Yonsei Medical Journal
Vol. 48, No. 4, pp. 727-730, 2007

Granular Cell Tumors of the Abdominal Wall

Jung-Suk An,[1] Sun-Hee Han,[1] Sung-Bae Hwang,[2] Ju-Han Lee,[1] Byung-Wook Min,[2] Jun-Won Um,[2] Eung-Seok Lee,[1] Heum-Rye Park,[1] and Young-Sik Kim[1]

Departments of [1]Pathology, and [2]General Surgery, Ansan Hospital, Medical College, Korea University, Ansan, Korea.

Granular cell tumors (GCT) are found in virtually any body site, including the tongue, skin, subcutaneous tissue, breast, rectum and vulva. However, they are rarely seen in the abdominal wall. We report here on a rare case of GCT in the rectus muscle of the abdominal wall. A 44-year-old woman presented with a non-tender, hard mass in the right lower abdominal wall. Upon microscopic examination, the tumor was found to comprise of large polygonal cells with an abundant eosinophilic granular cytoplasm and round to oval nuclei. Upon immunohistochemical staining, the large cells showed S-100 and CD68 positive granular aggregates in the cytoplasm. Many lysosomes of variable size were observed in the cytoplasm.

Key Words: Granular cell tumor, abdominal wall, ultrastructure

INTRODUCTION

Granular cell tumors (GCT) were first described in the skeletal muscle of the tongue by Abrikossoff as "myoblastic myomata" in 1926.[1] The histogenesis of these tumor is still rather controversial, but its immunohistochemical and ultrastructural features have been accepted as neural or neuroectodermal in origin.[2-4] Most granular cell tumors are benign, but a rare malignant variant has been documented.[5] GCTs can occur in patients of any age, but they are more common during the fourth to the sixth decades of life and are rare in children. The tongue is the single most common involved anatomic site, but GCTs can be found in virtually any body site, including the skin, subcutaneous tissue, breast, rectum and vulva.[6] GCT develops rarely in the abdominal wall, and to the best of our knowledge, only six cases of abdominal wall GCTs have been reported in the English literature.[5,7-10] We report a rare case of GCT arising in the rectus muscle of the abdominal wall.

Received May 16, 2006
Accepted July 13, 2006

Reprint address: requests to Dr. Ju-Han Lee, Department of Pathology, Ansan Hospital, College of Medicine, Korea University, 516 Gojan-dong, Danwon-gu, Ansan-si, Gyeonggi-do 425-707, Korea. Tel: 82-31-412-5321, Fax: 82-31-412-5324, E-mail: repath@korea.ac.kr

CASE REPORT

A 44-year-old female patient presented with a four-month history of a non-tender, hard mass in her right lower abdominal wall. She had no previous history of any significant illness. Ultrasonography revealed a well-defined, hypoechoic mass in the rectus muscle of the abdominal wall. Abdominal computed tomography (CT) defined a 3.6 × 2.5 cm sized ovoid mass in the right rectus muscle. The preoperative surgeon's diagnosis was desmoid tumor, and the mass completely excised. Upon gross examination, the mass was poorly demarcated from the surrounding skeletal muscle tissue and measured 3.6 cm across its largest dimension. The cut surface showed a solid grayish-white appearance with focal fibrotic changes (Fig. 1). The tumor was composed of large polygonal cells arranged in cord or sheets; these were divided by slender fibrous tissue septa which were interdigitated with the surrounding skeletal muscle fibers. Lymphoid aggregates were noted at the periphery of the tumor. The large cells had an abundant eosinophilic granular cytoplasm and poorly defined cellular borders (Fig. 2). The nuclei were round to oval with small nucleoli. There was no significant cytologic atypia; mitotic features and necrosis were not observed. The granules in

