

Received: 2018.01.30
Accepted: 2018.03.20
Published: 2018.06.05

e-ISSN 1941-5923
© Am J Case Rep, 2018; 19: 642-650
DOI: 10.12659/AJCR.909261

First Case Report of a Huge Giant Cell Tumor of Soft Tissue Originating from the Retroperitoneum

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: This work was financially supported by Hyogo Prefectural Kakogawa Medical Center

Patient: Male, 78
Final Diagnosis: Giant cell tumor of soft tissue
Symptoms: Fatigue • weight loss
Medication: —
Clinical Procedure: Surgical resection
Specialty: Surgery

Objective: Rare disease

Background: Giant cell tumor of soft tissue (GCT-ST) is a rare disease generally generated from superficial tissue. We report an extremely rare case of giant cell tumor of soft tissue arising from retroperitoneal tissue.

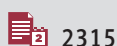
Case Report: A 78-year-old man visited our medical center with the chief complaint of fatigue and weight loss for 1 month. He had a hard and immobilized mass without pain in the left upper quadrant. Contrast-enhanced CT showed a huge tumor (22×20×16 cm) in the retroperitoneal space, and it invaded into the stomach, colon, pancreas, spleen, and left kidney. MRI demonstrated the tumor had a serous cystic component as T1 was low, T2 was high, and DWI was slightly high. We diagnosed the retroperitoneal malignant tumor, and tumor resection was performed with total gastrectomy, partial colectomy, distal pancreatectomy, left nephrectomy, and left adrenalectomy for complete resection, without any postoperative complications. The tumor predominantly consisted of a solid mass, and had necrotic lesions, cystic lesions, and calcification. The histological exam showed it was composed of spindle and multinucleated giant cells; however, there was no cellular atypia or pleomorphism. Immunohistochemical staining characterized the tumor with CD68+, SMA+, CD34-, Desmin-, and S-100-. We finally diagnosed it as GCT-ST with the intermediate group of malignancy, according to WHO criteria. Thereafter, the patient had no recurrence at 1 year after resection.

Conclusions: The huge GCT-ST arising from the retroperitoneal space, which has never before been reported, was successfully resected. We report it with pathological findings to add to the relevant literature.

MeSH Keywords: Giant Cell Tumors • Retroperitoneal Neoplasms • Soft Tissue Neoplasms

Abbreviation: CT – computed tomography; GCT-ST – giant cell tumor of soft tissue; HPF – high-power fields; MRI – magnetic resonance imaging; SMA – smooth-muscle actin; WHO – World Health Organization

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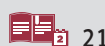
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Background

Giant cell tumor of soft tissue (GCT-ST) is generally generated from body surfaces and is classified as an intermediate malignancy due to its low risk of metastasis. In 1972, Salm and Sissons first reported GCT-ST, which clinicopathologically resembles giant cell tumor of bone [1]. In 1999, Folpe reported that some patients who were diagnosed with GCT-ST had few metastases [2]. In 2000, Oliveira suggested that patients with GCT-ST have good prognosis after complete resection [3]. The disease concept of GCT-ST was established to distinguish it from the “giant cell tumor”, which has a poor prognosis. In 2002, GCT-ST was addressed in the 3rd edition of the WHO Classification of Tumors of Soft Tissue and Bone, and was described as an independent disease in the 4th edition. GCT-ST is most likely to arise from the thighs, subcutaneous tissue, and the parotid gland, and has not been previously reported to arise from retroperitoneal tissue. Here, we provide the first report of a case of huge GCT-ST arising from retroperitoneal tissue, as well as presenting a review of the literature.

Case Report

A 78-year-old man came to our hospital with chief complaint of general fatigue and weight loss. He had been feeling fatigued for the past month. In the physical examination findings, an abdominal mass, which was hard and immobilized, was identified in the left upper quadrant, but he reported he did not feel any pain. Although he had not recognized the abdominal mass until we pointed it out based on the physical examination, he retrospectively noticed he seemed to have the mass from before. He had past history of diabetes, appendicitis, and left inguinal hernia. His diabetes was well-controlled with dipeptidyl peptidase-4 inhibitor and sulfonylureas. Blood exams showed no particular findings. The level of hemoglobin A1c was 6.2%, which was within normal range.

Abdominal contrast-enhanced CT revealed the huge irregular mass, 22×20×16 cm, surrounded with stomach, spleen, and left kidney, and it was strongly suspected that the tumor invaded the surrounding organs (Figure 1A, 1B). Additionally, the tumor had a certain low-density area suggesting degeneration or necrosis (Figure 1A3). There was no ascites, no distant metastases, and no swollen lymph nodes. On T2-weighted MRIs, the solid portion of the tumor was shown with heterogenous intermediate and slight high-intensity signal (Figure 2A1, 2A2). Cystic component was demonstrated as a low-density area in plain CT (Figure 2B1), low-intensity in T1-weighted imaging (Figure 2B2), high-intensity in T2-weighted imaging (Figure 2B3), and slightly high-intensity in DWI (Figure 2B4). These MRI findings suggested the cystic lesion of the tumor seemed to be serous content and not bleeding. Additionally, calcification in

