Undifferentiated Pleomorphic Sarcoma of the Spine in a patient with Li-Fraumeni syndrome: a case report

Linxiang Zhang
Ningbo University Medical School https://orcid.org/0000-0002-2645-9472
Jijie Yan
Ningbo University Medical School
Guangjian Bai
Changhai Hospital Department of Oncology
Yiwei Hu
Ningbo University Medical School
Lijun Jiang
Ningbo University Medical School
Kai Guo
Weifang Medical University
Shuming Hou
Changzheng Hospital
Xing Huang
Changzheng Hospital
Tielong Liu (liutielongvip@163.com)
Changzheng Hospital

Case report

Keywords: undifferentiated pleomorphic sarcoma, Li-Fraumeni syndrome, treatment

Posted Date: August 7th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-53509/v1

Abstract

Background Undifferentiated pleomorphic sarcoma (UPS) is an aggressive tumor that rarely occurs in the spine. We present a 38-year-old male patient with Li-Fraumeni syndrome and discuss the treatment and prognosis.

Case presentation A 38-year-old male patient presented with bilateral lower extremity weakness accompanied by radiation pain. He had been diagnosed with right adrenal cortical carcinoma previously and had a strong family history of cancer. PET/CT indicated increased uptake in many parts of the body, especially the right adrenal gland, the left occipital lobe, and the L4 vertebral body (VB). MRI also revealed the destruction of the L4 vertebral body and a paraspinal soft-tissue mass. The tumor was completely resected and pathological findings revealed UPS. Subsequent genetic testing revealed a mutation in the TP53 gene, which is consistent with Li-Fraumeni syndrome (LFS). The patient received postoperative adjuvant radiotherapy and did not develop local recurrence, metastasis, or secondary cancer during the 31-month follow-up.

Conclusions Spinal UPS is a rare aggressive tumor with a poor prognosis. Surgery alone can improve the survival of patients but cannot effectively control the disease. In spinal UPS patients with LFS, we think that the prognostic benefits of postoperative adjuvant therapy outweigh the risks of long-term secondary cancer. Family history of cancer and genetic testing can help diagnose LFS, and MRI of the spine can aid the early detection of microlesions. For these patients, early diagnosis and intervention can effectively improve survival.

Background

Undifferentiated pleomorphic sarcoma is an aggressive type of tumor with a poor prognosis, with 5-year survival rates ranging from 30–50%[1, 2]. Primary UPS arising from the spine is relatively rare, and only a small number of UPS cases involving the spine have been reported since its first description in 1975[3, 4]. Spinal UPS has poorer survival rates compared to UPS at other sites, with a 5-year survival rate of only 7.7%. The probability of having two rare primary malignancies in the same patient is very low and should raise suspicions concerning the implication of a hereditary disease. Li-Fraumeni syndrome (LFS) is a rare autosomal dominant cancer predisposition syndrome with exceptionally high lifetime cancer risks. It is predominantly caused by mutations of the TP53 gene. It is notable that chemoradiotherapy is not recommended for patients with LFS because it will increase the risk of secondary cancer. Whether postoperative adjuvant therapy should be used is currently controversial. The purpose of this study was to discuss the treatment and prognosis of spinal UPS in patients with Li-Fraumeni syndrome.

Case Presentation

A 38-year-old male patient presented with right lower back pain for one week. Computed tomography (CT) results suggested that there was a large circular low-density lesion in the right adrenal gland and

osteolytic destruction in the L4 vertebral body (Fig. 2C,D). The patient then had an adrenal biopsy, and the pathological findings revealed adrenal cortical carcinoma (ACC). The patient did not undergo surgery immediately because the tumor was too large, measuring 10*9*10 cm. A week later, the patient complained of bilateral lower extremity weakness accompanied by radiation pain in the left lower extremity. Physical examination revealed tenderness and percussion pain in the lumbar spine. The patient had a strong family history of cancer: two uncles had died of lung cancer, one was diagnosed before the age of 45 years old, and the other was unknown. ^{18}FDG PET/CT was performed and the rate of ^{18}FDG uptake was abnormally high in many parts of the body, especially in the L4 VB, right adrenal gland, and left occipital lobe. The results indicated that the L4 vertebral lesion may have derived from the ACC. Magnetic resonance imaging (MRI) revealed osteolytic destruction of the L4 VB and identified a paraspinal soft-tissue mass at the level of the L4 VB (Fig. 3E,F,G). The lesions showed low signal on T1-weighted images and mixed signal on T2-weighted images. A posterior spinal tumor resection and autograft with internal fixation was performed (Fig. 4H). During the surgery, we saw that the tumor was a white flesh colored and friable mass with incomplete capsule. After the surgery, the symptoms in the lower extremity were relieved. Postoperative pathological reports indicated undifferentiated pleomorphic sarcoma (Fig. 5I,J). Immunohistochemistry showed Vimentin (+), CD68 (kpl) (+), Ki67(30% positive). This patient had two primary malignancies and a strong family history of cancer, therefore we suspected that the patient had Li-Fraumeni syndrome (LFS) and recommended him for further genetic testing. The testing results revealed mutations of the TP53 genes. The information to date was consistent with the characteristics of LFS. Later the patient received postoperative adjuvant radiotherapy and did not develop local recurrence, metastasis, or secondary cancer during the 31-month follow-up.

