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Case Report

Malignant granular cell tumor of the multifidus muscle: Case report and review of the literature

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ABSTRACT

Granular cell tumors (GCTs) are uncommon soft tissue tumors characterized by cytoplasmic granular appearance of the neoplastic cells. Malignant GCTs comprise less than 2% of GCTs and are mostly found in the subcutaneous soft tissues of the lower extremities, especially the thighs. This report presents a case of malignant granular cell tumor in the right multifidus muscle. A 69-year-old woman presented to the surgeon with a 3 month history of light pain in the lumbar area and hip joint, with no particular history. CT and MRI revealed a soft tissue tumor with a maximum diameter of 7.5 cm. There is patchy unenhanced hypointense shadow in the mass. Widely excision was performed for the primary tumor, which was interpreted as an malignant GCTs. GCTs should be considered in the differential diagnosis in a rapidly growing intramuscular tumors. We investigated the CT and MRI findings of malignant granular cell tumor.

Introduction

Granular cell tumors (GCTs) were first described in 1926 by Abrikossoff et al [1], GCTs is a rare tumor with the incidence of 0.019%-0.03%. The presence of S100 protein, a Schwann-cell marker, suggested its neurogenic origin [2]. Although most GCTs had the excellent outcomes after surgical resection, less than 2% of GCTs was malignant [3].

Malignant GCTs had a wide anatomic distribution and carried a poor prognosis, with the recurrence or metastasis typically within one year after diagnosis. Malignant GCTs located in the sacrococcygeal muscles has not been reported in the literature. Here we reported a case of malignant GCTs showing an uncommon localization in the right multifidus muscle with the complete imaging data and reviewed the literature.

Case presentation

A 69-year-old woman presented to the surgeon with a three-month history of light pain in the lumbar area and hip joint, with no particular history. There were not fever, chills or

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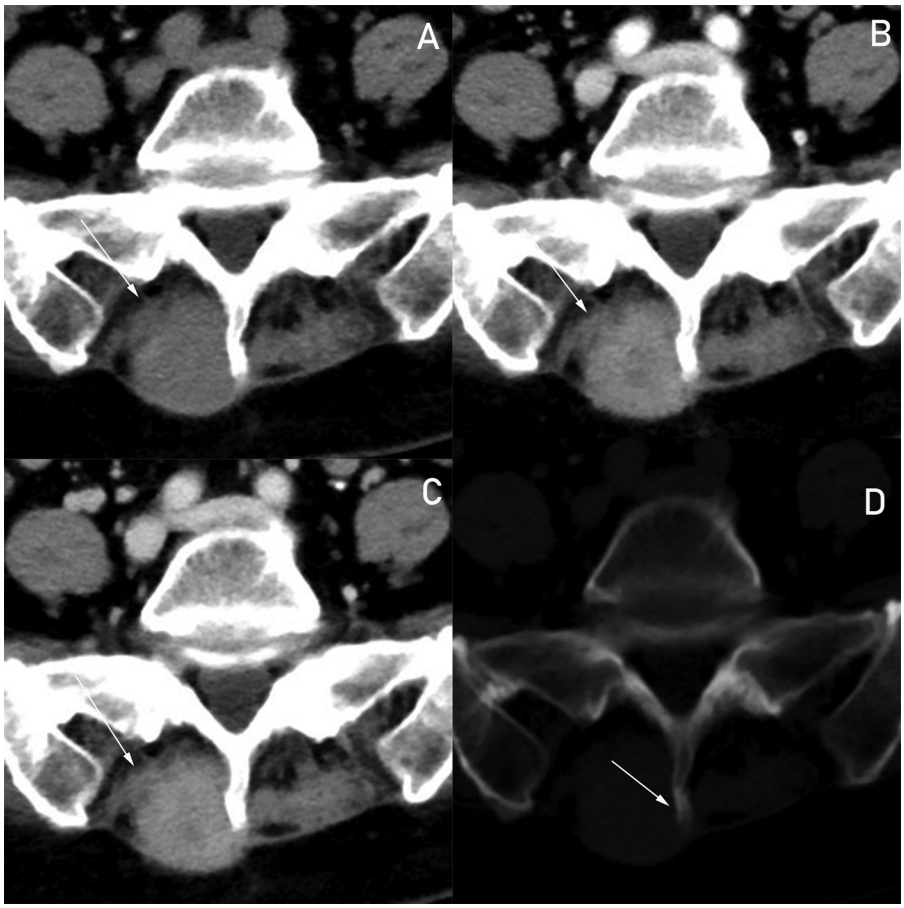

