Aggressive fibromatosis near the incision after cervical spinal cord ependymoma: A case report

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Abstract. Aggressive fibromatosis (AF), also known as ligamentoid fibromatosis and desmoid tumor, is a fibroblast clonoproliferative lesion located in the deep soft tissue. The present study reports the case of a 36-year-old female with AF who underwent cervical spinal cord ependymoma surgery. AF developed in the soft tissue of the neck adjacent to the incision site. The size of the neck AF increased rapidly over 2 years, and due to discomfort, the patient underwent initial surgical resection without any other combined treatment methods. When the patient was routinely reviewed at 6 months post-surgery, a recurrence of AF of the neck was found. The patient was recommended surgical resection and radiotherapy. This case report should improve the understanding of clinicians with regard to AF, and help the diagnostic process and treatment plan.

Introduction

Aggressive fibromatosis (AF), a borderline soft tissue tumor arising from fibrous connective tissue, occurs throughout the body. The incidence of AF is significantly higher in females compared to male patients (1,2). Emerging evidence has suggested that the etiology of this disease has several aspects, including genetic, endocrine and physical factors. Surgical trauma may accelerate the development of AF, the pathogenesis of which remains unknown. Two principal types of AF have been identified, namely the sporadic and the genetic type. The sporadic type is more common and its pathogenesis is associated with mutations in the β-catenin gene (3). In addition, the genetic type of AF is more common in familial adenomatous polyposis and Gardner syndrome (4). The genetic type is often intraperitoneally associated with an adenomatous polyposis coli disease gene mutation (5). AF can impact functionality and cause treatment-related morbidity and mortality. AF is a complex condition with numerous recognised treatments, including active observation, hormonal therapy, chemotherapy, radiotherapy and surgical resection. Hormonal agents and nonsteroidal anti-inflammatory drugs have benign side effect profiles but generally limited efficacy. Among patients with progressive, refractory or symptomatic AF, sorafenib significantly prolonged progression-free survival.

Case report

Case. In the present study, the case of a 36-year-old female with AF who underwent cervical spinal cord ependymoma surgery is reported. AF developed in the soft tissue of the neck adjacent to the incision site. The patient did not have any genetic family history of AF. In June 2019, the patient visited the China-Japan Union Hospital of Jilin University (Changchun, China), complaining of neck and shoulder pain for >3 months. An enhanced magnetic resonance imaging (MRI) scan of the cervical spine was then performed. The MRI scan showed uneven enhanced masses in the spinal cord at the medulla-C3 vertebral level (Fig. 1).

The patient was otherwise in good health and self-reported that she had no history of hypertension, coronary heart disease, diabetes, cerebrovascular disease, hepatitis, malaria or tuberculosis. The patient also denied any known familial genetic disease history. In August 2019, the patient underwent a posterior median approach at the Beijing Tiantan Hospital (Beijing, China) for complete removal of the medulla-C3 vertebral level intramedullary tumor. The patient had a good prognosis and the 7x1.5x2-cm mass was completely resected, with no residual lesions (Fig. 2). Postoperative pathological findings classified the mass as a World Health Organization II grade ependymoma (Fig. 3A). Immunohistochemical analysis revealed that the tumor was positive for glial fibrillary acidic protein (Fig. 3B) and S-100 (Fig. 3C), and negative for oligodendrocyte transcription factor 2, epithelial membrane antigen (data not shown), synaptophysin (Fig. 3D) and progesterone receptor expression (data not shown). The Ki67 positive nuclear expression rate was 2% (data not shown).