Discussion

UPS, previously termed malignant fibrous histiocytomas (MFH), is a common subtype of soft tissue sarcoma[5]. UPS is an aggressive tumor type and is associated with a high risk of local recurrence and distant metastasis[5–10]. UPS of the bones predominantly affects males and has a peak incidence between the ages of 50 and 70 years old[11, 12]. The prognosis of UPS is poor, with five-year survival rates ranging between 30–50%[1, 2]. UPS can appear throughout the body, but 60% of cases occur in the extremities[5, 13]. Primary UPS arising from the bone is relatively rare. The statistics have shown that skeletal involvement of UPS represents less than 2% of primary malignant bone tumors[3]. In most cases, UPS of the bone develops around knee joints and in proximal femurs and humerus[3, 14]. Only a small number of UPS cases involving the spine have been reported since its first description in 1975.

Currently, surgical resection is still the mainstay of treatment for spinal UPS, and complete resection with a negative margin can improve the survival of patients. Ozkurt *et al* reported that patients with wide surgical margins had a five-year survival probability of 81.9%, while for patients with marginal surgical margins this was 33.3%[14]. Goertz *et al* retrospectively studied 192 UPS patients and found that those with negative margins had better overall survival[5]. In the treatment of UPS, surgery alone is not sufficient and the rate of local recurrence (LR) and distant metastasis is high. LR occurs in between 25–

75% of cases[3, 15], especially for patients with inadequate margins[14]. Radiotherapy should be considered as an adjuvant therapy, especially for patients with non-wide margins. Dahlin *et al* [16] used radiotherapy to treat two cases of unresectable pelvic tumors, neither patient suffered distant metastasis or local recurrence during follow-up. In one large study, patients with high-grade MFH of the extremities who underwent excisional surgery, followed by postoperative radiotherapy, experienced a 10-year relapse-free survival of 62% and an overall survival rate of 80%[15, 17]. Ole Goertz *et al* found that adjuvant radiotherapy could decrease the risk of local failure and significantly improve overall survival (OS)[5]. The use of chemotherapy in spinal UPS treatment is controversial. UPS is also less sensitive to the first-line chemotherapeutics Doxorubicin and Ifosfamide[5]. Lehnhardt *et al* analyzed 140 patients with UPS in their extremities and found adjuvant chemotherapy to have no effect on prognosis[3, 8]. Nevertheless, Weiner *et al* treated three patients who suffered MFH of the bone with radical resection and adjuvant chemotherapy. All three patients remained disease-free with no complications over a follow-up period of 42–48 months[12]. Bacci *et al* reported that 70% of patients who received neoadjuvant chemotherapy combined with surgery survived 6.5 years during the follow-up period, which was significantly higher compared to the 20 patients who underwent surgical resection only[18].