Fig. 1 – Axial CT demonstrating a homogeneous solid mass (arrow) in the right multifidus muscle (A), After the injection of contrast, the mass was shown the obvious heterogeneous enhancement, and the low-density area with mild enhancement was seen in the center of mass (B, C). There is no osseous involvement (D) .

weight loss. Specialized examination: proneness to 60 degrees, back stretch 10 degrees, 10 degrees on the left side of the bend, the right side of the bending of 10 degrees, cervical test (-), abdominal sign (-), the straight leg-raising test on the left side of 45 degrees and on the right side of 50 degrees, 4 word test (-), femoral nerve pull test (-), mild tenderness near the spinous process of lumbar 4, taps pain (+), the left lateral crus hypoesthesia, muscle strength, normal bilateral knee tendon reflex (+ +), achilles tendon reflex (+ +), pathological reflex did not elicit . Tumor marker evaluation included, Carbohydrate antigen 242(CA 242), Carbohydrate antigen 50(CA 50), Carbohydrate antigen 72-4(CA 72-4), Carbohydrate antigen 15-3(CA 15-3), Carbohydrate antigen 19-9(CA 19-9), Carbohydrate antigen 125(CA 125), Cytokeratin 19 fragment (CYFRA21-1), Neuron-specific enolase (NSE), Human epididymal protein 4(HE 4), Squamous cell carcinoma antigen (SCC), AFP, and Carcinoembryonic antigen (CEA), all of which were normal.

Computed Tomography (CT, Philips Brilliance iCT, Shanghai, China) scan showed a homogeneous solid mass with the size of 3.2 cm**X**7.5 cm was shown in the right multifidus muscle, with the clear demarcation. There was no calcification in the mass and the CT value without contrast was 55 HU. After the injection of contrast, the mass was shown the obvious heterogeneous enhancement, and the low-density area with mild enhancement was seen in the center of mass. CT value after enhancement were 61-85 HU in the arterial phase and 67-95 HU in the venous phase. The lesion compressed the surface of the sacrum bone without infiltration and the sacrum bone was compressive sclerosis. (Fig. 1).

Magnetic resonance imaging (MRI, Siemens Skyro, Shanghai, China) scan of the lumbosacral region was performed using the spine coil. The saggital T1WI, T2WI, STIR sequence, and the axial fat-saturated T2WI sequence were acquired. Then, the contrast-enhanced MRI was performed with an intravenous administration of 30 mL gadolinium (at a speed of 2.0 ml gadolinium per second). Finally, the axial and sagittal T1WI sequences with fat suppression were carried out.

The lesion (Fig. 2) was located in the right multifidus muscle at the level of lumbar 4 to sacral 3. On T1WI, inhomogeneous isointense to the skeletal muscle were observed, and patchy hypotense was observed. STIR shows inhomogeneous and slightly high signal intensity, while low signal intensity is patchy. After enhancement, the tumor showed obvious heterogeneous enhancement and lamellar unenhanced low signal.

The tumor was widely excised. At surgery, the lumbosacral posterior midline incision was made at sacral 1 as the center. The tumor was located behind the vertebral body of the