Postoperatively, the female patient underwent a routine cervical spine plain MRI scan and was then fully reviewed at the China-Japan Union Hospital of Jilin University (Changchun,

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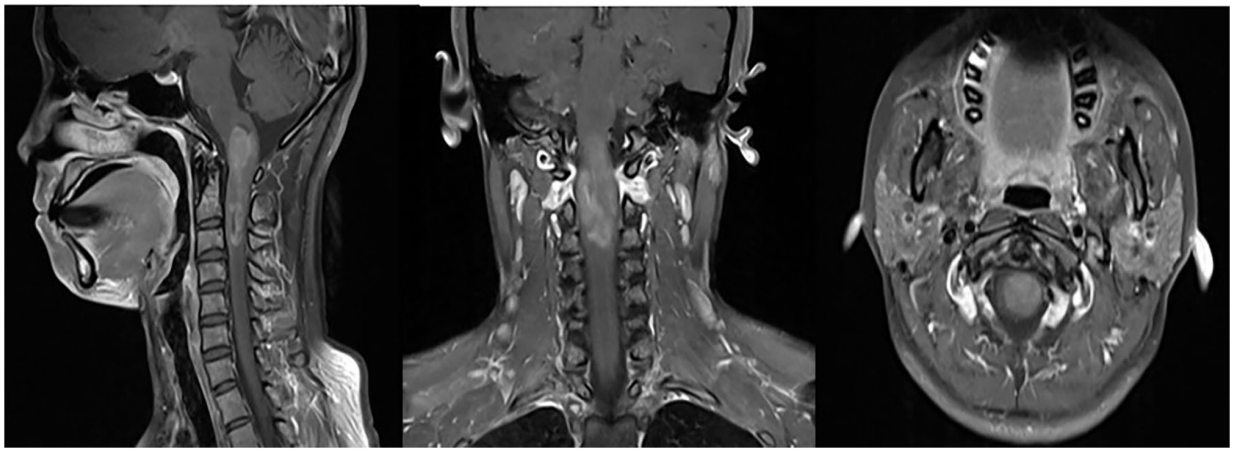

Figure 1. Enhanced magnetic resonance imaging of the patient's cervical spine.

China) in July 2020 (Fig. 4). As indicated in Fig. 4A-C, postoperative changes of the medulla-C3 vertebral level ependymoma were observed with no clear signs of recurrence. In addition, strips of abnormal enhancement were revealed in the soft tissue of the left side of the neck (Fig. 4D and E). A follow-up review or further examination were recommended. The patient did not experience any discomfort during follow-up. Therefore, re-examination was performed at two years after the last follow-up, while the patient was not treated for the soft tissue lesions in the neck. In July 2022, the patient arrived at the China-Japan Union Hospital of Jilin University (Changchun, China) for re-examination of the cervical vertebra by plain MRI scan with enhancement (Fig. 5). The results revealed abundant blood supply and occupying space in the left cervical semispinosus and splenius capitis muscles. The lesion showed infiltrative growth, while its volume was significantly increased compared with that in the previous scan. The clinicians recommended that the patient should undergo an ultrasound-guided puncture biopsy of the posterior neck. After one month, the lesion on the back of the left side of the patient's neck was surgically removed. The intraoperative tumor was located in the muscle space with apparent adhesion into the muscular layer with a complete capsule covering its surface. The tumor, 5x8x7 cm in size, was completely removed (Fig. 6). A needle biopsy revealed spindle-cell lesions originating from mesenchymal tissue. The nuclei were blunt and rounded at both ends, and atypia was not obvious. Division of the nuclei was rare. The postoperative pathology suggested that the mass consisted of spindle cells (including fibroblasts and myofibroblasts), and infiltrated the fat and the rhabdoid tissue. The postoperative pathology combined with immunohistochemical results indicated AF (Fig. 7). For immunohistochemistry, 5-μm tissue sections of formalin-fixed and paraffin-embedded material were prepared on glass slides. The relevant markers were detected by the immunohistochemical EnVision method (Agilent Technologies, Inc.). The immunohistochemical analysis results demonstrated that the tumor was positive for β-catenin (nucleoplasm) (Fig. 7B), smooth muscle actin (SMA) (Fig. 7C), calponin (Fig. 7D), vimentin, Ki-67 (1%) and desmin, and negative for CD34, actin, S-100, mucin 4 and Bcl-2 (data not shown). During the follow-up, the patient underwent cervical MRI half a year after surgery. The results