It is notable that in our case the patient's condition was unique. He suffered from two primary malignancies and had a strong family history of cancer. We suspected that the patient had LFS and recommended him for further genetic testing. The result showed mutation of the TP53 gene. These characteristics met the diagnostic criteria of LFS. Patients with LFS have an increased risk of malignancy and mutations in TP53[19]. The lifetime risk of cancer has been previously reported to be nearly 100% by the age of 60 years in women and 73% in men[19, 20]. Breast cancer, bone, soft tissue sarcomas, brain tumors, and adrenocortical carcinoma are 'core' LFS cancers. Radiation exposure should be avoided in patients with LFS because it may induce secondary cancers[21]. In terms of chemotherapy, patients with LFS should not be treated with alkylating agents because of their DNA-damaging properties. In patients with LFS, whether to give adjuvant therapy for the treatment of spinal UPS is a conundrum. For tumors with a high degree of malignancy and poor prognosis, we believe that the prognostic benefits of postoperative adjuvant therapy outweigh the risks of long-term secondary cancer. Potapov *et al* reported that surgery combined with chemotherapy has a good prognosis in the treatment of anaplastic oligodendroglioma[22]. Klein JD *et al* used surgery and adjuvant radiotherapy to treat mucosal melanoma with LFS, and there was no recurrence, metastasis, or second primary tumor at a 30-month follow-up[23]. While Hosoya T *et al* used both postoperative radiotherapy and chemotherapy to treat a 7-year-old boy who suffered anaplastic ependymoma with LFS, but the prognosis was poor, and recurrence could not be prevented[21]. In these studies, postoperative adjuvant therapy did not result in a secondary primary tumor. The difference in the effects of the treatments was mainly related to whether the primary tumor was sensitive to chemoradiotherapy. Spinal UPS is an aggressive malignant tumor, and some studies have shown that chemoradiotherapy is effective in reducing local recurrence and metastasis rates. In our case, the patient undertook postoperative adjuvant radiotherapy, and there was no local recurrence, metastasis and secondary cancer during the 31-month follow-up. So, we believe that for these

patients, the benefits of postoperative adjuvant chemoradiotherapy outweigh the risks of secondary primary cancer.

It is rare for a patient to have two primary malignancies at the same time. In our case, the patient already had confirmed ACC before coming to our hospital. PET/CT indicated increased uptake in many parts of the body. The lesion in the L4 VB was suspected to be derived from the ACC. ACC is a rare malignancy with poor prognosis and high rates of metastasis[24]. However, postoperative pathological findings indicated UPS. How to differentiate between spinal UPS and metastatic carcinoma of the spine is very important to determine the treatment regimen. For spinal UPS, computed tomographic scans revealed osteolytic destruction without periosteal reaction or new bone formation[25]. Moreover, magnetic resonance imaging showed a rapidly enlarged paraspinal soft tissue mass at the contiguous level, with a tendency to extensively invade surrounding structures around the vertebrae. As for osteolytic metastatic cancers of the spine like ACC, osteolytic destructions are visible on a plain radiograph. The cancellous bone was resorbed and cortical bone disappeared. In the sagittal position, double margin shadows could be observed at the upper margin of the vertebral body caused by pathological vertebral collapse. CT revealed moth-eaten changes, vertebral bodies, and pedicles which disappeared and were replaced by soft-tissue masses. MRI revealed an epidural soft-tissue mass or convex posterior vertebral body border. On T1-weighted images, the lesion showed a low signal change, while on T2-weighted images, this was a high signal change. These differences in imaging findings may help to differentiate spinal UPS from other metastatic carcinomas. Of course, the final diagnosis still depends on the pathological findings.

Many studies have shown that advanced age is an independent risk factor for poor prognosis[26, 27]. Lou *et al* [3]revealed that an age ≥ 55 years were independently associated with poor overall survival in spinal UPS. Therefore, early diagnosis is quite important. While the early diagnosis of spinal UPS is difficult and often not made until an advanced stage has been reached, when the lesion is large or nerve compression has been presented[25]. For asymptomatic patients with a family history of malignancy, genetic testing can be valuable. If LFS is apparent, monitoring for the occurrence of spinal UPS should be conducted vigilantly. An annual spine MRI can help to detect microscopic lesions early. Individuals who undergo cancer surveillance have significantly lower cancer-related mortality and higher overall survival compared with those who do not, suggesting that a comprehensive surveillance strategy is feasible and clinically relevant.

Conclusions

Spinal UPS is a rare aggressive tumor with a poor prognosis. Surgery alone can improve the survival of patients but cannot effectively control the disease. In spinal UPS patients with LFS, we think that the prognostic benefits of postoperative adjuvant therapy outweigh the risks of long-term secondary cancer. Family history of cancer and genetic testing can help diagnose LFS, and MRI of the spine can aid the early detection of microlesions. For these patients, early diagnosis and intervention can effectively improve survival.