the tumor was shown as high-density structures in plain CT (Figure 2B1). The angiography demonstrated the tumor stain from the splenic artery, inferior mesenteric artery, and left renal artery (Figure 3A–3C). The splenic artery was a main feeder artery of the tumor (Figure 3A). Additionally, the blood flow from the inferior mesenteric artery spread to the splenic flexure through the left colic artery, suggesting tumor invasion into the colon (Figure 3B). Similarly, the left renal artery was shown as a feeder artery of the caudal region of the tumor (Figure 3C). Upper gastrointestinal endoscopy revealed the exclusion at posterior wall and corpus of the stomach, whereas the colonoscopy had no significant findings of exclusion or invasion by the tumor. It was diagnosed as a malignant retroperitoneal tumor based on the radiological findings of a huge tumor in the retroperitoneal space that invaded into multiple organs, although the origin was unknown, and the symptoms of weight loss and fatigue were compatible with the diagnosis of a malignant tumor. The cause of cystic component was unclear, but it was inferred that the huge tumor might cause necrosis in the tumor due to ischemia and insufficient blood supply to feed the huge tumor. Radical surgical resection of the tumor was performed with total gastrectomy, partial colectomy, distal pancreatectomy, left nephrectomy, and left adrenalectomy due to tumor invasion. There were no findings of carcinomatous peritonitis and no swollen lymph nodes in the intraoperative findings.

The resected specimen revealed that the tumor invaded stomach, colon, pancreas, spleen, left adrenal gland, and left kidney (Figure 4A, 4B). The tumor was predominantly solid and had some large necrotic lesions (Figure 4B). It also had cystic lesions, calcification, and ossification inside. Pathological examination noted that many multinucleated giant cells were scattered, surrounded by spindle cells, and this finding was typical of GCT-ST (Figure 5A). The giant cells had little cellular atypia or pleomorphism but had grown invasively toward neighboring organs. This invasive behavior suggested the tumor had low-grade malignancy. Massive necrosis in GCT-ST is atypical and suggests that the growth in size caused ischemia in parts of the tumor. In the immunohistochemical findings, the multinucleated giant cells had strongly positive staining with cytoplasmic CD68 (Figure 5B). In addition, the tumor cells had positive staining of smooth-muscle actin (SMA, Figure 5C); however, CD34, desmin, and S-100 protein were not stained at all in the tumor. The mitotic ratio of the tumor cells was greater than 30/10 high-power fields (HPF). Ki-67 was stained at the histiocytes in the background cells, not at multinucleated cells (Figure 5D). The tumor was diagnosed as GCT-ST generated from the retroperitoneal tissue, which has never been reported before. The patient began oral intake on the third postoperative day, and he was discharged without any complications on the 18th postoperative day. To date, he is alive and has had no recurrence of GCT-ST as of 1 year after surgery.