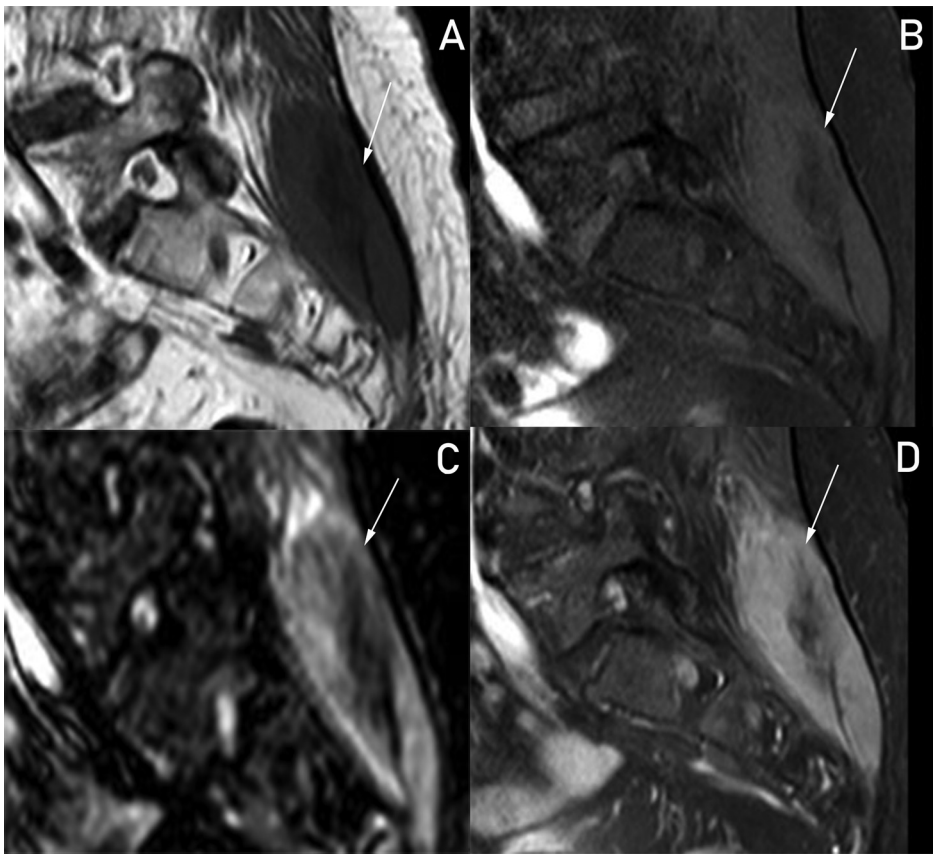

Fig. 2 – (A–D). Sagittal MRI show the intramuscular location of the mass. (A) An saggtial T1WI image shows the tumor with a signal isointense to the skeletal muscle (B) The mass shows a hyperintense heterogeneous signal intensity on T2-weighted sequences, is (C) isointense to skeletal muscle on T1-weighted fat-saturated images, and (D) shows obvious heterogeneous enhancement with contrast.

L4-S3 vertebrae, within the right multifidus muscle, with hard texture and unclear boundary. The surrounding muscle tissue was infiltrated, and no vertebral body and spinous process bone destruction was observed. The tumor tissue had no complete capsule and abundant blood supply.

On the frozen-section examination, the tumor was with the greatest dimension of 7.5 cm, yellowish gray in section and slightly tough. Histological study showed that the eosinophilic tumor with large cell volume, heteromorphic, rich in cytoplasm, acidophilic, enlarged in nucleus, with obvious nucleoli, and local nuclear division like 2 of 10 HPF. There was not definite invasion of the nerves, vessels and adjacent bone tissue. (Fig. 3). Immunohistochemical study showed positive in S100 protein, SOX-10, MDM2 and Bcl-2, and negative in Desmin, MyoD1, Myogenin, CD99, Syn, CK-pan, CD34, ERG and CD163. Proliferative activity (Ki 67) was high as more than 10% (Fig. 4).

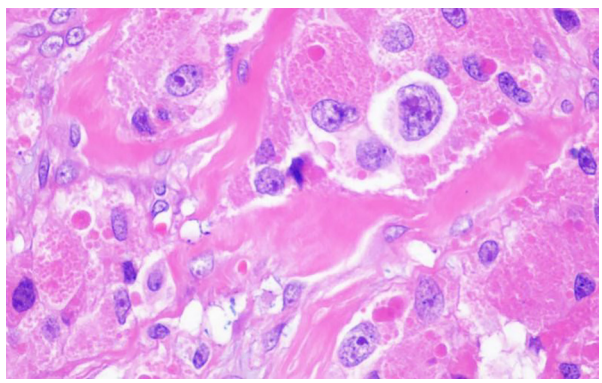

Fig. 3 – High-power hematoxylin and eosin stained-micrograph of tumor showing pleomorphic nuclei, elevated nuclear and/or cytoplasmic ratio, and spindled tumor cells (X400) .