Abbreviations

UPS
Undifferentiated pleomorphic sarcoma
LFS
Li-Fraumeni syndrome
VB
Vertebral body
ACC
Adrenal cortical carcinoma
MFH
Malignant fibrous histiocytomas
LR
local recurrence
OS
overall survival

Declarations

Acknowledgements

We would like to acknowledge the patient and his family for allowing us to use his medical records in our case report and allowing this case to be published.

Funding

We authors declare that we have not received any kind of fund from any source and do not have any conflict of interest in this present study.

Availability of data and materials

We respect the patient's rights to privacy and to protect his identity, so we do not wish to share our patient data. We presented, in the manuscript, all the necessary information about the case report. Raw data regarding our patient is in his admission file, a file that is strictly confidential, without the possibility of publishing raw data from it.

Authors' contributions

Author LXZ is mainly responsible for Conceptualization, Methodology, Writing - Review and Editing. Author JJY is mainly responsible for Data curation and investigation. Author GJB is mainly responsible

for Writing - Original Draft and software. Authors YWH, LJJ, KG, SMH and XH is mainly responsible for data collection and analysis. Corresponding author TLL is mainly responsible for validation, supervision and project administration. All authors read and approve the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

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

Ethics approval and consent to participate

This clinical study of the abovementioned case report was waived by the institutional review board at our center.