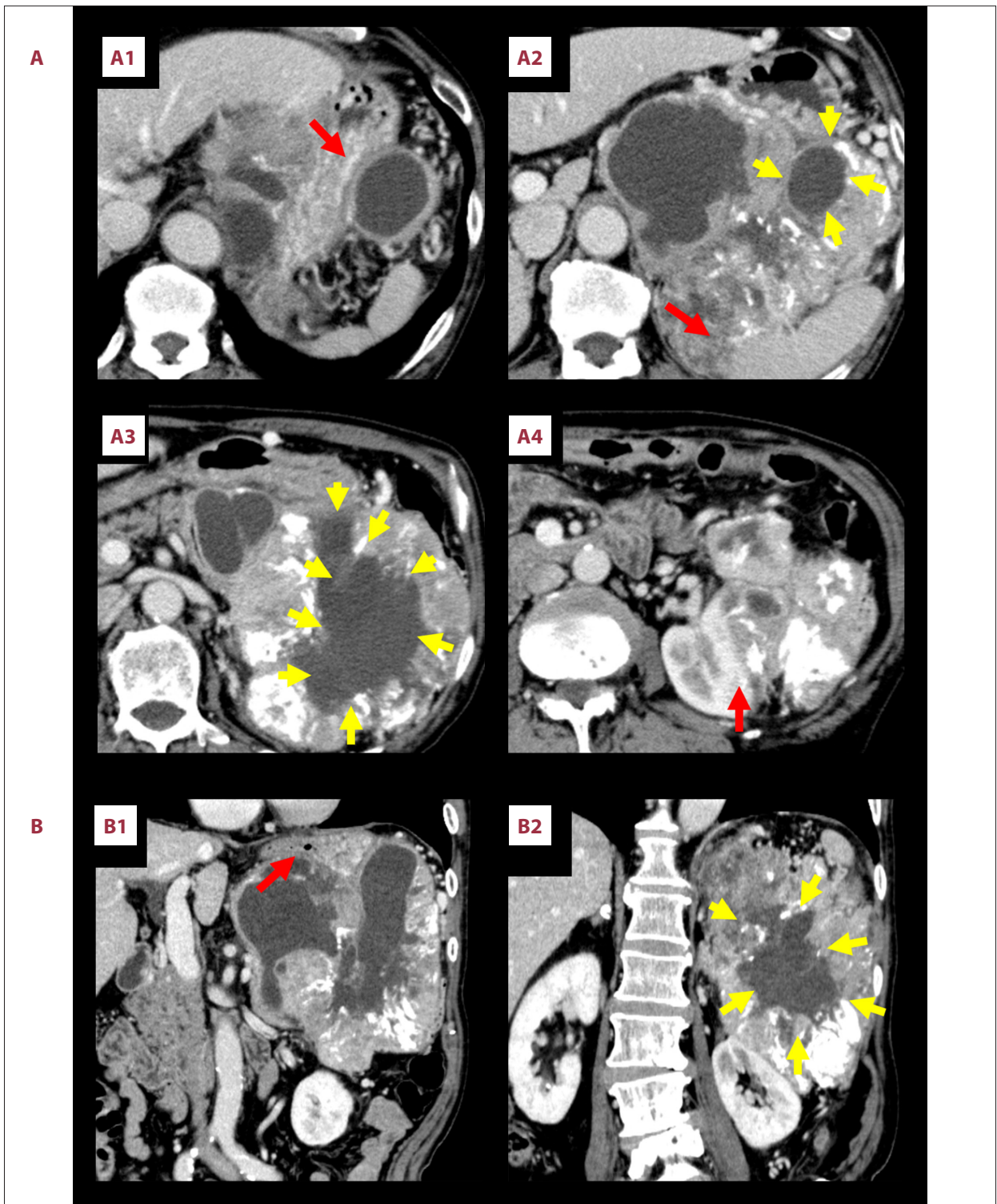


Figure 1. Radiological features of the tumor in contrast-enhanced computed tomography. (A) Axial views; the huge tumor was located in the abdominal cavity and surrounded by stomach (A1), pancreas, spleen (A2), adrenal gland, and left kidney (A4). It was rich enhanced in contrasted CT imaging (A3, A4). The low-density area shown by yellow arrows, which suggests necrosis or cystic lesions (A2, A3), existed inside the tumor. The tumor invaded to stomach (A1) and left kidney (A4), as indicated by the red arrow. (B) The tumor was demonstrated in coronal view of contrasted CT imaging. The tumor invaded to stomach pointed by red arrow (B1). The cystic lesion was pointed by yellow arrows in coronal view (B2).

