Giant spindle cell rhabdomyosarcoma in an adult thorax: A case report

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Abstract. Spindle cell rhabdomyosarcoma (SCRM), a rare and distinct subtype of RM, predominantly affects children. While SCRM can manifest in the head and neck regions of adults, primary occurrences in the thorax are exceedingly uncommon. In the present study, a 24-year-old female patient was admitted to the Affiliated Hospital of Zunyi Medical University (Zunyi, China) with a 10-month history of dull pain in the right side of the chest. The patient had previously received treatment for right-sided tuberculous pleurisy at another hospital for 6 months, but the symptoms persisted, and the chest pain progressively worsened. A chest computed tomography scan now revealed a large mass in the right thorax. Pathological examination following surgical resection confirmed a diagnosis of SCRM. The patient did not undergo standardized postoperative chemoradiotherapy and the 5-year follow-up examination indicated tumor recurrence. Primary thoracic SCRM is a rare tumor that morphologically resembles other spindle cell tumors. Immunohistochemistry is crucial for an accurate diagnosis, and surgical resection remains the primary treatment approach. The clinicopathological features, molecular genetic characteristics and biological behavior of SCRM are largely unknown due to its rarity. Consequently, large-sample studies are essential to enhance the understanding of this tumor and advance precision medicine treatments.

Introduction

Rhabdomyosarcoma (RM), a prevalent soft-tissue malignancy in children, consists of rhabdomyoblasts at various stages of differentiation. RM predominantly affects the head and neck, genitourinary tract, retroperitoneum and extremities (1). The occurrence of RM, particularly spindle cell RM (SCRM), in the adult thorax is exceptionally rare. To the best of our knowledge, only one case of SCRM in the thoracic cavity has been reported to date (2). The present study details a case of primary thoracic SCRM in an adult patient and includes a literature review to enhance the understanding of this rare tumor type.

RM is a common soft-tissue sarcoma in children and adolescents, and accounts for 3% of all pediatric tumors (3,4). The World Health Organization (2013) classifies soft-tissue tumors into four subtypes based on their morphology: Acinus-shape, embryonal, pleomorphic and sclerotic/SC RM (5). SCRM, first described by Cavazzana *et al* (6) in 1992, is a specific and rare subtype of RM that primarily occurs in the paradidymal region, followed by the head and neck, in children. The first adult case of SCRM was reported by Rubin *et al* (7) in 1998. Unlike in children, adult SCRM predominantly occurs in the head and neck region, with cases also reported in the prostate, uterus and bones (8-10). However, primary thoracic SCRM is extremely rare in clinical settings, with only one case involving a 5-year-old female patient reported to date (2), to the best of our knowledge.

The present study aims to enhance the understanding and awareness of this rare tumor by providing a detailed report of a case of a giant SCRM in the thorax of an adult. By describing the clinical characteristics, pathological findings and treatment outcomes of this case, the study offers valuable insights for the diagnosis and management of similar cases. Additionally, it contributes to the early clinical identification of this tumor and supports the development of individualized therapeutic strategies.

Case report

A 24-year-old female patient was admitted to the Affiliated Hospital of Zunyi Medical University (Zunyi, China) in November 2012 due to right chest pain for 10 months and aggravation for 4 months. The patient initially experienced dull pain in the right side of the chest without any apparent cause. The patient had no symptoms, such as a cough, phlegm, cold, fever, abdominal pain or distension. At 10 months prior to admission, the patient was treated at Affiliated Hospital of Guiyang Medical College (Guiyang, China) for dull right-sided chest pain. A chest and abdominal computed tomography (CT) scan revealed a large space in the right upper diaphragm and right pleural effusion. Despite 6 months of

