Chondromyxoid Fibroma-Like Osteosarcoma in Thoracic Spine with Azygos Tumor Thrombosis, A Case Report

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Case report

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Abstract

Background: Chondromyxoid fibroma-like osteosarcoma (CMF-OS) is extremely rare subtype of osteosarcoma, its clinical data is scarce, understanding of it is far from enough. Besides, it is short of typical imaging manifestations, it is not uncommon to be misdiagnosed clinically. Meantime azygos vein thrombosis is also a rare entity, and there is a big controversy over treatments for it.

Case presentation: Herein, we report a case of CMF-OS that occurred in spine, coincidently, azygos vein thrombosis was found. A young male patient came to our clinic because of continuous back pain, then neoplastic lesion was suspected in thoracolumbar vertebrae. The pathological results of the biopsy showed low grad of osteosarcoma, and chondromyxoid fibroma-like osteosarcoma was the primary diagnosis. Since the tumor cannot be en-bloc resected, he received palliative decompression surgery, followed by radio and chemotherapy. Azygos vein tumor thrombosis was not intervened, unfortunately, he died of heart failure caused by the thrombus migrated from azygos vein to right atrium. Before the palliative decompression surgery, both the patient and the clinical team were trapped in the dilemma of how big surgery should be done to maximize the benefits of this patient.

Conclusions: CMF-OS is indeed more aggressive than its pathological sections look like. Guidelines for osteosarcoma should be followed. Besides, it is important to recognize the danger of tumor thrombosis in azygos vein. Preventive measures have to be done timely to avoid catastrophic results.

Background

CMF-OS is an extremely rare type of low-grade osteosarcoma [1]. It has the imaging and pathological manifestations of osteosarcoma-like focal osteogenesis. A lot of myxoid stroma is usually found among loose aggregated cells, which are separated by fibrovascular septa. The tumor cells usually have low grad of atypia and mitotic phase [2]. However, CMF-OS is more biological aggressive than it looks like, and the prognosis is commonly poor [2]. Because of its atypicality, misdiagnosis is more likely to occur. Here, we report a case of CMF-OS involving extensive thoracolumbar (T10-L1) vertebrae and paravertebral tissues. Worse still, azygos vein tumor thrombosis was found, and its diagnosis and treatments were little known [3]. The young patient and the treatment team were entangled in the benefits and losses that surgery can bring. This is a dilemma that exists widely between doctors and patients. The presentation of this case is expected to provide a reference.

Case Presentation

A 17 years old male patient came to our clinic with back pain for 7 months with movement restriction in the morning, while symptoms got partially relieved 1 hour after exercises. In the beginning, he was diagnosed as "kidney stones" in a local hospital, and was given lithotripsy. However, his lower limbs got progressive weakness during the past 3 months, and had to get assistance during climbing up stairs.
Physical examinations found more than half of the key muscles’ strength of lower limbs were 4/5 (American Spinal Cord Injury Association, ASIA D) [4].

Lumbar X-ray films undertaken in a local hospital showed signal changes in T11 vertebra (Figs. 1A and B), CT scan images demonstrated osteogenic lesions in vertebrae and appendix of T11 and T12 (Figs. 1C and D). MRI scan images furtherly showed signal changes in vertebrae, pars and paravertebral tissue from T11 to L1, furthermore, spinal canal was partially occupied and spinal cord was compressed (Figs. 2A and B). Then, needle biopsy was undertaken at L1 vertebra under CT navigation, and CMF-OS was the primary diagnosis. High metabolic level was found in the above sites (including azygos vein at T11 level) in systemic metabolic nuclide images. No previous medical history was declared.

Pathology report

T11 paravertebral soft tissue was basically highly calcified myxoid stroma tissues with disordered structure, tumor cells were sparsely distributed and separated by cells rich sheath. Vertebral bone tissue was partially replaced by multi-nodular lesions. The myxoid stroma can be seen in the lesions with focal calcification and osteogenesis, and the peri-nodular interstitial cells were rich and nuclei had heteromorphism. From the results of immunohistochemistry, chordoma was excluded, and chondromyxoid fibroma-like osteosarcoma was considered.

In details, S-100(-), SOX9(-), P53(-), Osteopontin (+), Osteonectin (+), CD34(-), Ki67(6%), brachyury (-), vimentin (+). From pathology report, chondromyxoid fibroma-like osteosarcoma was considered a kind of low-grade osteosarcoma. The pathology sections were consulted with top pathologists from several Hospitals, and reconfirmed the primary diagnosis.