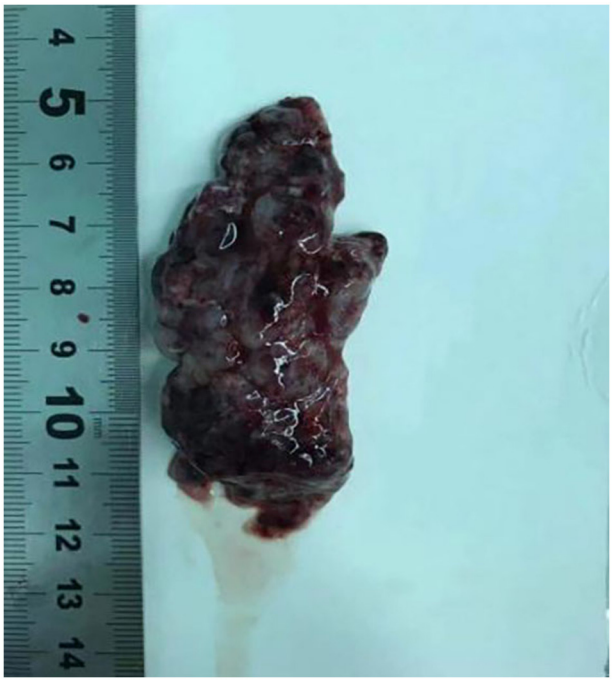

Figure 2. Gross visual observation of the surgically excised cervical spinal cord ependymoma (scale bar, cm). The removed specimen was dark red, with a hard texture and a lobulated shape.

suggested AF recurrence and the patient was re-admitted for radical surgery and volumetric modulated arc therapy. An MRI scan of the neck was recommended semi-annually after discharge.

Methods. Histological analysis and immunohistochemical staining for EnVision were performed according to standard protocols. The following primary antibodies were used: Anti-β-catenin (cat. no. ab32572; working solution), anti-SMA (cat. no. ab108424; working solution), anti-Calponin (cat. no. ab227667; working solution), anti-Vimentin (cat. no. ab92547; working solution), anti-Ki-67 (cat. no. ab92742; working solution), anti-Desmin (cat. no. ab32362; working-solution), anti-CD34 (cat. no. ab81289; working solution), anti-Actin (cat. no. ab32575; working solution), anti-S-100 (cat.