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treatment for right-sided tuberculous pleurisy, the symptoms persisted, and a mass puncture performed 4 months prior to the current admission identified a spindle cell tumor. In the last 3 months, the patient's chest pain on the right side continued to worsen, prompting a transfer to the Affiliated Hospital of Zunyi Medical University for further treatment. The patient was admitted with a diagnosis of a right thoracic tumor. Upon physical examination, the following findings were noted: Decreased respiratory motion of the right lung, pain induced by light pressure on the right chest wall, a solid sound on percussion of the right lung and a leftward shift of the relative border of cardiac dullness. Laboratory tests for tumor markers and biochemical indicators were normal. A chest CT scan showed irregular masses in the right lower thorax, the right middle mediastinum and the diaphragm area, with unclear borders and uneven density. CT values ranged from 25-65 Hounsfield units, with a maximum cross-sectional area of ~173x140 mm. Multiple nodular and small dot-like high-density shadows were observed. Enhancement scans indicated heterogeneous enhancement, significant compression and deformation of the right inferior pulmonary vein and right atrium, a poor display of the right atrium, and a leftward shift of the mediastinum and heart. No adjacent bone destruction was observed (Fig. 1). The patient had no specific past medical or family history. The patient underwent a thoracotomy for a suspected primary thoracic tumor. Intraoperatively, yellowish effusion was noted in the right thorax, and the tumor occupied approximately three-quarters of the right thorax, displaying a large lobulated morphology. The tumor exhibited aggressive growth, invading the diaphragm, lower lung, mediastinum and part of the chest wall, with an incomplete capsule. The tumor protruded downward into the abdominal cavity, but did not invade the liver and heart, with a clear demarcation between the tumor and the pericardium.

The pathological findings were of a mass of gray-white and gray-red fragmented tissue measuring 25.0x20.0x8.0 cm, with some well-defined areas. The cut surface had a fish meat-like appearance, gray-white and gray-red in color, with a solid and soft texture. The specimens were fixed in 4% neutral formalin at room temperature for 12 h, followed by routine dehydration, paraffin embedding and sectioning at a thickness of 5 μm. Hematoxylin and eosin staining was then performed at room temperature for 5 min each. Examination under a light microscopic examination revealed an incomplete tumor capsule with infiltrative growth, and tumor cells were observed to invade the surrounding muscle and adipose tissue. The tumor predominantly consisted of long spindle cells arranged in bundles, featuring darkly stained nuclei, inconspicuous nucleoli, mitosis and eosinophilic cytoplasm (Fig. 2). In a few regions, the tumor cells were naive, stellate or irregularly shaped, with interstitial mucinous edema-like changes. Some tumor cells showed lamellar necrosis and calcification (Fig. 3).

The specimens were fixed in 10% neutral formalin, followed by routine dehydration, paraffin embedding and sectioning at a thickness of 3 μm. Immunohistochemistry using the Envision two-step method was employed to assess the expression of relevant proteins in the tumor tissue. The staining procedures were performed strictly according to the manufacturer's instructions (all primary antibodies used were rabbit and mouse anti-human monoclonal antibodies, purchased from

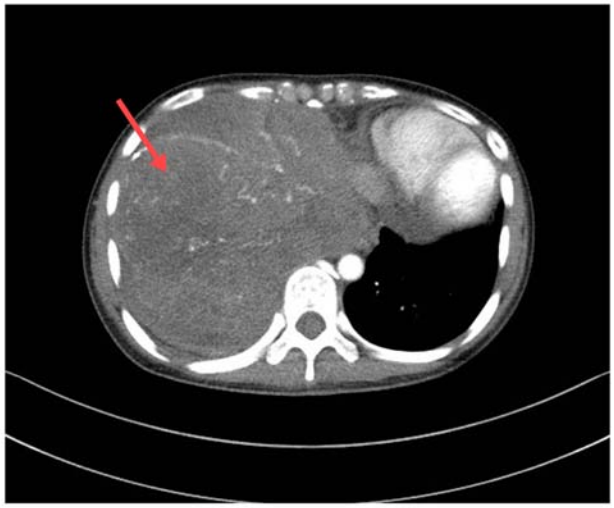

Figure 1. Enhanced computed tomography image showing an irregular mass (red arrow) in the right thorax.

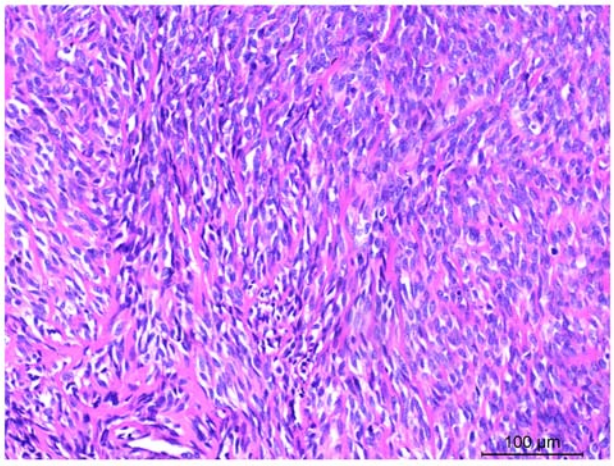

Figure 2. Hematoxylin and eosin staining showing that the tumor is primarily comprised of spindle cells arranged in bundles, with deep-stained nuclei, inconspicuous nucleoli and abundant eosinophilic cytoplasm. Scale bar, 100 μm.