Discussion

GCTs were first described in 1926 by Abrikossoff et al [1]. At first, GCTs had been considered to arise from Schwann cells, histiocytes, fibroblasts, myocytes or intestinal mesenchymal cells. Lack et al were the first authors to use the term "granular cell tumor" [4]. Based on the positive results of S-100 protein in the tumors, it is believed that GCTs arise from Schwann cells or neural tissue. On pathological examination they can be identified by both microscopic and immunohistochemi-

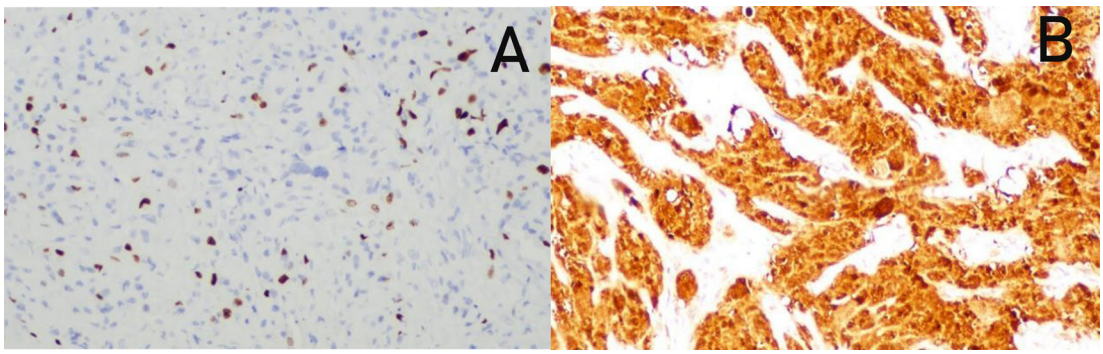

Fig. 4 – (A–B) A S100 positive. The neoplastic cells are strongly and diffusely immunore-active with S-100 protein, showing nuclear and cytoplasmic staining (X100) . B Ki-67 stain showing an area of high proliferative activity manifested by nuclear staining involving >10% of cells (X100) .

cal features. The cells of tumor had a distinctive granular eosinophilic cytoplasm associated with typical nuclei [5].

GCTs are rare and have been reported in many different locations, which are more common in the head and neck region, skin or subcutaneous tissue and less common in the breast, thyroid, mediastinum, respiratory tract and gastrointestinal tract [5]. GCTs occurring in deep soft tissues are extremely rare, especially those in the intramuscular area [6,7]. Some reports described that the incidence of GCTs in females were twice as high as in males [8], but a larger epidemiological study of 263 patients showed that most GCTs occurred in males (68 %) [9]. The lesion most frequently occured in the fourth to sixth decades and was rare in children [10].

Malignant GCTs are rare, aggressive neural tumors that were first reported by Ravich et al [11] in 1945. These tumors were accounted for 0.5%-2% of all GCTs [3]. Malignant GCTs were similar in epidemiology to their benign counterparts and usually presented as painless masses [12]. The 2 distinct clinical characteristics of malignant granular cell tumors were larger average size as a median size of 4.0 to 5.0 cm and frequent localization to the lower limbs [13–16]. Thus, the following factors in patients were highly indicative of the malignancy of tumor: a tumor that was large (the diameter more than 5.0 cm), deep location (intramuscular) at the lower extremities and showed rapid recent growth, local recurrence and distant metastasis, and the elder patients and female patients were another rich factors [13,17] Due to the difficulties to diagnose malignant GCTs, Fanburg-Smith et al [17]. proposed the following histological criteria in order to differentiate the benign from malignant tumors: necrosis, spindling, vesicular nuclei with large nucleoli, nuclear pleomorphism, high nuclear to cytoplasmic ratio, and increased mitotic activity (>2 mitoses/10 high-power fields). Neoplasms that met three or more of these criteria were classified as malignant. Although Fanburg-Smith criteria could be used to diagnose malignant GCTs. However, it should be noted that these histological features were subjective and might be pathologist-dependent [15]. Malignant GCTs with distant metastases had been reported. The common sites for metastasis were the lungs, lymph nodes and bones [18]. Nasser et al [19] considered metastases as the only definitive criterion of malignancy regardless of the histopathologic features. Thus, the diagnosis of a malignant GCTs required the evaluation of both the clinical findings and histological results [20].

In the present case, the tumor cells showed large volume, enlarged in nucleus, with obvious nucleoli, and local nuclear division like 2 of 10 HPF. Staining for Ki-67 showed a high proliferation index of more than 10%, so malignant GCTs was confirmed.