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Figures

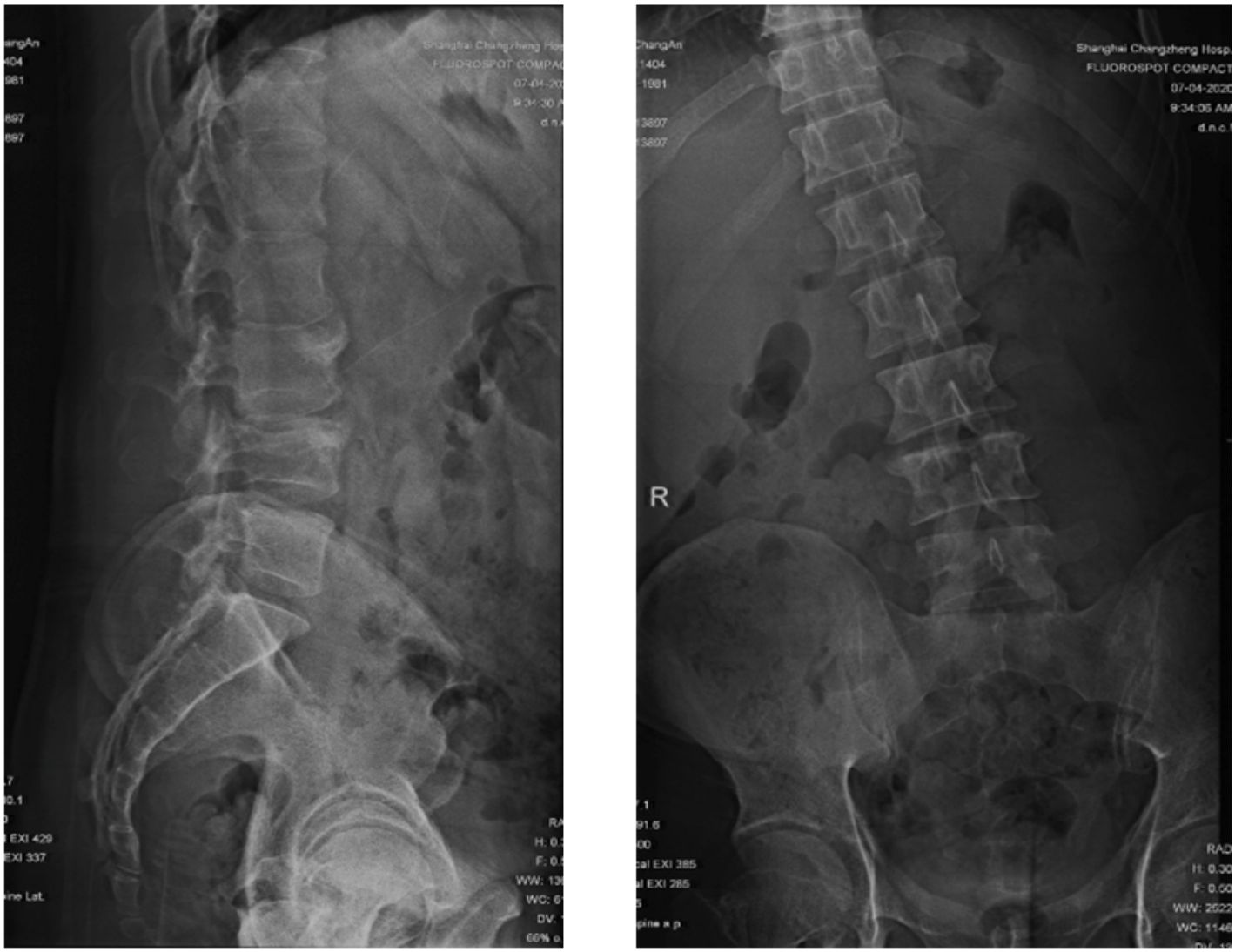
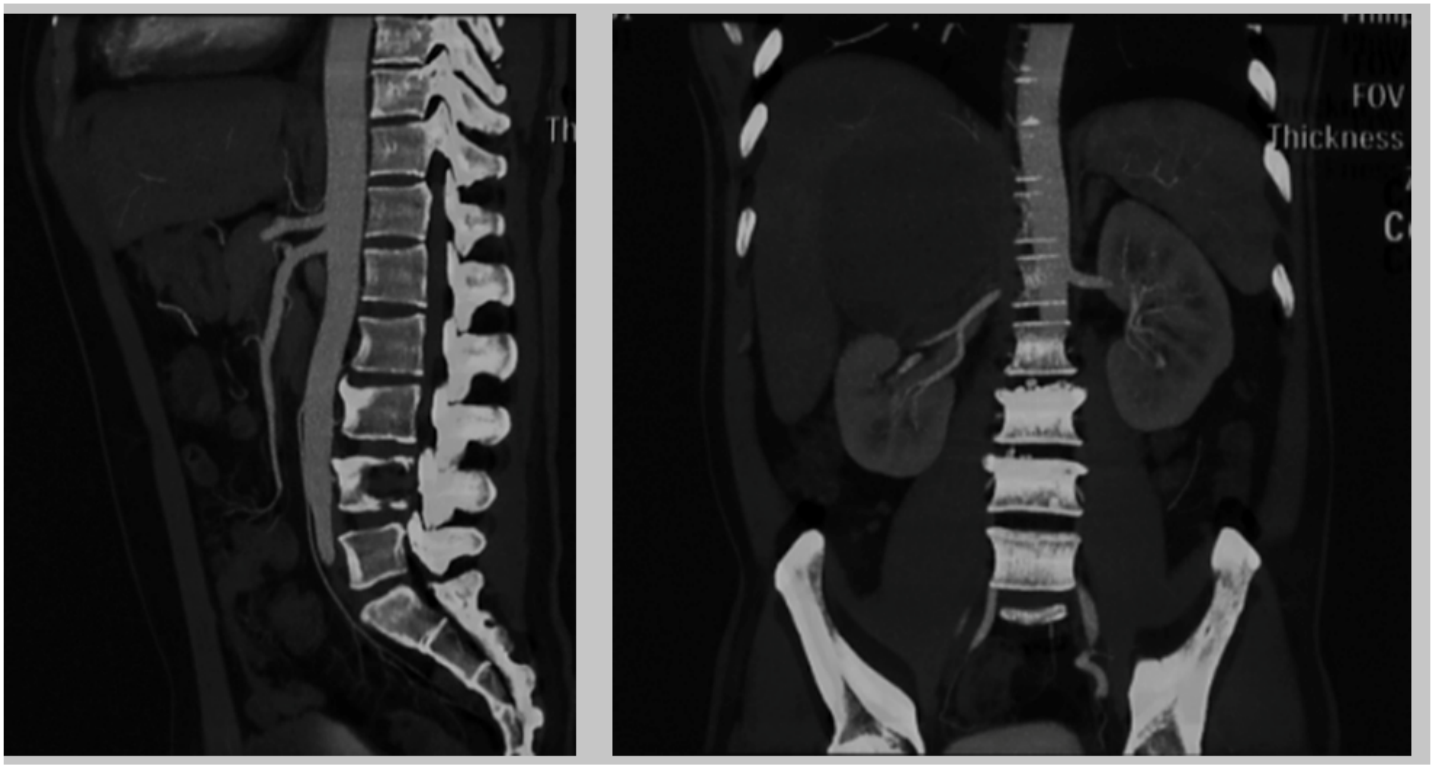


Figure 1

(A) and (B), The lateral and anterior view of X-ray, showing the destruction in L4 vertebral body.