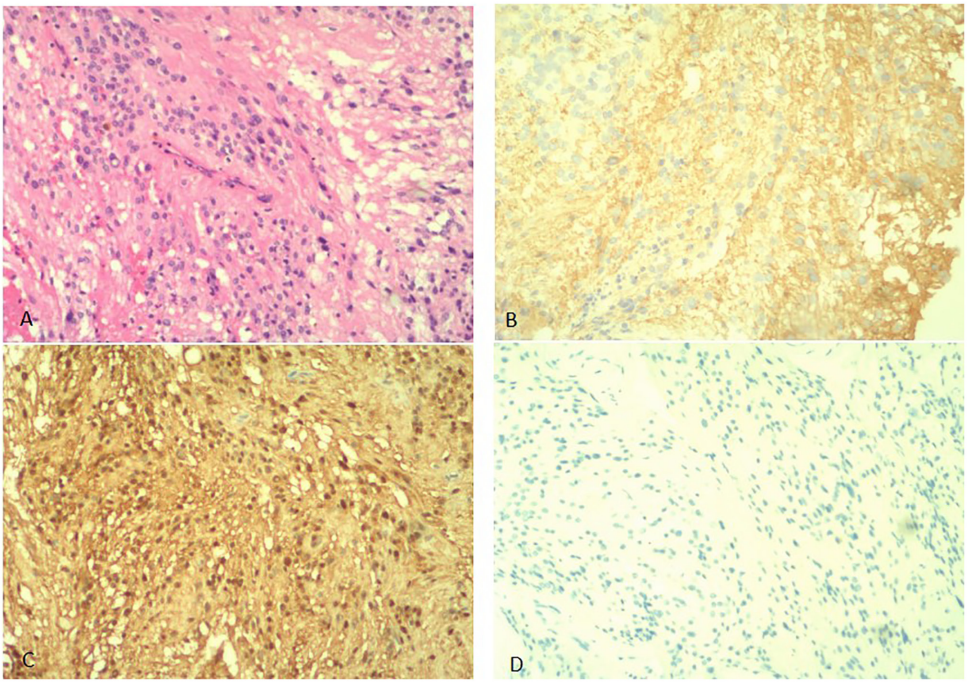

Figure 3. (A) Hematoxylin and eosin-stained pathological sections of the intraspinal ependymoma at the level of the medulla-C3 vertebral body. Immunohistochemical analysis results demonstrated (B) glial fibrillary acidic protein (positive), (C) S-100 (positive) and (D) synaptophysin (negative) (magnification, x100).