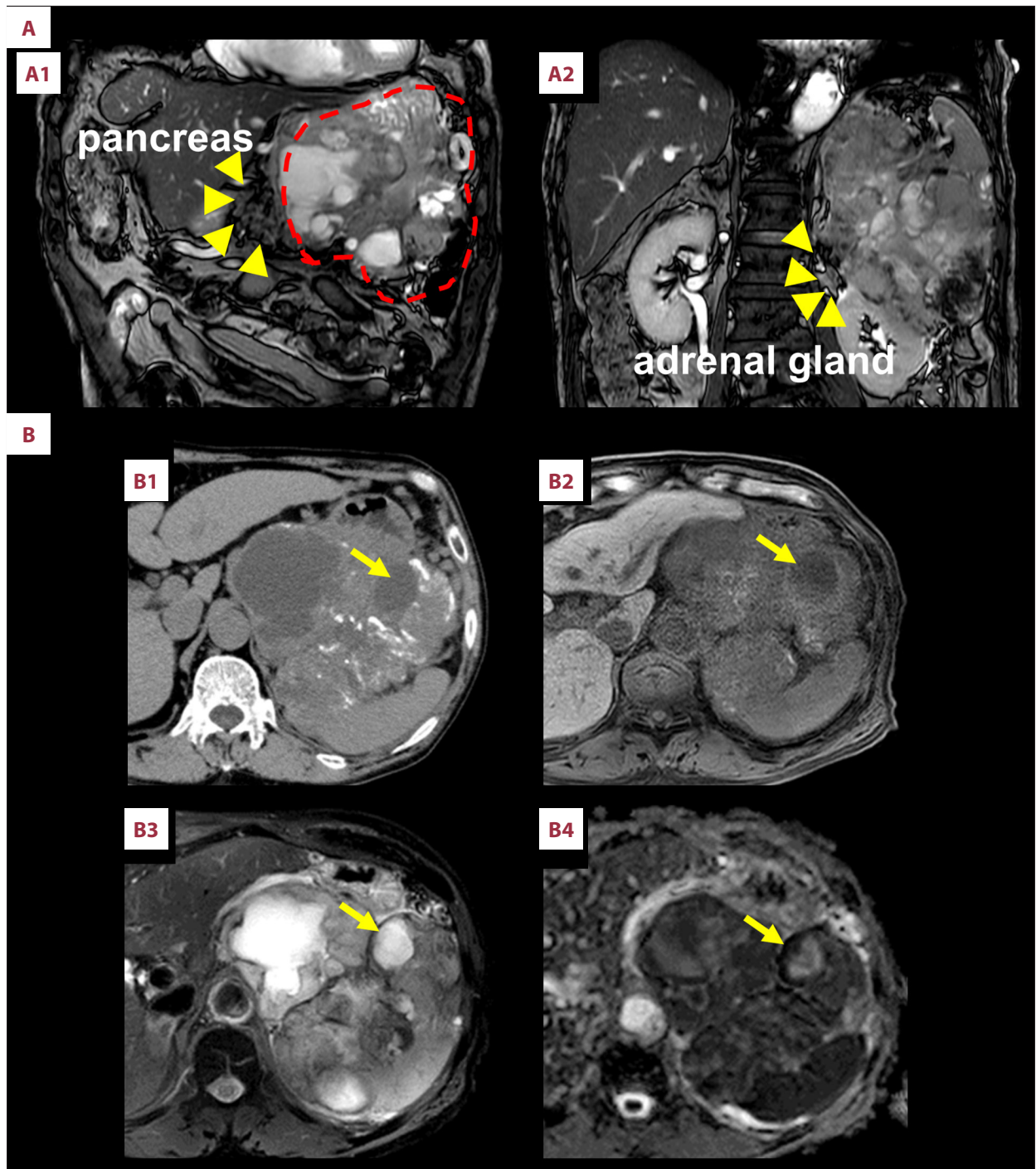


Figure 2. Radiological findings of the tumor in MRI. (A) MRI demonstrated the tumor as heterogeneous of intermediate and slightly high-intensity on T2-weighted imaging. The tumor contacted the pancreas (shown by arrows in **A1**) and adrenal gland (shown by arrows in **A2**) but did not seem to invade them. (B) Cystic component indicated by arrow was demonstrated as low-density area in plain CT (**B1**), low-intensity in T1-weighted imaging (**B2**), high-intensity in T2-weighted imaging (**B3**), and slightly high-intensity in DWI (**B4**). Calcification was demonstrated as high-density structures in plain CT (**B1**).

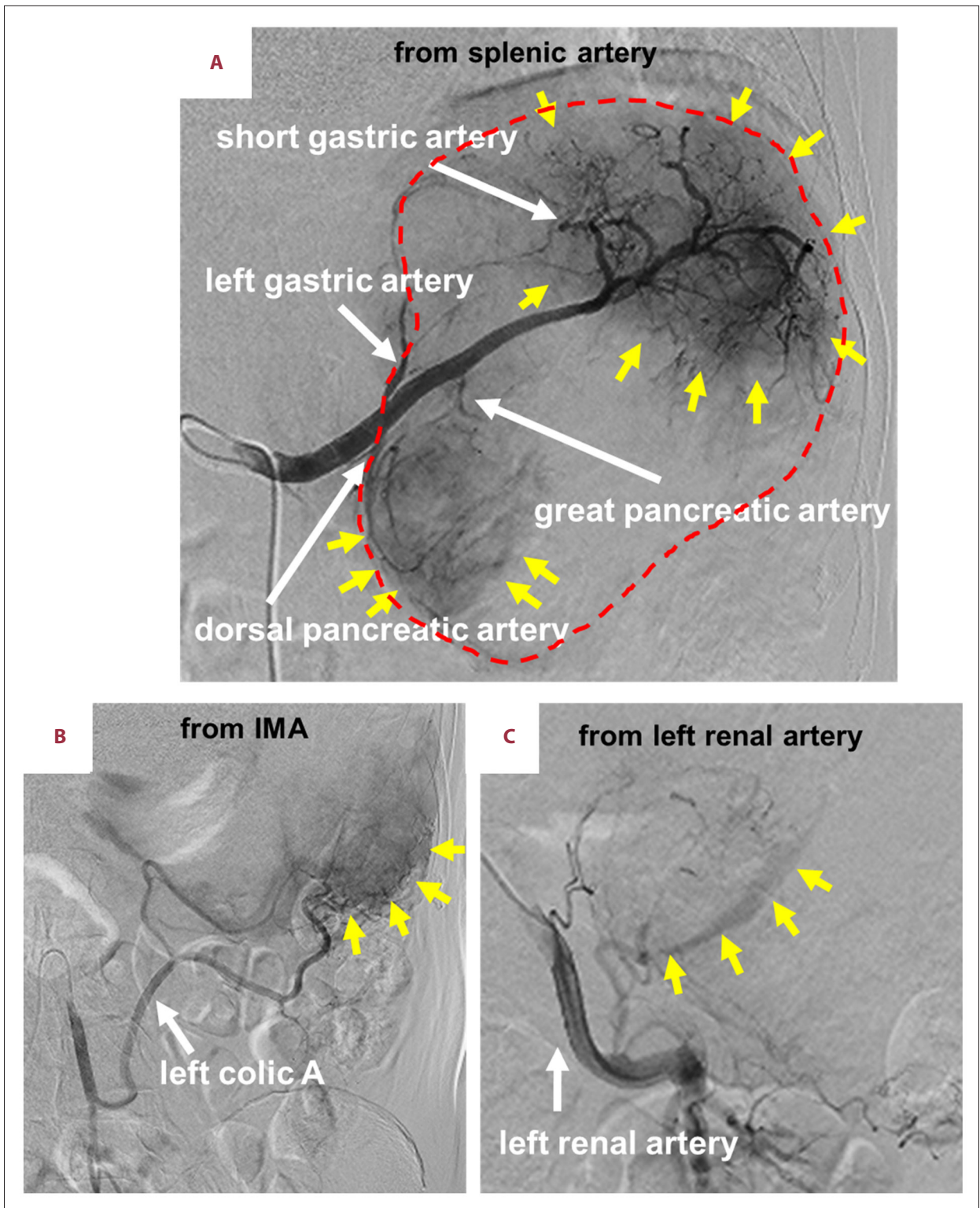


Figure 3. Findings of angiography. The angiography demonstrated the tumor stain from splenic artery, inferior mesenteric artery, and left renal artery. (A) The splenic artery was a main feeder artery of the tumor. The tumor staining is indicated by yellow arrows, and tumor configuration is shown by a red broken line. (B) The blood flow from inferior mesenteric artery spread to the splenic flexure through the left colic artery, suggesting tumor invasion into the colon. (C) Left renal artery was shown as a feeder artery of the caudal region of the tumor.