(C) (D)

Figure 2

The sagittal CT scan, showing the osteolytic lesions in L4 VB with soft tissue involving (C). The coronal CT scan, showing a large circular low-density lesion in the right adrenal gland (D).

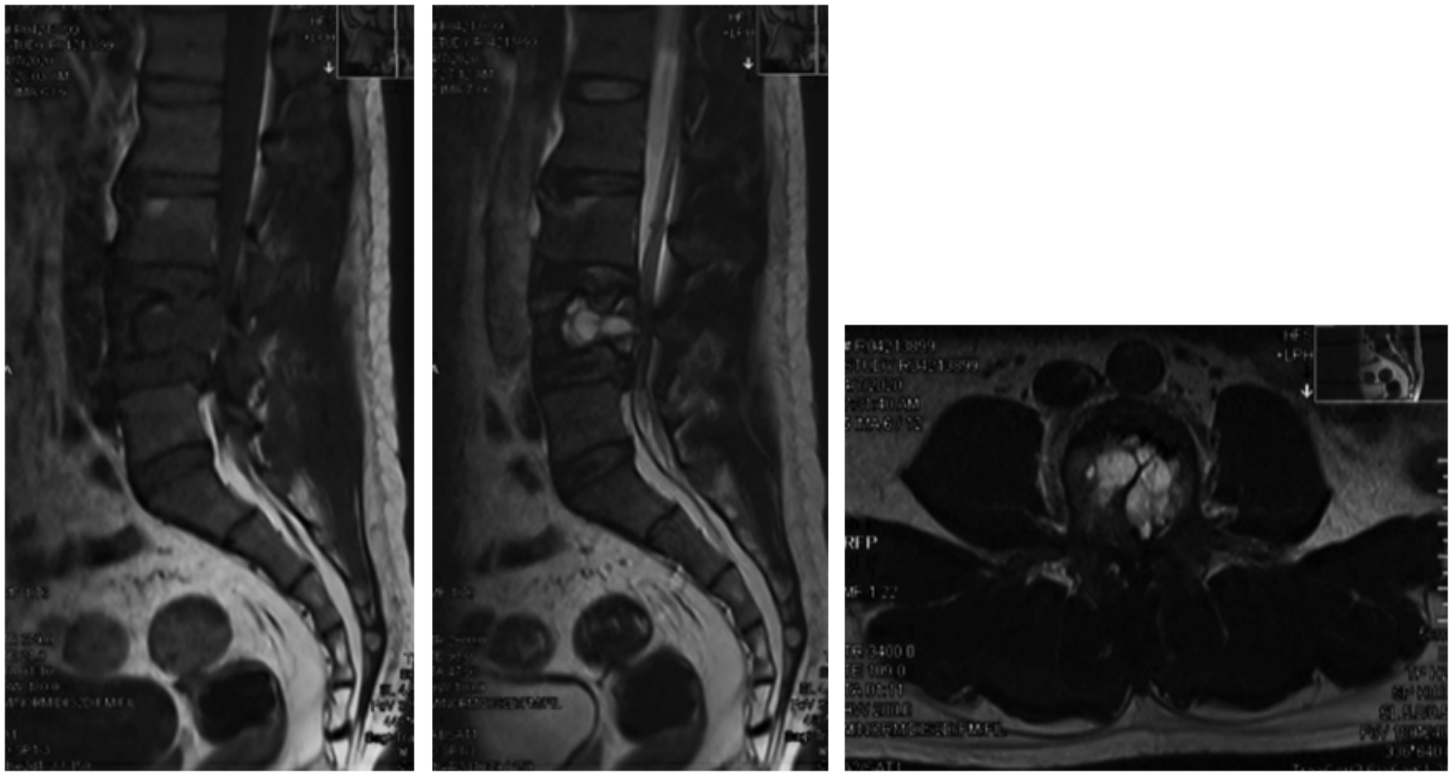
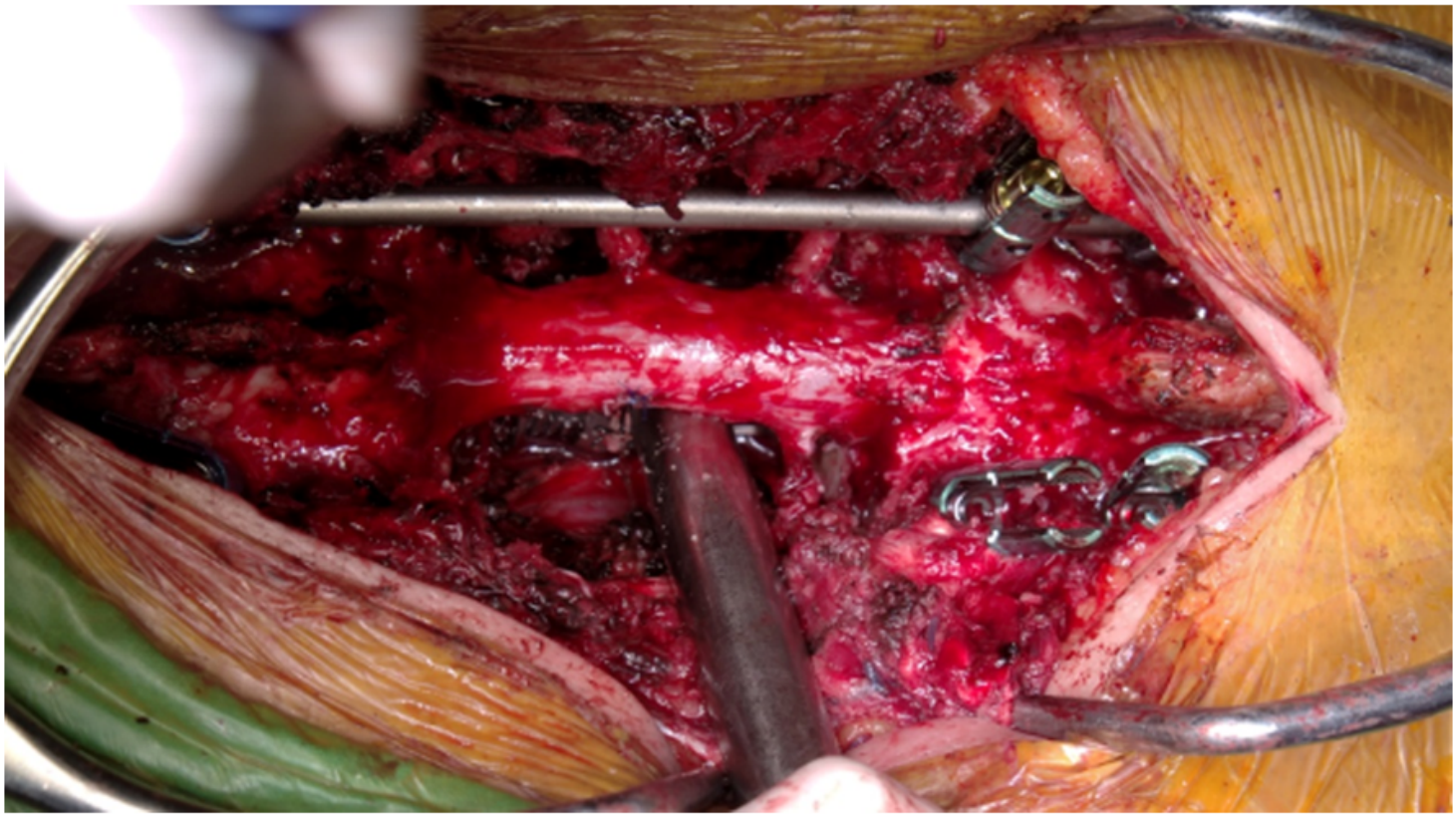