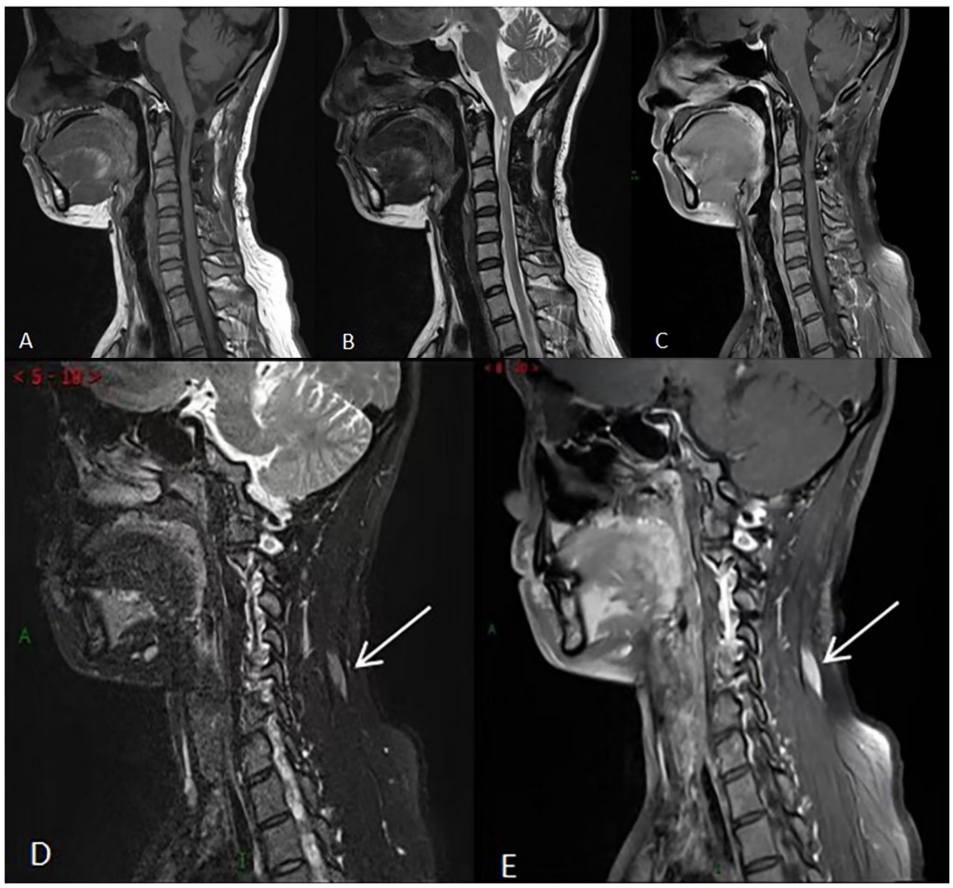

Figure 4. The cervical spine was reviewed with a plain magnetic resonance imaging and enhanced scan at the first follow-up 1 year after surgery. (A) The sagittal T1WI showed a low signal in the medulla-C3 vertebral spinal cord. (B) The sagittal fat-suppressed T2WI showed a high signal in the medulla-C3 vertebral spinal cord. (C) The sagittal T1WI enhancement scan indicated postoperative changes in the medulla-C3 vertebral spinal cord ependymoma. Moreover, the absence of the spinous process of the cervical 2-3 vertebra appeared after surgery. (D) The sagittal fat-suppressed T2WI showed an abnormal subcutaneous stripe signal in the neck at the left side (indicated by a white arrow). (E) T1WI enhancement scanning revealed significant uniform enhancement of the abnormal subcutaneous signal in the left side of the neck (indicated by a white arrow). T1WI, T1-weighted imaging.