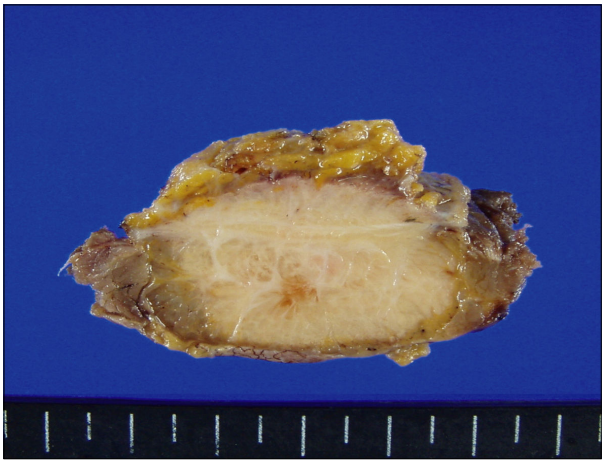

Fig. 1. Upon gross examination, the cut surface of the mass shows a solid grayish-white appearance with focal fibrotic changes. This mass is poorly demarcated from the surrounding skeletal muscle tissue.

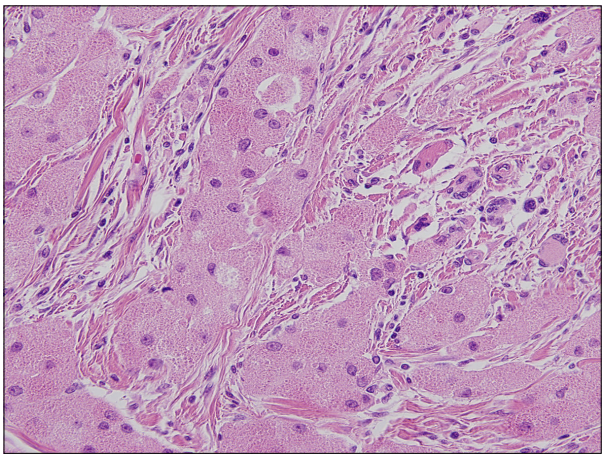

Fig. 2. Upon microscopic examination, the tumor is composed of large polygonal cells arranged in cord or sheets that are divided by slender fibrous tissue (H&E, ×400).

the cytoplasm were positive for Periodic acid Schiff (PAS) staining. Upon immunohistochemical staining, the granular cytoplasm was strongly reactive for S-100 protein (Fig. 3), CD68 and calretinin, but was negative for c-kit, CD34, smooth muscle actin, desmin and vimentin. Ultrastructural examination revealed numerous membrane-bound vacuoles in the cytoplasm that were presumably lysosomes, which were filled with electron-dense materials, fragmented rough endoplasmic reticulum and myelin components (Fig. 4).

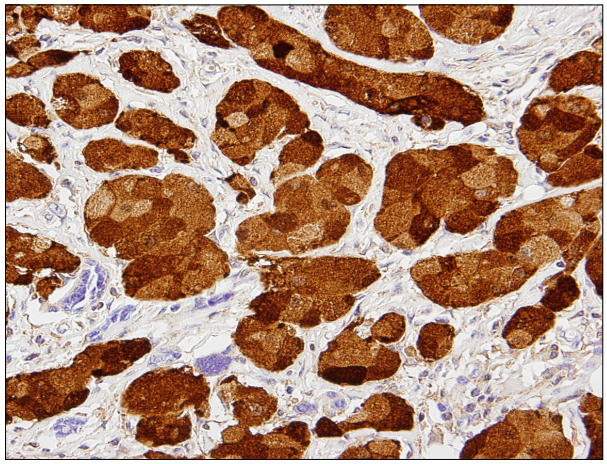

Fig. 3. Upon immunohistochemical staining, the granular cytoplasm is strongly reactive for S-100 protein (× 200).