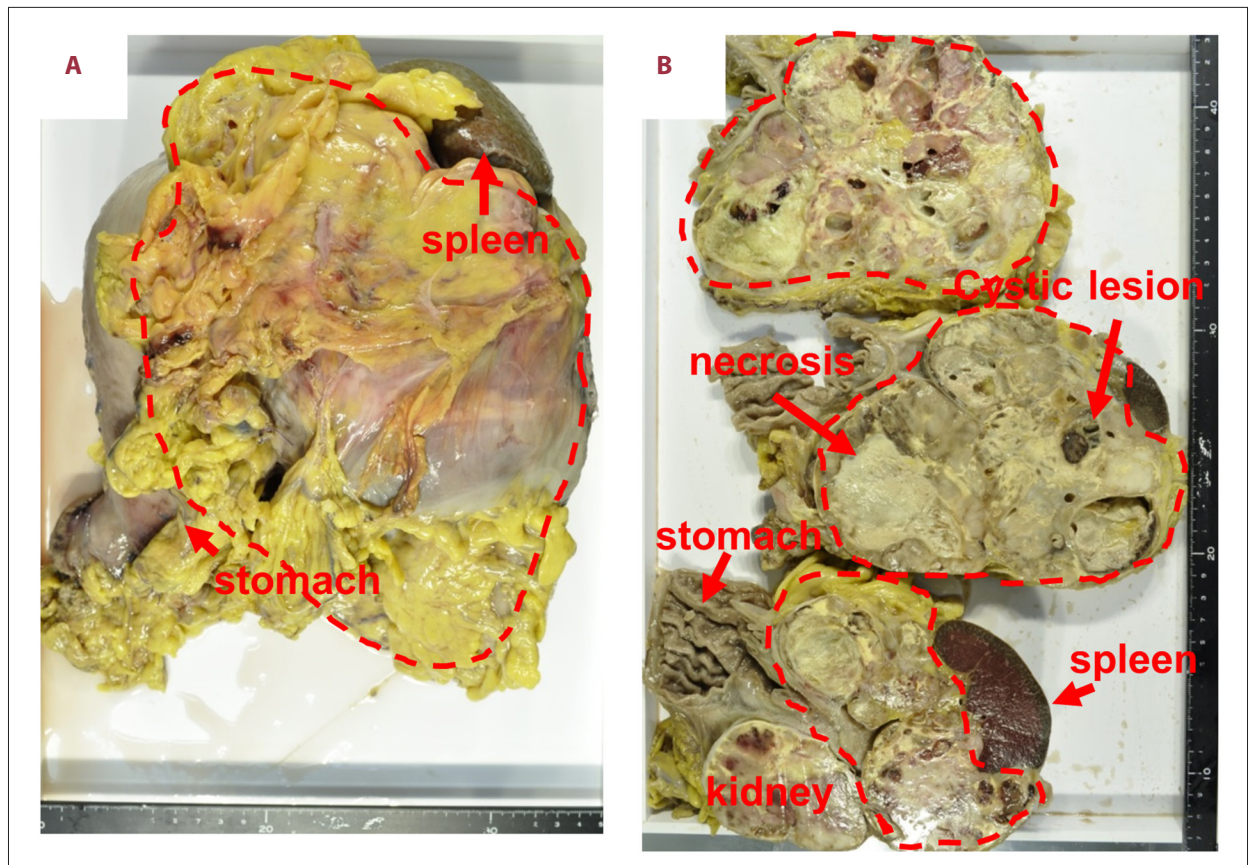


Figure 4. Morphological findings of the tumor. (A) The size of the resected tumor was 22×20×16 cm (surrounded by red broken line). (B) The tumor invaded into stomach, left kidney, spleen, and pancreas. It had multinodular features, central necrosis in the nodules, and multiple small cystic lesions.

Discussion

GCT-ST is a rare neoplasm that clinicopathologically resembles a giant cell tumor of bone. GCT-ST usually arises from the thigh, parotid gland, or subcutaneous tissue [4–6]. It is also possible for GCT-ST to arise in the head, neck, or mediastinum. Since the first case report of Salm and Sissons, approximately 120 GCT-STs have been reported [1]; however, there is no previous report of GCT-ST arising from retroperitoneal tissue. In this case, the huge GCT-ST was detected in the retroperitoneal space, and this is the first case report of the GCT-ST arising from retroperitoneal tissue.