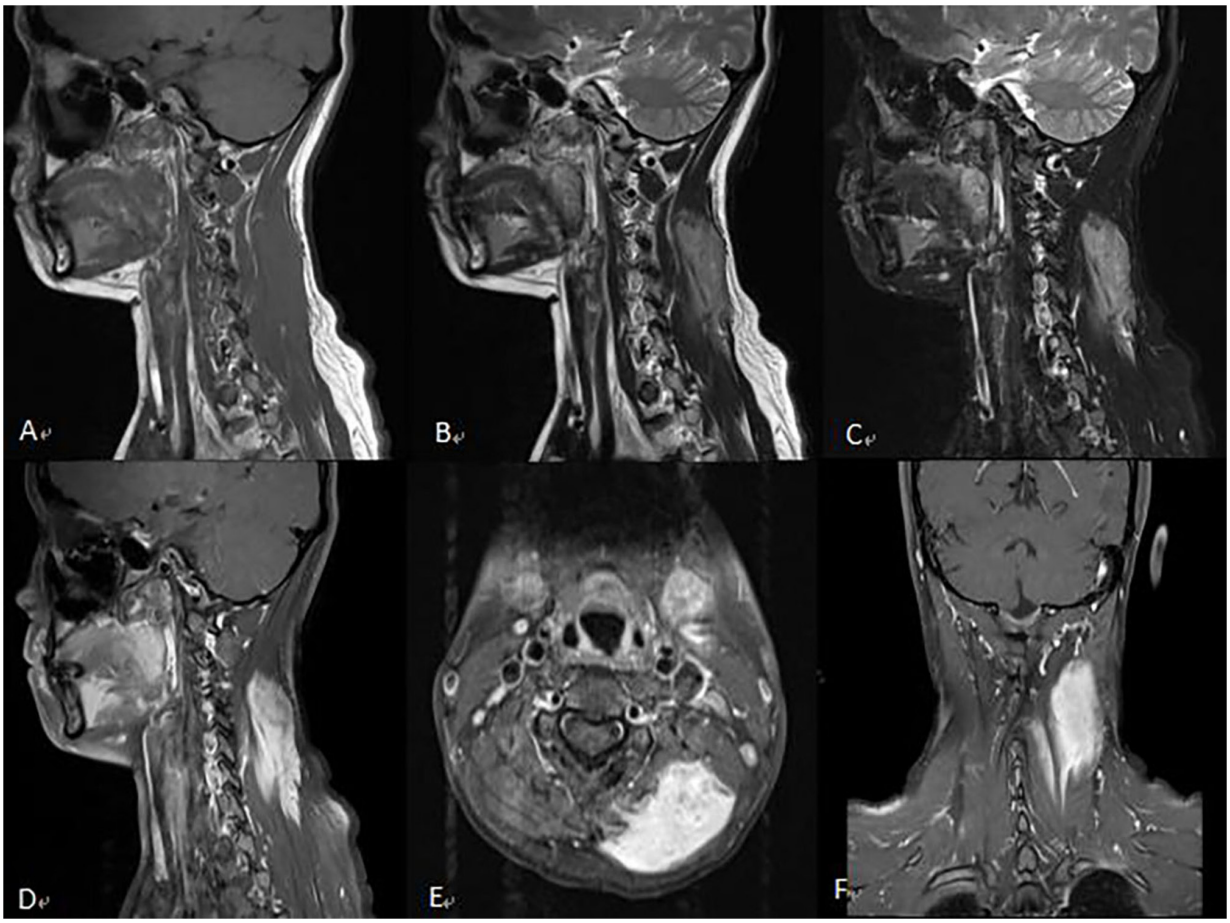

Figure 5. The cervical spine was examined by plain magnetic resonance imaging and enhanced scan at the second follow-up ~3 years after surgery. (A) The sagittal T1WI revealed an abnormal signal under the left side of the neck. In addition, the lesion exhibited a low signal. (B) Sagittal T2WI images. (C) Sagittal fat-suppressed T2WI images. The lesions showed a high signal on the T2WI sequences. (D) Enhanced sagittal T1WI images. (E) Enhanced axial T1WI images. (F) Enhanced coronal T1WI images. The lesions demonstrated apparently homogeneous improvement on the enhanced images. T1WI, T1-weighted imaging.

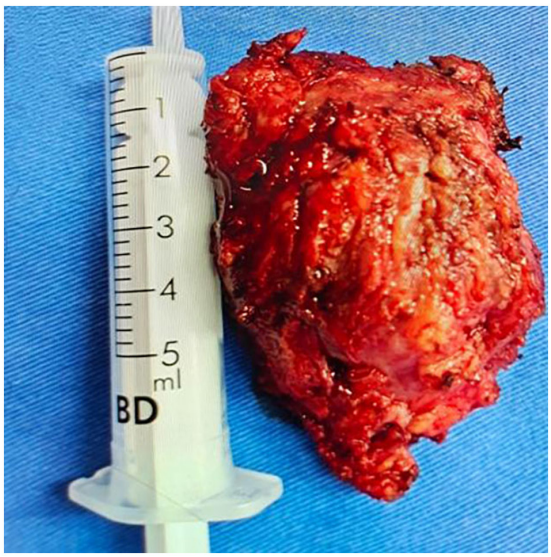

Figure 6. Gross appearance of the surgically resected posterior mass of the left side of the neck.

no. ab197896; working solution), anti-MUC4 (cat. no. ab243921; working solution), anti-Bcl-2 (cat. no. ab238042; working solution), anti-GFAP (cat. no. ab68428; working solution), anti-Olig2 (cat. no. ab109186; working solution), anti-MUC1 (cat. no. ab109185; working solution), anti-Synaptophysin (cat. no. ab32127; working solution) and anti-Progesterone Receptor (cat. no. ab32085; working solution) (all Abcam).

Discussion

The incidence of AF is higher in women during pregnancy and postpartum, while the abdominal wall scar is the most common tumor site. Trauma and endocrine factors may be associated with AF. Previous studies demonstrated that positive estrogen receptor β and cyclin D1-mediated immune responses were associated with a high proliferation rate of AF, and estrogen receptor upregulation was able to predict postoperative tumor recurrence (6,7). It was therefore hypothesized that estrogen could modulate AF. However, evidence of the efficacy of antiestrogen therapy in AF has been limited to case series and single-arm trials (8). Treatment guidelines do not routinely recommend treatment with hormones and non-steroidal anti-inflammatory drugs (NSAIDs), including celecoxib, which are commonly used for pain control. Although treatment approaches for AF continue to evolve, several directions are clear. For the majority of patients with AF, surgery is no longer the preferred primary therapeutic approach, which has been replaced by active surveillance (9).