Chemotherapy and Surgery

Chemotherapy was firstly considered for osteosarcoma to eradicate the malignant cells in circulation, reduce the tumor size, and create opportunities for tumor resection [5]. He received two courses of chemotherapy with methotrexate (16 g) and vincristine (2 mg). During the course of chemotherapy, the neurological status of lower limbs furtherly deteriorated, and the muscle strength dropped to 0 grade, while the function of defecation and urination was normal. After multidisciplinary consultation, it was recommended that surgery be performed emergently to save nerve function, and then chemotherapy or other treatments was continued.

Preoperative physical examination found pinprick and temperature sensation in the skin below the groin disappeared, while proprioception sensation existed. Muscle strength of lower limbs below the iliopsoas muscle is 0/5 grade. Hyperreflexia was found in both patellar tendons, and Babinski sign was negative on both sides.

Pedicle screw fixation was implanted for vertebrae of T7,8,9 and L2,3,4. Intralesional resection was executed for T10,11,12, and L1 (lamina, upper and lower articular processes and pedicles), and tumor in
intraspinal canal was also resected, however, there was still much tumor tissue remained in paravertebral and vertebrae. Operation took 5 hours, and bleeding volume was 1500 ml.

Nerve function recovered partially, e.g., iliopsoas, quadriceps muscle strength recovered to level Ⅴ/Ⅴ. The general condition was good and nutritional status was basically normal (albumin 39 g/L, hemoglobin 107 g/L). Post-operative pathology confirmed the diagnosis of CMF-OS, but tumor cells did not proliferate fast, therefore, the patient was not suitable for high-throughput genetic testing. Besides, no obvious tumor necrosis was found after chemotherapy, which verified the tumor was not sensitive to chemotherapy of Methotrexate (MTX) and vincristine.

Discussion

CMF-OS low grade, but high aggressive.

CMF-OS is an extremely rare type of malignant tumor, and shares the same biological behavior as osteosarcoma, so it is defined a subtype of osteosarcoma and follows the same principles of treatment [2]. After medical history collection and physical examination, regional lesion was initially evaluated by CT and MRI, distal metastasis was excluded by Pet/CT. Besides, bone metabolism, e.g., alkaline phosphatase (ALP), Lactic Dehydrogenase (LDH), should also be tested to evaluate bone metabolism [5].

For low-grade osteosarcoma, it is well established that extensive resection should be firstly considered, followed by sensitive chemotherapy or radiotherapy if there was residual tumor tissue. Although first line chemotherapy for osteosarcoma are cisplatin and doxorubicin with or not with high dose of methotrexate, obviously, the regular chemotherapy plan is not fit for the low proliferative osteosarcoma as CMF-OS, and the poor results of chemotherapy for this patient confirmed the idea. Methotrexate plays an anti-tumor effect mainly by inhibiting the DNA synthesis of tumor cells [6]. While the vincristine targets at microtubules, which mainly inhibit the polymerization of tubulin, affect the formation of spindle microtubules, and finally stop mitosis in the metaphase [7]. The reasons for choosing MTX and vincristine are experimental treatment, considering their relatively low toxicity. However, after two courses of chemotherapy, the neurological status deteriorated very quickly, and palliative decompression had to be carried out emergently to preserve neural function.

According to NCCN guideline, radiotherapy should be considered for patients with positive margins of resection, partial resection or unresectable cases [8]. For this patient, he received large fractionation radiotherapy of total 60 Gy. Until he passed away (6 months after operation), no local or distant recurrence was found.

Proactive treatments are suggested for azygos vein with tumor thrombosis
Azygos vein is usually located at the right anterior side of spine (from T1 to L2), it connects with right subcostal vein, inferior vena cava, ascending lumbar vein, accessory hemiazygos vein and intercostal veins. During en bloc spondylectomy, attention should be paid to this venous system [9]. For this case, medical images showed venous thrombosis in azygos vein. Without intervention, the patient died from heart failure caused by thrombus in atrium which probably came from azygos. Therefore, resection of azygos with thrombosis should be actively considered in case of migrating to atrium. As far as we know, this was the first report about heart failure caused by azygos tumor thrombus.