Fuzhou Maixin Biotechnology Development Co. Ltd., and were used at a working concentration of 1:100). The primary antibodies were added to the sections and incubated overnight (12 h) at 4˚C. Immunohistochemical staining revealed, under a light microscope, that the tumor cells expressed vimentin (catalog no. RMA-0547) (Fig. 4), myoblast determination protein 1 (MyoD1) (catalog no. MAB-0822) (Fig. 5) and desmin (catalog no. MAB-0766) (Fig. 6), but did not express CD117 (catalog no. Kit-0029), CD34 (catalog no. MAB-1076), CD68 (catalog number: Kit-0026), epithelial membrane antigen (EMA) (catalog no. Kit-0011), smooth muscle actin (catalog no. ZM-0003), pan cytokeratin (AE1/AE3) (catalog no. Kit-0009), cytokeratin (CK)7 (catalog no. MAB-0828), CK19 (catalog no. MAB-0829), CD99 (catalog no. MAB-1012), transcription factor SOX-10 (SOX-10) (catalog no. RMA-1058), synaptophysin (catalog no. MAB-0742), neuron-specific enolase (catalog no. MAB-0791), S100 (catalog no. RAB-0150) and anaplastic lymphoma kinase (catalog no. MAB-0848) (Fig. S1).

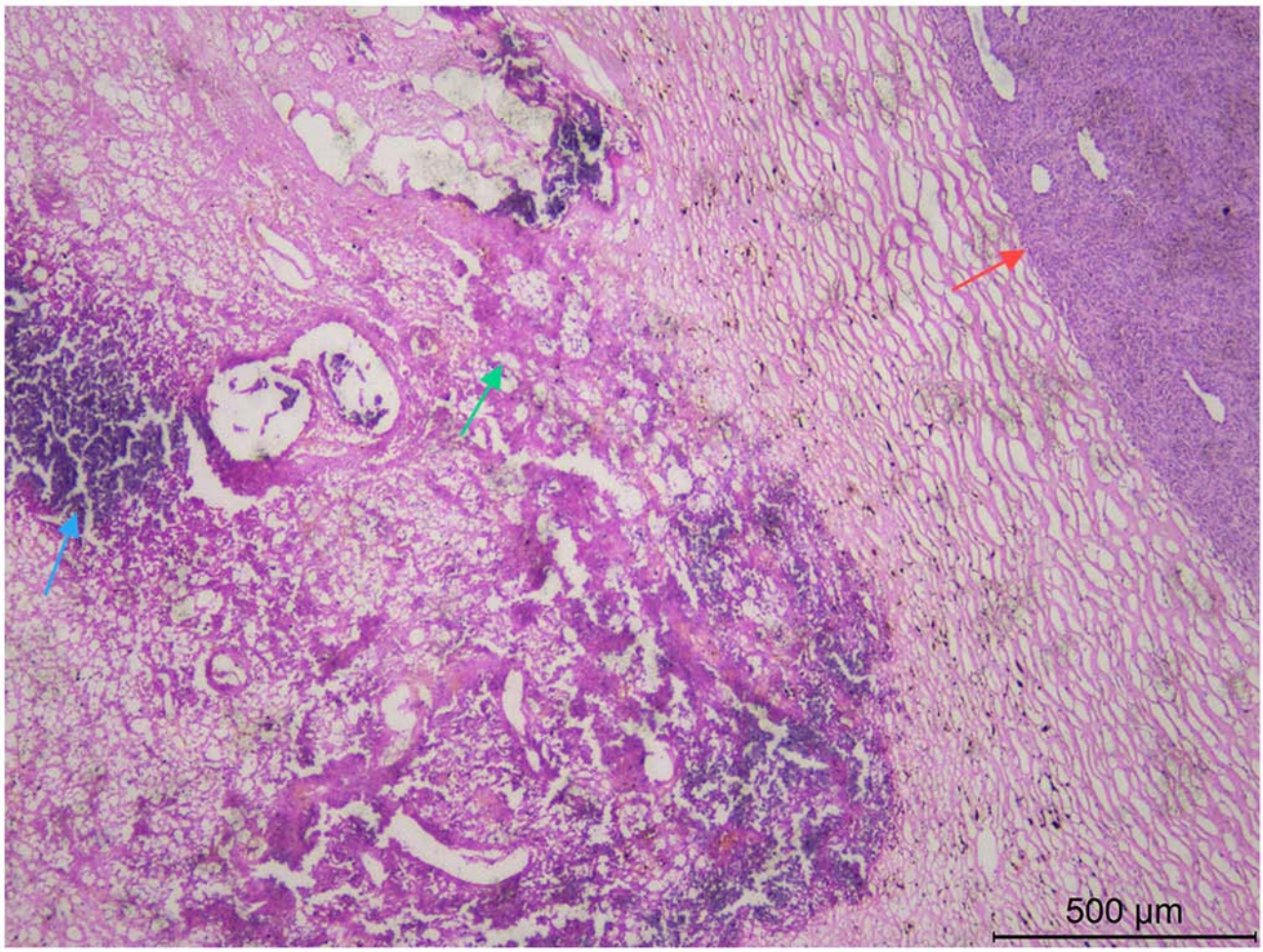

Figure 3. Hematoxylin and eosin staining showing lamellar necrosis and calcification in some areas of the tumor. Scale bar, 500 μm. The red arrow indicates tumor cells, the green arrow indicates necrosis and the blue arrow indicates calcification.

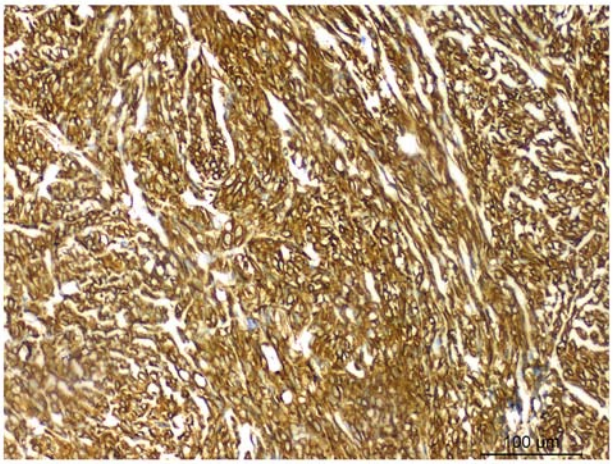

Figure 4. Immunohistochemistry showing vimentin positivity, as evidenced by EnVision staining. Scale bar, 100 μm.

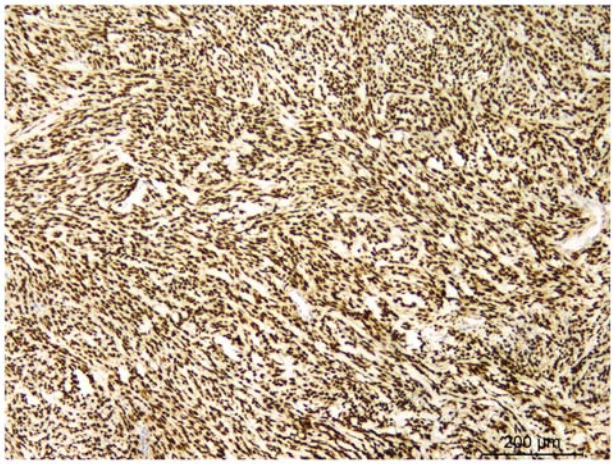

Figure 5. Immunohistochemistry showing diffused nuclear staining for myoblast determination protein 1, as evidenced by EnVision staining. Scale bar, 200 μm.

The Ki-67 index was ~30%. The patient was pathologically diagnosed with a right thoracic SCRM.