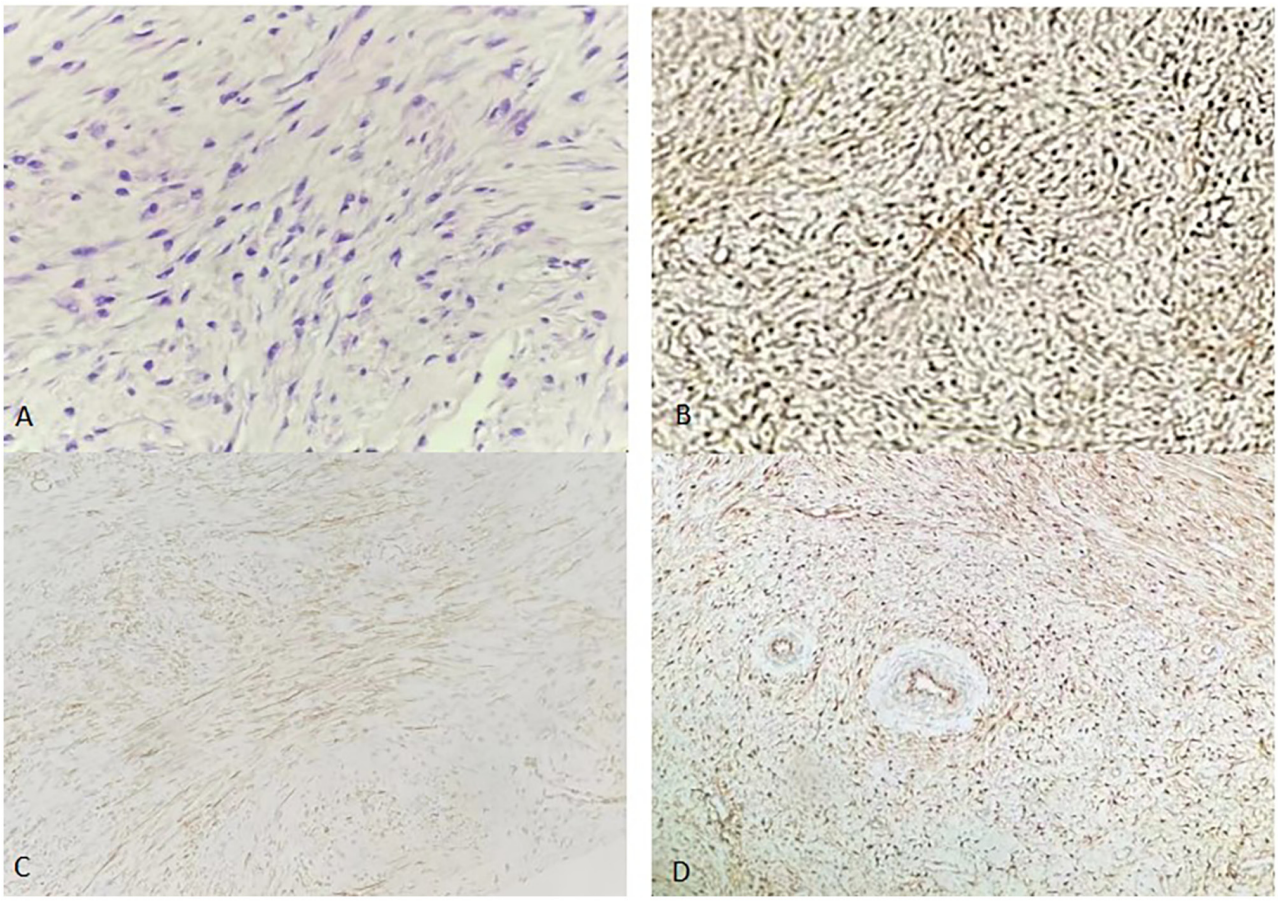

Figure 7. (A) Hematoxylin and eosin-stained pathological section of the aggressive fibromatosis on the left side of the neck. The immunohistochemical analysis results indicated (B) β-catenin (partial nuclear positive), (C) smooth muscle actin (positive) and (D) calponin (positive) (magnification, x100).