**The dilemma of benefits and loses**

To the beginning, tumor tissue should be resected as much as possible, including vertebrae, paravertebral tumor tissue, and azygos vein with tumor thrombosis. Two stages were needed to finish the operation. Firstly, azygos vein with thrombosis should be resected, and tumor tissue in the anterior and lateral side should be freed through anterior approach. Secondly, 3D-Printed prosthesis vertebrae or titanium mesh can be used to achieve spine reconstruction through posterior approach. However, tumor tissues were so extensive that it was hard to complete en bloc resection. The possibility of complete resection was pretty low, and the complication rate was very high, even made his life in danger. Therefore, en bloc resection was impossible, and intrallesional resection was chosen to preserve neurological function.

Besides, tumor thrombosis was found in azygos vein, which was also a rare phenomenon and difficult to treat. The question was whether should we have an excision of azygos vein with thrombosis at great risk. Even though it is a major operation [3], the resection of azygos vein with thrombosis may save his/her life. Because thrombus formed in azygos vein may migrate upward, and finally result in superior vena cava and heart thrombosis [10]. However, reconsider the tumor can only be partially resected, and both the patient and surgeons did not want to take the risk of resection of an azygos vein with thrombosis. Furthermore, poor prognosis was deduced considering the unresectable tumor and poor responsive to neoadjuvant chemotherapy. Based on the above issues, palliative resection of tumors by posterior approach was chosen with the main purpose of saving nerval function. Then chemotherapy plan was readjusted according to postoperative pathology results, similarly, whether to remove the anterior vertebral body depended on postoperative pathology report and the results of multidisciplinary consultation.

The balance of benefit and lose was hard to achieve when we just considered the state of illness, let alone the very poor financial compensation he could get. However, it is common to see families suffer extreme poverty because of serious diseases in many countries. Furthermore, life expectancy is not always easy to judge according to tumorous classification and stage. All in all, it is difficult to balance possible complications, benefits and the financial burden after operation.

Finally, this patient received palliative decompressive surgery. Unfortunately, he died of heart failure caused by thrombus from azygos vein, which was not anticipated. In other words, resection of azygos vein with thrombosis in time may save his life. This was a bitter lesson, worthy of our attention.
Conclusions

Restate the major findings and address their potential implications or applications. In this report, a case with spine CMF-OS was reported, and it was much more malignant than its pathology looked like. The patient did not well respond to chemotherapy, and the prognosis was very poor. Besides, it should be emphasized that that azygos vein thrombosis was present, and the patient died of heart failure caused by thrombus in right atrium. Therefore, we recommend active intervention to deal with azygos vein thrombosis, and prevent thrombus from upward migrating.

Abbreviations

CMF-OS: Chondromyxoid fibroma-like osteosarcoma
ASIA: American Spinal Cord Injury Association
MTX: methotrexate
ALP: alkaline phosphatase
LDH: Lactic Dehydrogenase

Declarations

Ethics approval and consent to participate

The study received approval from the Ethics Committee for Medical Science Research of Peking University Third Hospital, and got the informed consent of patients.

Consent for publication

The patient agreed to make their medical information public and signed on the patient’s consent. All authors agreed to publish this manuscript in World Journal of Surgical Oncology, and the corresponding author will submit the manuscript on their behalf.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to patient privacy but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

Chuanchao Du: Conceptualization, Methodology, Writing-Original Draft, Submission. Shanshan Liu: Visualization, Software. Yu Liu: Validation, Formal analysis, Visualization. Xiaoguang Liu: Resources, Writing - Review & Editing. Feng Wei: Writing: Review & Editing, Supervision.

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**Figures**

**Figure 1**

X-ray films (A, B) and CT images (C, D) showed the high-density osteogenic changes (* in red) in the T11 vertebrae body (A, B, C, D) and appendages (C, D), and involved with the upper and lower stages of the spinal canal (C, D).
Abnormal signals were found in T11, T12 and corresponding spinal canal in contrast-enhanced magnetic resonance images both in sagittal and axial images (T1-weighted imaging). Tissues suspected of being tumors can be significantly enhanced in MRI images (* in red).

**Figure 2**
Figure 3

The azygos vein (* in red) was occupied by tumor like tissues (A), and the tissues were significantly enhanced in MRI T1-weighted imaging (B).

Figure 4
Haematoxylin-eosin staining of T11 paravertebral tissue showed nodular calcification and osteogenesis separated by cells rich septa (A, 100×). Under high-power microscopy (B, 400×), tumor cells were loosely aggregated in myxoid stroma and osteoid was produced, nuclei heteromorphism can be found. Vimentin staining of the same section was positive (C, 100×; D, 400×).