GCT-ST has been recently named and defined in the WHO Classification of Soft-Tissue Tumors. First, Salm and Sissons reported 10 benign primary soft-tissue tumors resembling giant cell tumors of bone in 1972 [1], and they described the tumors with the term “giant cell tumor of soft tissue”. In the same year, Guccion and Enzinger reported 32 tumors, using the term “giant cell tumor of soft parts” [7]; however, half of the cases died of distant metastasis, suggesting some of them might be “malignant fibrous histiocytoma” with a high-grade

malignancy. Thereafter, both “malignant giant cell tumor” and “giant cell tumor of soft parts” were used; however, Folpe proposed that they should be termed “giant cell tumors of low malignant potential” in order to distinguish them from “malignant giant cell tumor of soft parts” and “malignant fibrous histiocytoma, giant cell type” [2]. In 2000, Oliveira et al. reported 22 cases of primary GCT-STs [3], and they demonstrated that only 1 patient died of local recurrence and distant metastasis, but the other patients survived after complete resection of tumors. In the same year, O’Connell reported 11 cases of benign GCT-ST, with no instances of local recurrence or metastases during the observation period (range; 2–80 months, average; 24 months) [8]. In 2002, the term “giant cell tumor of soft tissue” was addressed in the 3rd WHO Classification of Soft-Tissue Tumors. GCT-ST was defined as a tumor that sometimes causes local recurrence but rarely undergoes distant metastasis. The term and disease concept of “giant cell tumor of soft tissue” remained in the 4th WHO Classification of Soft-Tissue Tumors published in 2013.

In Japan, data on 5948 cases of soft-tissue tumors were collected from 2006 to 2008 by the Bone and Soft Tissue Committee

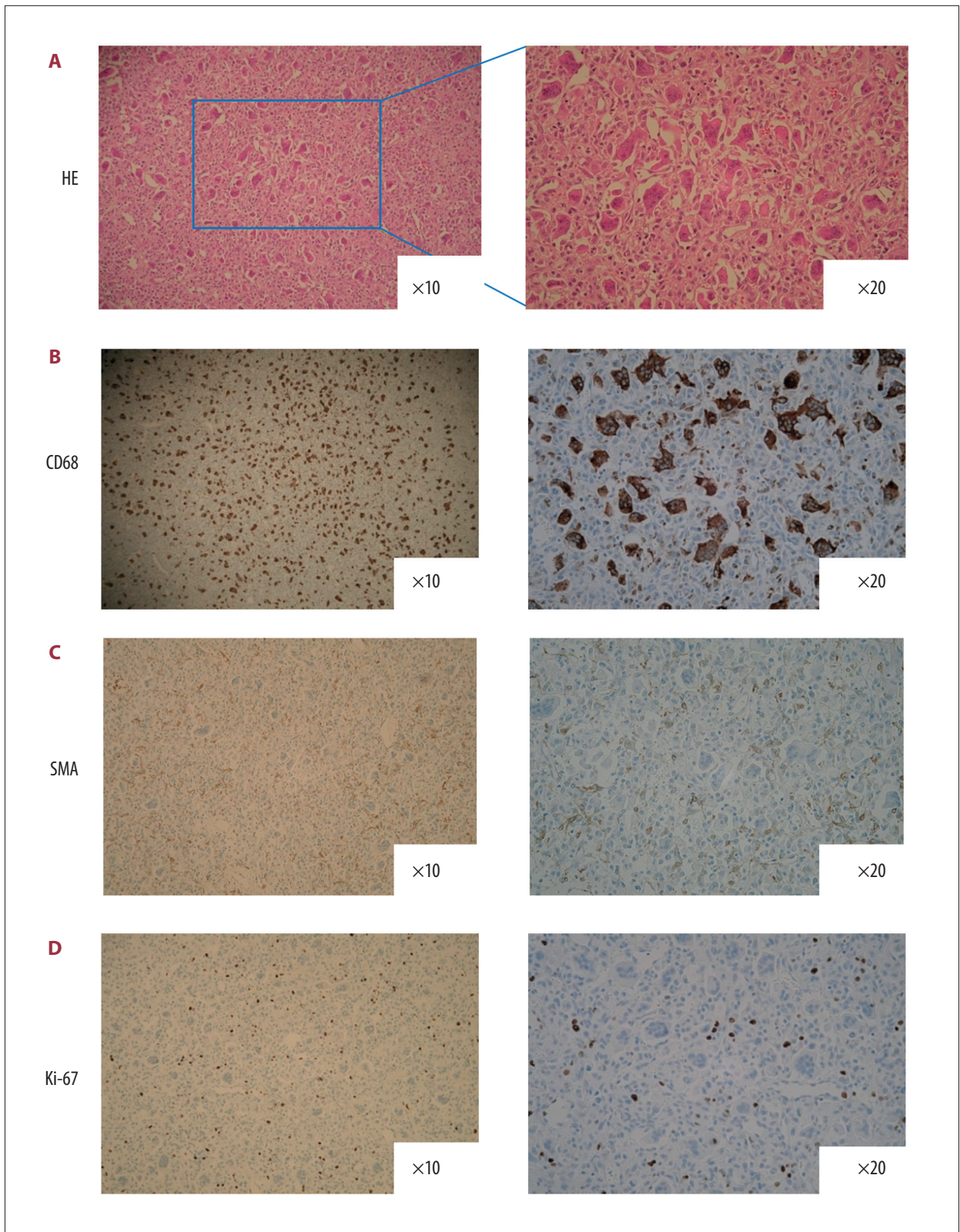


Figure 5. Pathological features of the tumor. (A) The tumor had many multinuclear cells, compatible with specific features of giant cell tumor. (B) CD68 on multinuclear cells was strongly stained. (C) SMA was weakly stained in 40% of tumor cells. (D) Ki-67 was stained at histiocytes in the background.

