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Images Combined With Surgical Procedures and Pathological Identification to Distinguish a Reactive Histiocytosis With Organized Hematoma From a Malignant Peripheral Nerve Sheath Tumor

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Abstract. *Background/Aim: Malignant peripheral nerve sheath tumors (MPNST) are rare soft tissue malignant tumors. To the best of our knowledge, there have been no previous reports of benign reactive histiocytosis with hematoma that mimics MPNST on medical images. Case Report: A 57-year-old female with past history of hypertension came to our clinic due to low back pain with radiculopathy which was diagnosed with a tumor arising from L2 neuroforamen with L2 pedical erosion. Initial tentative diagnosis on the images was MPNST. However, after surgical resection, the pathologic report revealed no evidence of malignancy but only an organized hematoma with reactive histiocytosis. Conclusion: Images cannot provide enough diagnostic evidence for distinguishing a reactive histiocytosis from MPNST. Proper surgical procedures and expert pathological identification can correct the mistaking of the ambiguous identification as MPNST. Images can only provide precise and personalized medication accompanied by proper surgical procedures and expert pathological identification.*

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Malignant peripheral nerve sheath tumors (MPNSTs), also known as nerve sarcomas or nerve fiber sarcomas, are rare malignant tumors of the soft tissues (1). Their incidence is 0.001% in the general population and 3-5% in patients with neurofibromatosis Type 1 (NF1) (2, 3). Despite the use of radical surgery along with adjuvant therapy as a standard approach against MPNST for several decades, the prognosis for patients with MPNST remains poor, with less than 50% surviving for 5 years (4). In contrast, benign reactive histiocytosis (BRH) is a benign disorder characterized by the proliferation of histiocytes, including the monocyte/macrophage series and Langerhans cell/dendritic cell series (5). MPNST and BRH differ significantly in their pathophysiology and histology, leading to distinct clinical management and outcomes. Therefore, we aimed to address this issue by providing appropriate diagnostic and management solutions for these two distinct conditions.

In the literature, there is no clinical study to have examined the two disorders spontaneously. Herein, we report a novel case of BRH with hematoma in the lumbar spine that was initially suspected to be MPNST. We successfully distinguished between MPNST and BRH by employing surgical procedures and pathological identification, rather than relying solely on imaging findings. This is the first report to describe the differential diagnosis of these two conditions using such an approach.