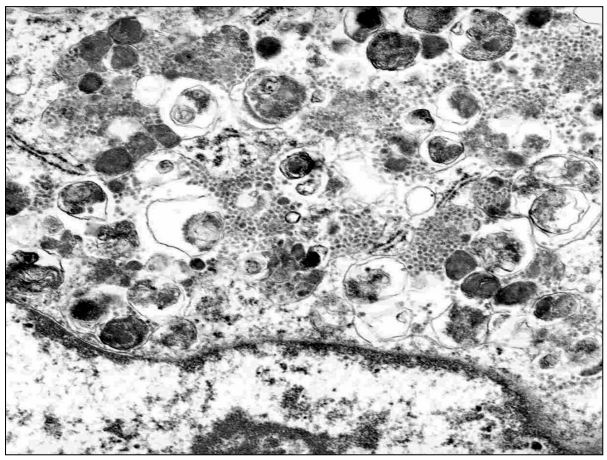

Fig. 4. Ultrastructurally, the cytoplasm shows numerous membrane-bound vacuoles, presumably lysosomes, which are filled with electron-dense materials, such as fragmented rough endoplasmic reticulum and myelin components.

DISCUSSION

Granular cell tumors (GCT) are rare and almost always benign. It usually develops as a painless mass, and most patients present with a mass as the primary symptom. GCT occurs in a wide variety of visceral and cutaneous sites, yet finding this lesion in the abdominal wall is rare. Gorelkin et al.[7] first described GCT in the abdominal wall. We found only six case reports of GCTs in the abdominal wall in the medical literature (Table 1).[5,7-10]

GCTs are characterized by large polygonal

Table 1. Characteristics of Reported Granular Cell Tumors of the Abdominal Wall Since 1978

Authors (yr)	Sex	Age (yrs)	Tumor size (cm)	Nature
Gorelkin L et al. (1978)	Female	58	8	Benign
Vamsy CM et al. (1992)	Female	30	9	Malignant
Fanburg-Smith JC et al. (1998)	Female	49	11	Malignant
Fanburg-Smith JC et al. (1998)	Male	32	5.5	Malignant
Joshi AH et al. (2003)	Male	37	2.7	Benign
Chelly I et al. (2005)	Female	67	6	Malignant

tumor cells with an abundant granular cytoplasm and relatively small nuclei. The granules in the cytoplasm are PAS-positive and diastase-resistant. The tumor cells may on rare occasion show a moderate degree of the nuclear atypism. The cells are arranged in nests or cords separated by fibrous connective tissue. The periphery of the tumor is not sharply defined, and this creates an appearance of infiltration that is highlighted when lymphoid tissue envelops the tumor cells. When a GCT lies immediately beneath the skin or mucosa, marked acanthosis or pseudoepitheliomatous hyperplasia may be present in the overlying epithelium. In such cases, the lesion may be mistaken for squamous cell carcinoma.[6,11]

The tumor cells show strong cytoplasmic and nuclear staining for S-100 protein and are positive for CD68, neuron-specific enolase and myelin basic protein, although they lack expression of neurofilament protein and glial fibrillary acidic protein.[4,12] The positive immunoreactivity for CD68 may be a reflection of the intracytoplasmic accumulation of phagolysosomes, but this does not imply a histiocytic origin for this tumor.[12] Ultrastructurally, the tumor cells vary in size and are separated by bands of collagen and fibroblasts. The cytoplasm contains many large lysosomes with various cellular debris, such as myelin components, remnants of mitochondria and fragmented rough endoplasmic reticulum.[5,11] These lysosomes confer the cytoplasmic granularity observed on light microscopy.

Abrikossoff et al.[1] postulated a myogenic origin for these tumors. This hypothesis is supported by a morphological similarity between granular cells and skeletal muscle cells. The histogenesis of these tumors is still rather controversial, but the ultrastructural features, the immunohistochemical reactivity with S-100 protein and its relationship with peripheral nerves favor a neural or neuroectodermal origin.[2-4]

The differential diagnosis of GCT includes rhabdomyoma, hibernoma, oncocytoma, extragastrointestinal stromal tumor (EGIST), and the reactive changes associated with trauma and injury. The histologic characteristics and reactivity toward S-100 and CD68 distinguish GCT from rhabdomyoma, which contains glycogen and hibernoma, which in turn contains lipid droplets. Ultrastructurally, the lack of mitochondria differentiates GCT from oncocytoma. GCTs can mimic gastrointestinal stromal tumors with epithelioid cells. The negative reaction to c-kit and CD34 distinguish GCT from EGIST. The inflammatory cells and areas of necrosis in the reactive change from trauma and injury are absent in GCT. The frozen section diagnosis of GCT can be difficult. Diagnosis based on frozen sections is problematic in general, e.g. one-third of frozen section diagnoses are erroneous in the breast.[13] The infiltrating character of this lesion and the blurred cytoplasm contours are most often suggestive of carcinoma. As such, the awareness of this entity can lead to the appropriate treatment.