In the present case, following cervical spinal cord ependymoma surgery, the lesion was located in the soft tissue of the neck adjacent to the incision site. Within two years after surgery, the lesion had rapidly grown and caused marked discomfort for the patient. The tumor could be associated with the massive reactive proliferation of fibroblasts and myofibroblasts triggered by the external impact and intrinsic injury of the neck muscles and fascia after surgery. Therefore, surgical treatment was applied. During follow-up, the patient underwent cervical MRI half a year after surgery. The MRI scanning results revealed abnormal signals within the soft tissue of the neck and therefore, further examination was recommended. The results suggested AF recurrence and the patient was re-admitted for radical surgery and volumetric modulated arc therapy. More specifically, the pathology suggested recurrence of invasive fibromatosis with infiltrative growth in striated muscles and adipose tissues. Through the follow-up of this case, the diagnosis and treatment patterns of AF were thoroughly explored. The choice of treatment modality may depend on the extent and location of the lesion, and the capacity of the medical facility. Based on the clinical condition and patients' preferences, any of the aforementioned treatment options may be potentially applied as a first- or second-line therapy. In general, surgery is not considered a first-line treatment strategy. Among patients with progressive AF, those with symptoms, systemic therapies, surgery and ablative therapies are considered. Systemic therapy is commonly applied as a first-line therapy. However, the choice of other treatment approaches, such as surgical resection and medical or ablative therapies, partially depends on the location of the tumor (10).

In a previous case report, unresectable AF of the neck was successfully treated with chemotherapy combined with NSAIDs for ~21 months (11). The most recent National Comprehensive Cancer Network guidelines recommend the systemic treatment of tumors with symptoms and impaired or threatened functions with common chemotherapy drugs, including sorafenib and methotrexate combined with vinorelbine, and methotrexate combined with vinblastine (12). The treatment of AF has gradually changed from surgical resection with active intervention to conservative treatment with follow-up monitoring.

Accurate diagnosis is crucial for AF treatment. In terms of rare AF in the neck, a differential diagnosis should be made to exclude the possibility of a solitary fibrous tumor or nodular fasciitis. In the case of solitary fibrous tumors, the incidence in the pleural cavity is >50%. The incidence of extrapleural disease is only 0.6% and rarely affects the head and neck (13). In terms of MRI scan, T1-weighted imaging (T1WI) showed an equivalent signal, T2WI an uneven hypersignal and enhancement a moderate to obvious enhancement. It was difficult to distinguish a solitary fibrous tumor from AF on the image. Therefore, imaging should be combined with a review of the patient's medical history, pathological findings and immunohistochemistry. In the case

of the present study, immunohistochemical staining showed that the solitary fibrous tumor was mostly positive for CD34, vimentin, Bcl-2 and CD99, and negative for S-100 and SMA. In addition, the female patient had a clear history of neck surgery, thus assisting the preoperative differential diagnosis. In nodular fasciitis, the benign lesion originates from the fascia tissue and its essence is considered a benign hyperplasia of the fibrous tissue. It most commonly occurs in the extremities, followed by the trunk and the head and neck (14). Nodular fasciitis is an isolated lesion, with a generally small size, which is characterized by rapid growth for no more than three months. Nodular fasciitis of the head and neck, which is commonly caused by local trauma and inflammation, is relatively rare (15,16). It is usually treated by local complete excision. Previous reports have suggested that it may spontaneously resolve, while preoperative diagnosis is difficult. The diagnosis of nodular fasciitis requires a combination of imaging findings, pathological diagnosis and immunohistochemical expression results (17,18).

In conclusion, AF near the incision site after cervical spinal cord ependymoma surgery is relatively rare. However, imaging examination alone cannot diagnose AF. In the case of the present study, immunohistochemical examination of AF indicated that the tumor cells expressed vimentin and SMA in the cytoplasm and β-catenin in the nucleus. The diagnosis of AF requires pathological results combined with immunohistochemical results.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

XZ, SL and BY conceived the study, participated in the design of the study, and collected the data and the images. XZ, GC, SL and BY drafted the manuscript. JD participated in the data acquisition and interpretation, was involved in drafting the manuscript and critically revised the manuscript. GC, TL and YG collected the clinical data and performed the literature research. XZ and TL confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

The patient provided written informed consent for publication of the medical data and images for this case.

Competing interests

The authors declare that they have no competing interests.

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