of the Japanese Orthopedic Association, and only 3.5% of them arose from the retroperitoneal area. Retroperitoneal tumors include a variety of benign and malignant neoplasms, and they are generally difficult to detect at an early stage because they begin asymptotically, in contrast to tumors generated from superficial tissue such as subcutaneous tissue. Therefore, retroperitoneal tumors are often detected as large or progressive tumors. Even after complete resection of the tumor, local recurrence or distant metastasis frequently occurs. Thus, the patients with malignant retroperitoneal tumors often have poor prognosis, while GCT-ST can be cured after complete resection.

Yakushiji et al. reported the diagnostic utility of diffusion-weighted MR images in primary soft-tissue tumors, and the apparent diffusion coefficient value of GCT-ST was significantly lower than that of benign tumors. Hu et al. reported the tumor exhibited predominantly slight hyperintensity on T2 images and intensely heterogeneous enhancement on contrast-enhanced T1-weighted images [6]. Moris reported a case with a hypointense rim on T2-weighted images [9]. In our MRI, the viable solid lesion was shown as the lower intensity of T2-weighted images, and the necrotic lesion was shown as irregular shape of isointensity on T2-weighted images. MRI was more informative than CT in differentiating the surrounding organs, as we recognized the pancreas and adrenal gland. Contrast-enhanced MR imaging revealed that the solid regions enhance diffusely, reflecting hypervascular tissue. Yaghmai et al. reported on 2 angiograms of GCT-ST, which were hypervascular, as well as GCT of bone [10–13]. In our case, the splenic artery mainly supplied blood flow into this huge tumor along with a part of IMA and left renal artery. The tumor was diagnosed as a primary retroperitoneal malignant tumor by the imaging examinations. At this point, a gastrointestinal stromal tumor was considered as the most likely diagnosis due to the huge hypervascular tumor. Differential diagnosis also considered left adrenal tumor, pancreatic tumor, left renal cancer, liposarcoma, and malignant lymphoma. Some reports suggested cytology and biopsy for preoperative diagnostic confirmation [14,15]. However, fine-needle aspiration and core-needle biopsy were not strongly recommended to make the diagnosis in our case, because it is often difficult to make an accurate diagnosis due to insufficient or inappropriate samples to perform an immunohistochemical analysis or a genetic exam, and there is some risk of implantation on the needle tract during cytology or biopsy. In addition, cytology and biopsy for hypervascular retroperitoneal tumor might induce bleeding into the abdominal cavity. Hence, it is difficult to make a histological diagnosis preoperatively. The optimal treatment of a retroperitoneal tumor without distant metastasis is curative surgical resection. In our case of GCT-ST, there was no metastasis, although the tumor invaded into multiple organs such as stomach, transverse colon, and left kidney. In addition, the patient had severe fatigue and body weight loss

due to the huge tumor compressing the gastrointestinal tract. The surgical treatment was required for the cure of disease as well as relief from the symptoms.

GCT-ST and giant cell tumor of bone are histologically similar in multiple aspects. However, GCT-ST seems to have different behavior from giant cell tumor of bone. GCT-ST is considered a tumor of low malignant potential, but giant cell tumor of bone is a locally aggressive tumor. Lee et al. suggested the genetic distinction between GCT-ST and giant cell tumor of bone [16]. They analyzed the genotype of H3F3A in 15 cases of GCT-ST. Despite the high prevalence of H3F3A Gly34 mutations in giant cell tumor of bone, no mutation of the H3F3A gene was revealed in any of the 15 GCT-ST cases.

Clinicopathologically, GCT-ST frequently shows a multinodular pattern, and many multinucleated giant cells are dispersed among spindle cells without cellular atypia or pleomorphism. The surface marker of GCT-ST has not been characterized before. In this case, immunohistological staining showed positive CD68 and SMA and lack of desmin, CD31, CD45, and S-100 of the tumor. CD68 was seen in multinucleated cells and was slightly positive in mononucleated cells, as in some previous reports [17]. CD68 is widely used as a macrophage marker and stain to bind lysosomal protein [18]. Smooth-muscle actin (SMA) was only weakly positive in mononuclear spindle cells. Desmin is a muscle-specific protein. Lack of desmin staining confirmed the tumor was not a myogenic stromal tumor. CD31, which plays a role in adhesive interaction between adjacent endothelial cells, is used as a marker of endothelial differentiation [19,20]. Lack of CD31 staining supported that the tumor was not angiogenetic. S-100 protein, which is used as a marker of neurogenic tumors such as schwannoma, is negative in tumor cells [21]. The mitotic ratio varies, and Oliveira reported it was from 2 to more than 30 mitoses per 10 HPF, and from 7 to 53 mitoses per 10 HPF in O'Connell's report [3,8]. Ki-67, which is well known as a cellular marker of proliferation, was relatively higher in our cases, so prudent follow-up was required even with low malignant potential.