Generally, GCT is benign, but complete excision has been recommended to prevent recurrence.[6] The prognosis of GCT is very good in most cases, except for the rare malignant cases. Malignant GCTs are encountered in only 2% of the cases. They are characterized by necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity (>2 mitoses/10 fields at $200\times$

magnification), a high nuclear to cytoplasmic (N : C) ratio, and pleomorphism.[5] The prognosis of malignant GCT is poor due to local recurrence and metastasis. Interestingly, four cases of malignant GCTs of the abdominal wall have been reported. However, only two cases of benign GCTs of this site were reported (Table 1). Therefore, careful histopathologic examination is recommended in the case of GCT of the abdominal wall. Our case showed the typical pathological features of GCT, and it exhibited only focal pleomorphism, while it met none of the other criteria for malignant GCT.

We describe here a rare case of GCT that occurred in the rectus muscle of the abdominal wall. This is the first reported Korean case and only the seventh case in the literature. We expect that this report will play a role in understanding the characteristics of GCT and for helping to correctly diagnose this disease.

REFERENCES

1. Abrikossoff A. Über myome, ausgehend von der quergestreiften willkürlichen muskulatur. Virchows Arch 1926;260:215-33.
2. Fisher ER, Wechsler H. Granular cell myoblastoma–a misnomer. Electron microscopic and histochemical evidence concerning its Schwann cell derivation and nature (granular cell schwannoma). Cancer 1962;15:936-54.
3. Altavilla G, Brotto M, Busatto G, Boccu C, Ragni L. Granular cell tumor of the intrapancreatic common bile duct: one case report and review of the literature. Ultrastruct Pathol 2004;28:171-6.
4. Mazur MT, Shultz JJ, Myers JL. Granular cell tumor. Immunohistochemical analysis of 21 benign tumors and one malignant tumor. Arch Pathol Lab Med 1990;114:692-6.
5. Fanburg-Smith JC, Meis-Kindblom JM, Fante R, Kindblom LG. Malignant granular cell tumor of soft tissue: diagnostic criteria and clinicopathologic correlation. Am J Surg Pathol 1998;22:779-94.
6. Lack EE, Worsham GF, Callihan MD, Crawford BE, Klappenbach S, Rowden G, et al. Granular cell tumor: a clinicopathologic study of 110 patients. J Surg Oncol 1980;13:301-16.
7. Gorelkin L, Costantino MJ, Majmudar B. Granular cell tumor of the abdominal wall musculature. South Med J 1978;71:857-8.
8. Vamsy CM, Smile SR, Ratnakar CR, Veliath AJ. Malignant granular cell tumour. A case report and review of literature. Indian J Cancer 1992;29:31-3.
9. Chelly I, Bellil K, Mekni A, Bellil S, Belhadjsalah M, Kchir N, et al. Malignant granular cell tumor of the abdominal wall. Pathologica 2005;97:130-2.
10. Joshi AH, Aqel NM. Educational case report-self assessment. An anterior abdominal wall tumour. Cytopathology 2003;14:172, 221-2.
11. Ordóñez NG, Mackay B. Granular cell tumor: a review of the pathology and histogenesis. Ultrastruct Pathol 1999;23:207-22.
12. Filie AC, Lage JM, Azumi N. Immunoreactivity of S100 protein, alpha-1-antitrypsin, and CD68 in adult and congenital granular cell tumors. Mod Pathol 1996;9:888-92.
13. Lellé RJ, Park H, Brow CA. Benign granular cell tumor mimicking carcinoma of the breast. Report of a case. Eur J Gynaecol Oncol 1992;13:390-3.