Figure 3

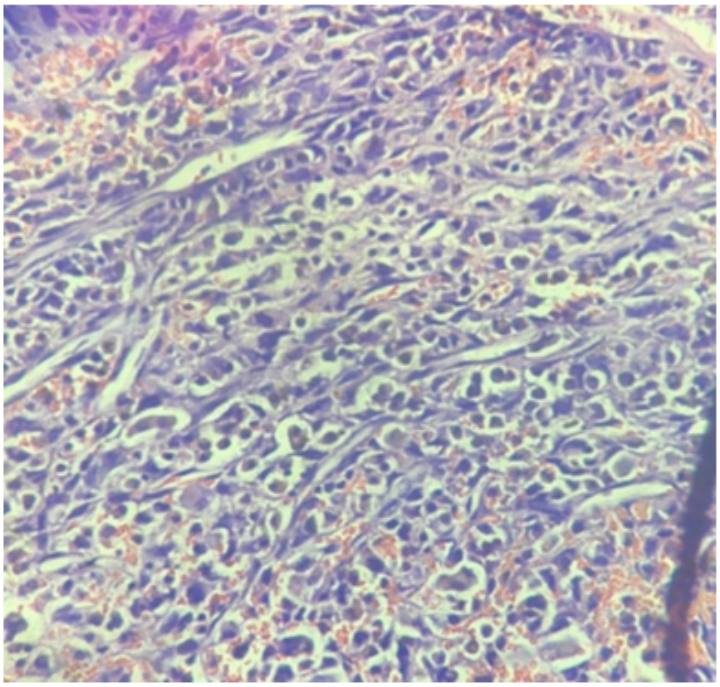
The sagittal section of the T1-weighted magnetic resonance image, revealing a soft tissue mass in and around the L4 VB, which has compressed the spinal cord (E). The sagittal and transverse section of the T2-weighted magnetic resonance image, revealing the destruction of L4 VB with soft tissue involving, and the mass compressed the nerve root (F and G).