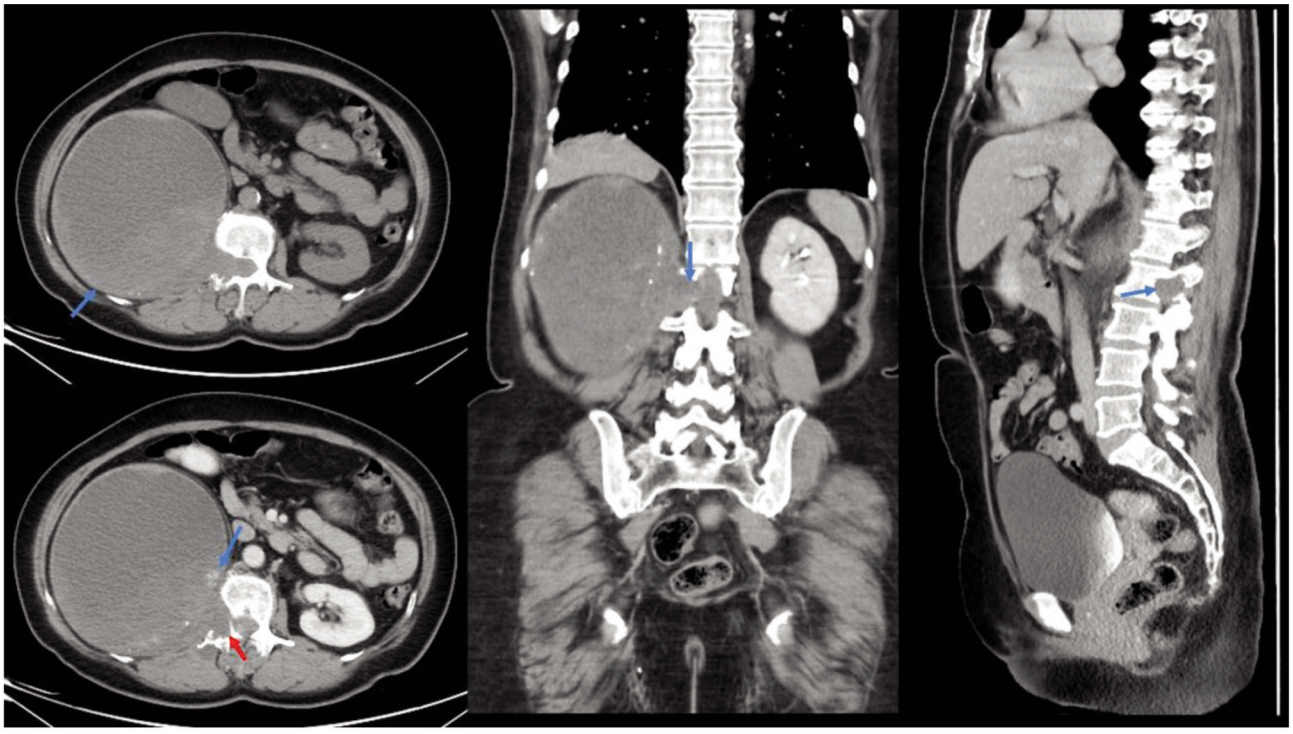

Figure 1. *Abdominal CT revealed a suspected retroperitoneal cystic tumor. A 15.4×15.3×15.8 cm tumor arisen from the right neuroforamen of L2 showed cystic, solid, blood product and calcified content (blue arrows). Destruction of perifocal vertebral bone and pedicle are also noted (red arrow). CT: Computed tomography.*

Case Report

Patient characteristics. A 57-year-old woman with a medical history of hypertension, receiving regular treatment presented to our hospital with severe low back pain persisting for approximately two weeks. She had been experiencing chronic low back pain for several months prior to her visit. She reported experiencing intense pain with a sensation of stinging and cramping that radiated from her flank to her right thigh. The patient also presented with weakness in her right thigh, exhibiting a muscle power grading of 2 out of 5, and intermittent claudication. Her visual analogue pain score was 8 out of 10, and she denied any history of trauma.

Physical examination revealed a significant decrease in muscle power upon right hip flexion and a positive straight leg raising test (SLRT) on the right leg. Furthermore, a large, immobile, non-tender mass was observed in the right upper abdomen. Abdominal computed tomography (CT) scans revealed a suspected 15.4×15.3×15.8 cm retroperitoneal cystic tumor originating from the right neuroforamen of L2, which resulted in bone erosion at the right L2 pedicle (Figure 1). Contrast-enhanced magnetic resonance imaging (MRI) of the lumbar spine depicted a substantial cystic mass in the right retroperitoneum with heterogeneous contrast-enhanced smaller components in the enlarged right L2-L3 foramen, right L2 pedicle bone erosion, and a long posterior epidural lesion with slight enhancement from T10 to the upper L5 level (Figure 2). Based on the images, it was concluded that a tumor originating from the L2/3 foramen, with bone erosion, had extended into the retroperitoneal cavity and the epidural space. Due to positive neurological deficits, surgical intervention was deemed necessary for the removal of the tumor.

Imaging. The patient was subjected to routine examination with a computed tomography (CT) scan since a huge and noted firm mass at right upper abdomen was found by visiting the China Medical University Hospital immediately after an emergent diagnosis. Since a huge retroperitoneal cystic tumor arose from right neuroforamen of L2 with bone erosion at right L2 pedicle was identified by the CT scan, in favor of MPNST by experienced radiologists, the L-spine contrast-enhanced magnetic resonance imaging was conducted immediately after the CT outcome. The study has been approved and supervised by China Medical University Hospital (CMUH111-REC3-053).

Surgical procedures and pathological identification. The suspicious diagnosis could be MPNST, sarcoma, metastatic