The patient was in good condition after surgery, and telephone follow-ups were performed at 1, 3 and 5 years after surgery. However, due to personal economic conditions and other factors, the patient declined postoperative radiotherapy and chemotherapy, and regular physical examinations. After 5 years, the patient exhibited symptoms of chest pain and dyspnea. A chest CT scan at the 5-year follow-up visit suggested a recurrence of the thoracic tumor (Fig. 7), and the

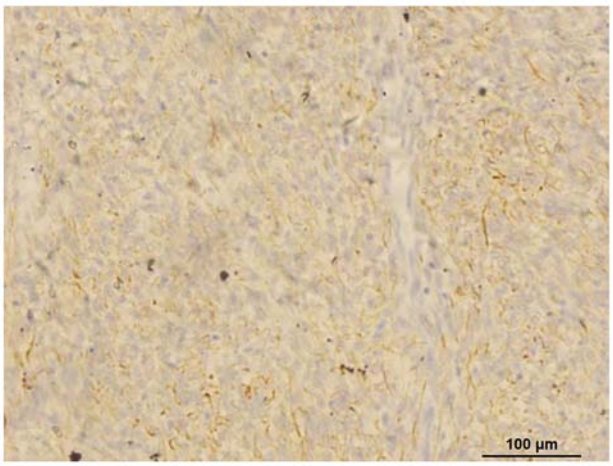

Figure 6. Immunohistochemistry showing weak positive staining for desmin, as evidenced by EnVision staining. Scale bar, 100 μm.

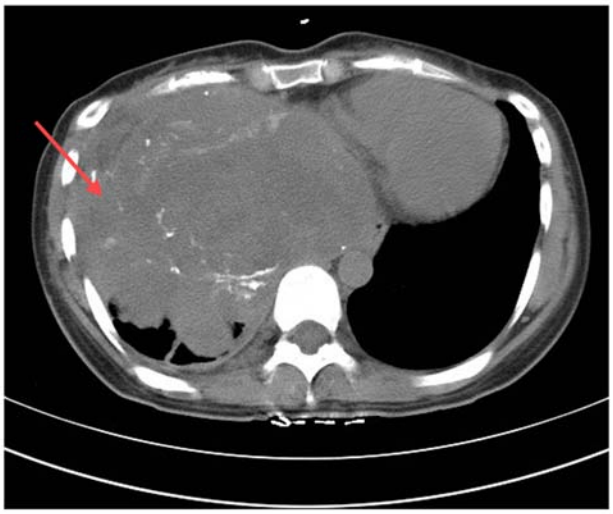

Figure 7. Computed tomography image at the 5-year follow-up suggesting a right-sided thoracic mass (red arrow).

patient continued to refuse treatment. The patient has been lost to follow-up.

Discussion

The clinical presentation of primary thoracic SCRM lacks specificity. The severity of symptoms depends on primary site and size of the tumor, the degree of compression and infiltration, and the extent of tissue destruction caused by the tumor cells. A preoperative diagnosis of SCRM is challenging due to the non-specific nature of imaging findings (2,11,12). In the present case report, the patient primarily presented with chest pain, without additional symptoms such as hemoptysis or a cough. Microscopically, the tumor predominantly consisted of spindle cells arranged in interlacing bundles, resembling fibrosarcoma and leiomyosarcoma. The spindle cells exhibited abundant red-stained cytoplasm, oval or elongated nuclei with deep staining, and inconspicuous or small nucleoli. Additionally, a small number of spindle or polygonal rhabdomyoblasts were interspersed among the spindle cells. The presence of rhabdomyoblasts suggested a diagnosis of SCRM, with mitotic figures ranging from 1 to 30 per 10 high-power fields. Immunohistochemical staining demonstrated varying degrees of expression of myogenic markers, including desmin and MyoD1, in the SCRM (13), with strong positivity for MyoD1. However, epithelial markers (such as CK and EMA) and neurogenic markers (such as S-100 and SOX-10) were not expressed.

Molecular genetic studies have identified genetic differences between young children with SCRM and older children or adults with the same condition. Young children often present with vestigial-like family member 2, serum response factor, TEA domain transcription factor 1 or nuclear receptor coactivator 2-associated gene fusions, which are associated with a better prognosis (3). By contrast, older children and adults frequently have mutations in the MYOD1 gene, leading to a poorer prognosis. Tsai *et al* (14) reported the cases of a group of patients aged 8-64 years with SCRM, finding that the mutation rate in MYOD1 was 30-67%. MYOD1 was diffusely expressed, and myogenin showed patchy expression in all MYOD1-mutated patients. Additionally, Dashti *et al* (10) reported a case of bone SCRM with fused in sarcoma-transcription factor cellular promoter 2 gene fusion. Further research on SCRM is expected to uncover more molecular genetic alterations, providing a basis for improved treatment strategies. However, no genetic analysis was performed in the present case for economic reasons.