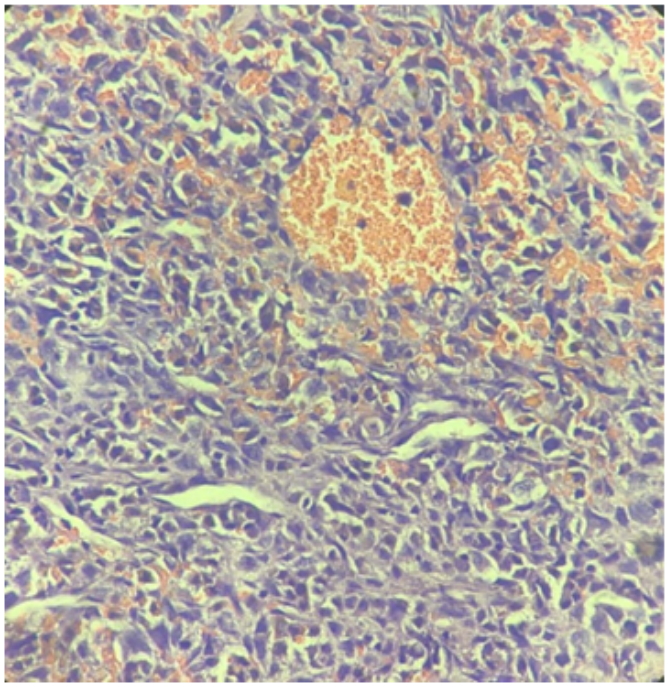
(H)

Figure 4

The graph of exposed spinal cord after laminectomy (H).



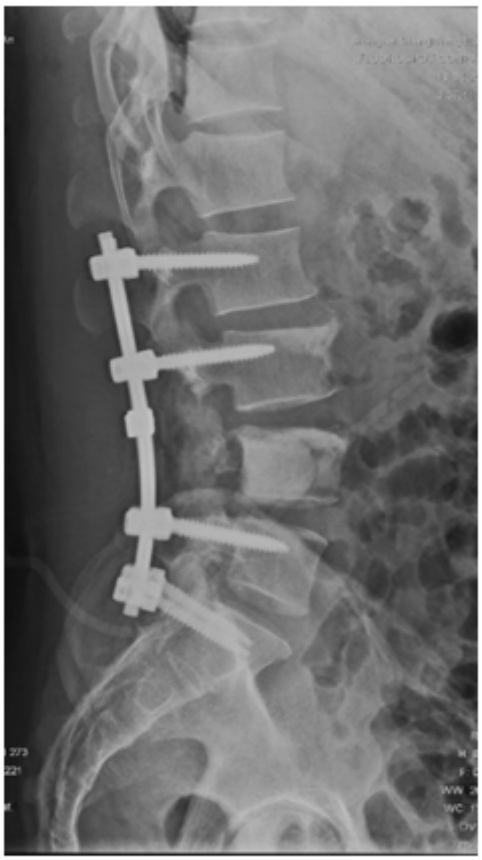
(I)



(J)

Figure 5

Photomicrograph showing highly heterotypic fusiform, round, polygonal cells were in clumps and some of the single cells were arranged in a way that looked like papillary growth. The tumor giant cells were visible, the nuclei were more delicate, some nucleoli were visible, and there was extensive hemorrhage in the stroma (hematoxylin & eosin staining×400) (I and J).



(K)

Figure 6

The postoperative X-ray image, showing the internal fixation position is good (K).