GCT-ST should be completely resected with negative surgical margin for radical treatment, as well as the other retroperitoneal tumors. A major problem of GCT-ST is not distant metastasis, but rather a local recurrence. All of the reported patients who had local recurrence after surgery had a positive surgical margin. In other words, radical resection is the most important way to eliminate any recurrence in retroperitoneal GCT-ST, although it is often difficult to secure the negative surgical margin. If the differential diagnosis suggests a tumor is a GCT-ST, complete resection should be performed to achieve long survival after surgery.

Conclusions

This is the first report of GCT-ST arising in the retroperitoneal tissue. GCT-ST is a tumor of low-grade malignant potential; however, the tumor in our case was huge and invaded into surrounding organs, possibly due to arising from the retroperitoneal space, as most of other retroperitoneal tumors are asymptomatic. In contrast to the poor prognosis in most other retroperitoneal tumors, a patient with GCT-ST arising in the retroperitoneal tissue can have long survival without recurrence after complete resection.

References:

1. Salm R, Sissons HA: Giant-cell tumours of soft tissues. *J Pathol*, 1972; 107(1): 27–39
2. Folpe AL, Morris RJ, Weiss SW: Soft tissue giant cell tumor of low malignant potential: A proposal for the reclassification of malignant giant cell tumor of soft parts. *Mod Pathol*, 1999; 12(9): 894–902
3. Oliveira AM, Dei Tos AP, Fletcher CD, Nascimento AG: Primary giant cell tumor of soft tissues: A study of 22 cases. *Am J Surg Pathol*, 2000; 24(2): 248–56
4. An SB, Choi JA, Chung JH et al: Giant cell tumor of soft tissue: A case with atypical US and MRI findings. *Korean J Radiol*, 2008; 9(5): 462–65
5. Boneschi V, Parafioriti A, Armiraglio E et al: Primary giant cell tumor of soft tissue of the groin – a case of 46 years duration. *J Cutan Pathol*, 2009; 36(Suppl. 1): 20–24
6. Hu Q, Peng J, Xia L: Recurrent primary mediastinal giant cell tumor of soft tissue with radiological findings: A rare case report and literature review. *World J Surg Oncol*, 2017; 15(1): 137
7. Guccion JG, Enzinger FM: Malignant giant cell tumor of soft parts. An analysis of 32 cases. *Cancer*, 1972; 29(6): 1518–29
8. O'Connell JX, Wehrli BM, Nielsen GP, Rosenberg AE: Giant cell tumors of soft tissue: A clinicopathologic study of 18 benign and malignant tumors. *Am J Surg Pathol*, 2000; 24(3): 386–95
9. Meana Moris AR, Garcia Gonzalez P, Fuente Martin E et al: Primary giant cell tumor of soft tissue: Fluid-fluid levels at MRI (2010: 3b). *Eur Radiol*, 2010; 20(6): 1539–43
10. deSantos LA, Prando A: Synovial hyperemia in giant cell tumor of bone: Angiographic pitfall. *Am J Roentgenol*, 1979; 133(2): 281–84
11. Swan JS, Heiner JP, Rao VK, Weber DM: Preoperative evaluation of giant cell tumors of the radius with magnetic resonance angiography. *J Hand Surg Am*, 1993; 18(3): 499–503
12. Yaghami I: Malignant giant cell tumor of the soft tissue: angiographic manifestations. *Radiology*, 1976; 120(2): 329–31
13. Prando A, deSantos LA, Wallace S, Murray JA: Angiography in giant-cell bone tumors. *Radiology*, 1979; 130(2): 323–31
14. Asotra S, Sharma S: Giant cell tumor of soft tissue: Cytological diagnosis of a case. *J Cytol*, 2009; 26(1): 33–35
15. Kulkarni MM, Joshi AR, Patil V, Ansari T: Giant cell tumor of soft tissues of low malignant potential: A rare diagnosis on fine needle aspiration cytology. *J Cytol*, 2016; 33(2): 106–8
16. Lee JC, Liang CW, Fletcher CD: Giant cell tumor of soft tissue is genetically distinct from its bone counterpart. *Mod Pathol*, 2017; 30(5): 728–33
17. May SA, Deavers MT, Resetskova E et al: Giant cell tumor of soft tissue arising in breast. *Ann Diagn Pathol*, 2007; 11(5): 345–49
18. Gottfried E, Kunz-Schughart LA, Weber A et al: Expression of CD68 in non-myeloid cell types. *Scand J Immunol*, 2008; 67(5): 453–63
19. Parums DV, Cordell JL, Micklem K et al: JC70: A new monoclonal antibody that detects vascular endothelium associated antigen on routinely processed tissue sections. *J Clin Pathol*, 1990; 43(9): 752–57
20. Pisacane AM, Picciotto F, Risio M: CD31 and CD34 expression as immunohistochemical markers of endothelial transdifferentiation in human cutaneous melanoma. *Cell Oncol*, 2007; 29(1): 59–66
21. Kahn HJ, Marks A, Thom H, Bauml R: Role of antibody to S100 protein in diagnostic pathology. *Am J Clin Pathol*, 1983; 79(3): 341–47

Acknowledgements

We gratefully acknowledge the writing assistance of Gumpei Yoshimatsu and the pathology assistance of Yuka Idei.

Conflicts of interest

None.