Primary thoracic SCRM must be distinguished from the following tumors: i) Fibromatosis: Occurring primarily in adults with aggressive growth, fibromatosis features long, spindle-shaped tumor cells with minimal cellular atypia, low mitotic activity and abundant interstitial collagen fibers. Immunohistochemically, SMA and catenin are expressed, while MyoD1 and myogenin are not (15-18). ii) Adult-type fibrosarcoma: Comprised of fibroblasts, these tumors present with long, spindle-shaped cells with pointed nuclei arranged in bundles or a herringbone pattern, and abundant interstitial collagen. Hemangiopericytoma-like structures are common in congenital fibrosarcoma. Immunohistochemical markers are positive for vimentin but negative for desmin, MyoD1 and myogenin (19,20). iii) Leiomyosarcoma: Primarily occurring in the retroperitoneum, extremities, trunk, head and neck of adults, leiomyosarcoma consists of fasciculated spindle cells with abundant eosinophilic cytoplasm arranged longitudinally and transversely. Tumor cells feature rod-shaped nuclei with blunt ends. Immunohistochemical assays typically show SMA positivity and MyoD1 negativity (21,22). iv) Synovial sarcoma: Often found around large joints in patients aged 15-40 years, synovial sarcoma consists of epithelial and spindle cell components. Spindle cells are uniform with scant cytoplasm, ovoid nuclei, and inconspicuous nucleoli; localized hemangiopericytoma-like structures are common. Poorly differentiated synovial sarcoma cells can resemble RM. Immunohistochemically, CD99 and BCL-2 are positive, while myogenic markers are negative (23,24). Fluorescence *in situ* hybridization assays frequently reveal synaptotagmin gene translocation (25,26). v) Mixed malignant tumors of neuroepithelial origin:

Affecting the extremities, head and neck, retroperitoneum, abdominal wall, perineum, scrotum and brain, these tumors exhibit multiple differentiations, including ganglion cells, neuroblastoma cells and RM cells. RM is characterized by the absence of a neuroepithelial component (27).

RM is primarily treated with surgery combined with chemoradiotherapy. The study by Yasui *et al* (5) emphasized that complete resection of the tumor, along with adjuvant chemotherapy and radiotherapy, could prevent local recurrence. Prognostic factors for RM include the location of the tumor, the completeness of its resection, its size and its histological subtype (28,29). The highly aggressive nature of SCRM in adults contributes to a poor prognosis (30). A previous study has shown that adult RM generally has a worse prognosis compared with that of pediatric RM, with 24.6% of patients dying from the cancer or treatment-associated complications, The overall 5-year survival and metastasis-free survival rates were recorded as 52.9 and 62.9%, respectively, The sole predictor of metastasis was the National Federation of Cancer Centers tumor grade (31). Although most RM cases present as large tumors, lymph node or distant metastases are rare at the time of diagnosis. In one study, RM initially showed a good response to vincristine, actinomycin and cyclophosphamide chemotherapy, but >50% of tumors recurred or progressed. These data suggest that SCRM has a worse prognosis compared with the infantile fetal variation (5). In the present adult patient, despite complete resection of the tumor, no standardized radiotherapy and chemotherapy regimen was available, and disease progression was observed over a 5-year follow-up period. Therefore, standardized postoperative radiotherapy and chemotherapy are crucial components of the treatment plan.

In conclusion, RM is a rare soft-tissue malignancy. Adult SCRM is particularly aggressive and associated with a poor prognosis. Due to its rarity, the clinicopathological features, molecular genetic characteristics and biological behavior of SCRM are not well understood. Consequently, large-sample analyses are essential to enhance the understanding of this tumor and facilitate the development of more effective precision medicine strategies.

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Authors' contributions

YQL and JJW analyzed the data and were the primary author of the manuscript. SL acquired the CT scan images. YL performed the immunohistochemical staining. XM analyzed patient data. JJW and YQL confirm the authenticity of the data. JJW and XH conducted the histopathological evaluation and assisted in writing the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

This case report was approved by the Ethics Committee of the Affiliated Hospital of Zunyi Medical University (Zunyi, China; approval no. KLLY-2020-064).

Patient consent for publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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