Preoperative imaging examination was helpful to distinguish this tumor from other soft tissue tumors based on some characteristic findings [15,18,21-24] CT scan could offer important information to reveal the regional involvement and identify the distant metastases [5]. But at present, only a few literatures had described the CT manifestations of malignant GCTs. JOHN et al [21] reported a case of malignant GCTs located in the short head of the right biceps femoris muscle, and the lesion was demonstrated as a heterogenous soft tissue mass. Positron emission tomography (PET)-CT demonstrated no additional abnormal fludeoxyglucose up-take. In this case, the enhanced CT presented an inhomogeneous soft-tissue mass with patchy, unenhanced low-density areas in the center of tumor. The lesion was close to the sacrum, which showed the characters of compression and absorption and no involvement. This was similar to the malignant GCTs performance reported by JOHN et al [21]. Therefore, it was difficult to judge benign and malignant lesions from CT appearances alone.

MRI played an important role in diagnosis and making preoperative plan for the treatment of this neoplasm [22] There have been a few reports of MR images of benign and malignant granular cell tumors of the extremities and the trunk [15,16,24]. Mihir et al [18] reported a patient with a histologically benign tumor in the left gluteal musculature which metastasized to the lung later. The mass was heterogeneously slightly high signal relative to skeletal muscle and the posterior part of the mass showed a spoke-wheel fashion from a central round area of intermediate signal on T1WI. T2WI showed intermediate signal intensity and two concentric rings of higher signal in the posterior part of the mass. They also reported another malignant GCTs which showed heterogeneous hyperintense signal on T2WI, slightly hyperintense to skeletal muscle on T1WI with fat-saturation and mild homogeneous enhancement with contrast. MRI description of some of the neoplasms in the report by Marcia et al [15] states that

masses often was either higher than or isointense to the adjacent muscle on T1WI, the single malignant lesion was deep in location, frankly infiltrating the adjacent bone. Our case subject showed isointense to the skeletal muscle on T1WI, consistent with the above report. Toshihisa et al [23] presented a case of malignant granular cell tumor in the deltoid muscle, and the tumor showed heterogeneously low to intermediate intensity on both T1WI and T2WI. After the administration, the tumor demonstrated heterogeneous enhancement. Meanwhile, they emphasized the correlation between imaging and pathological findings. They found the intermediate-intensity areas on T2WI were obviously enhanced after gadolinium administration, low–intensity areas on T2WI were shown no enhancement, which was histologically correlated with a cellularity and abundant collagen. Our patient presented lower signal intensity than fat tissue, but slightly higher than muscle tissue on T2WI. Low–intensity areas on T2WI were non-enhanced, which was accordant with the report of Toshihisa et al [23].

The definitive features of malignant GCTs were not present. On CT, this case presented as a homogeneous soft tissue mass with well-defined boundaries and only a hypodense area in the center of the enhanced lesion. Adjacent bones showed compressive sclerosis without destruction. On MRI, patchy low-signal areas can be seen at T1WI and T2 WI as well as after enhancement, which corresponds to low-density areas without enhancement after CT enhancement, and may indicate that there are a lot of fibrous components in this area. The boundary of the lesion was not clear on T2WI, but no obvious infiltration was observed in the surrounding tissues and bone. Therefore, no matter benign or malignant GCTs, CT and MRI features had many overlaps, and malignant GCTs could also show no invasion of adjacent bones. Therefore, it was difficult to make a diagnosis of benign or malignant lesions solely based on imaging manifestations. This would need the combination of the histological manifestations and imaging characters.

There were several other distinct conditions that demonstrated the low signals on T2WI, including proliferative myositis, myositis ossificans, muscle sarcoidosis, desmoid tumor and fibrous tumors. Most tumors with a low signal on T2WI were benign, but we should still consider malignant granular cell tumor as a differential diagnosis.

In all malign and benign GCTs, the best treatment was complete resection of the mass. Although this was not always possible because of lacking a surrounding capsule or proximity to the structures such as nerves or vessels, the surgical excision with a safe and clean margin was the first choice of treatment for this tumor [8,24]. If the resection margins were involved, the wider local excision might be recommended to decrease the risk of recurrence [7]. The role of adjuvant chemotherapy and radiotherapy was uncertain, but should be considered in patients with recurrent malignant GCTs or metastatic disease [20]. So, long-term follow-up was necessary for GCTs.

In conclusion, GCTs should be considered in the differential diagnosis in a rapidly growing intramuscular tumors. In our case, we had complete radiological, morphological and immunohystochemical data to understand this rare tumor.

Declaration of Interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work. there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of the manuscript entitled.

Patient consent

The Institutional Review Board of Shuguang hospital has approved this retrospective case report, and we have obtained informed consent from the patient for the publication of this case report.

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