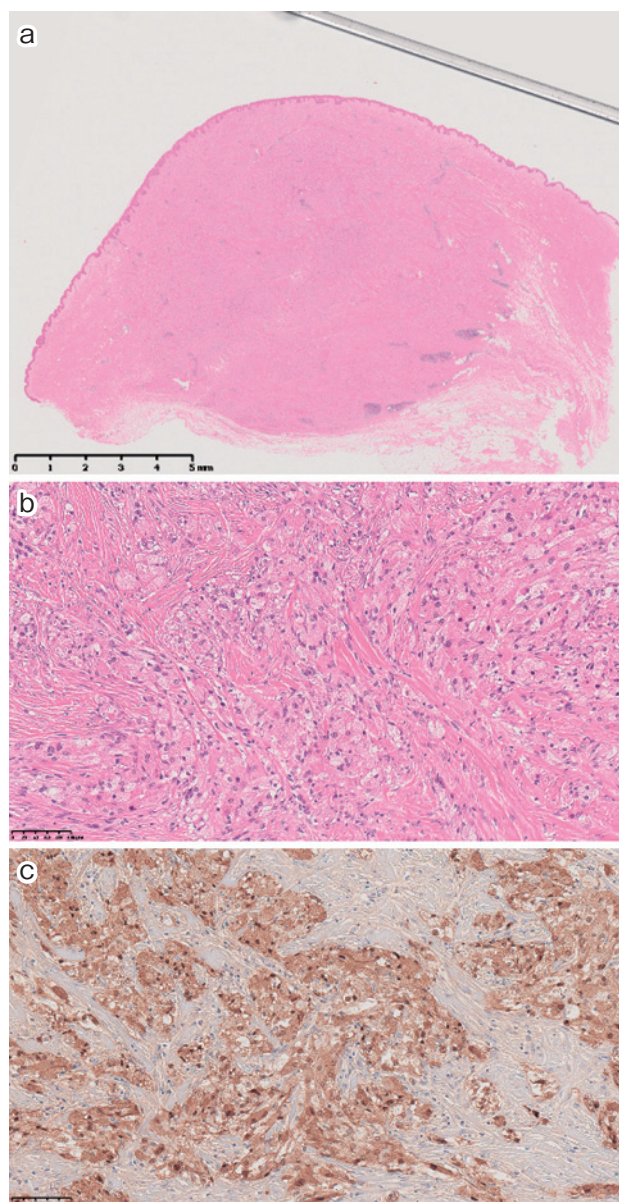


Fig. 4 Histopathological findings of Case 2. (a) The lesion was located in the dermis and subcutis, and was a well-circumscribed nodular lesion. (b) The tumor was composed of characteristic granular cells that (c) expressed S-100 protein.

**Conflict of Interest:** None declared.

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