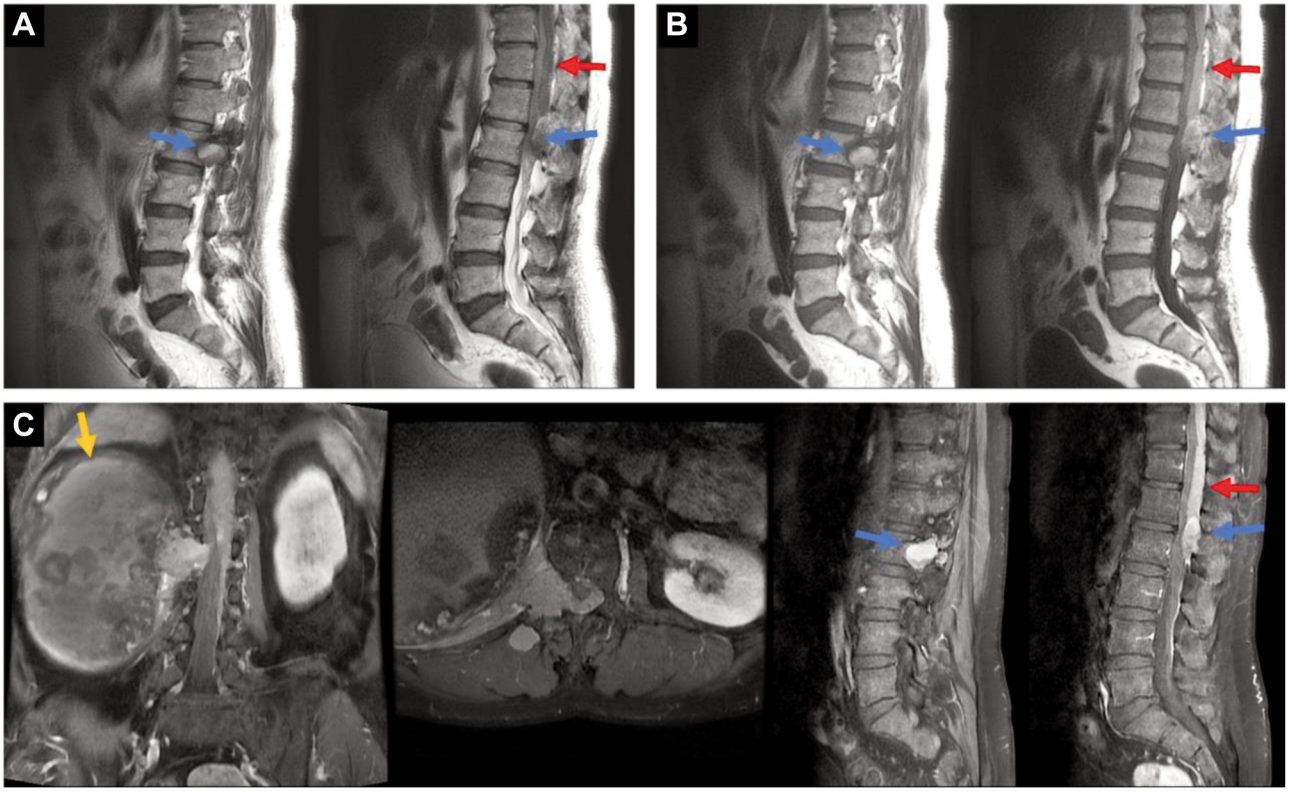

Figure 2. *L-spine contrast-enhanced MRI showed the precise location of the suspected tumor. A huge mass can be seen in the right retroperitoneum (orange arrow), with smaller components in the enlarged right L2-L3 foramen (blue arrow), continuously with long posterior epidural lesions from at least T10 to upper L5 level (red arrow). The tumor has hemorrhage or melanin content. (A) T2-weighted. (B) T1-Weighted. (C) Gadolinium enhanced coronal, axial and sagittal views. MRI: Magnetic resonance imaging.*

tumor or multiple myeloma. Due to her intractable pain, severe radiculopathy and unknow tumor origin, surgical resection of tumor lesions for root decompression and pathologic diagnosis was indicated. Long segment posterior decompression could lead to iatrogenic instability; therefore, instrumented fixation was suggested.

A two-stage surgical approach was utilized in the treatment of this unique case. The initial stage involved a posterior approach T12-L3 laminectomy for the removal of the epidural tumor while utilizing intra-operative neuromonitoring (IONM) and fixation of T12 to L3 transpedicular screws and rods. The second surgery involved an anterior approach for the resection of the retroperitoneal tumor. During the first spinal surgery, a soft, brownish, cake-like epidural lesion adhered to a mass lesion on the dura was observed. Intracystic dark-tan fluid was drained from the cyst at the right L2 foramen (Figure 3). Following foraminectomy, a severe adhesive, fibrotic mass lesion that compressed the L2 and L3 nerve roots, extended into the retroperitoneum, and the L1-L3 epidural space was discovered (Figure 4). The frozen section examination revealed no malignant cells but many inflammatory cells.

A second-stage surgery employing an anterior approach was conducted three days later to excise the retroperitoneal tumor. A capsulated, well-defined cystic tumor with much dark-tan hemorrhagic fluid inside (Figure 5) combined with solid part at paraspinal region compressing the right L2 root were removed. No evidence of malignancy was found on the frozen section biopsy either.

Histological analysis. Postoperative histological examination revealed no evidence of malignant cells that CK-, EMA-, SOX-10-, SYN-, ALK- on immunostaining. However, it showed the diffuse infiltration of foamy histiocytes that were CD68+, CD163+, S100-, CD1a- and BRAF- on immunostaining (Figure 6) which confirmed the diagnosis of BRH with organized hematoma.

Abdominal CT demonstrated a much decreased size of tumor at post operative day 7 (Figure 7A-D). Four months at OPD follow-up, abdominal CT revealed only minimal residual lesion at L2 extraforamen and well position of the instruments (Figure 7E-F). Her symptoms had greatly improved after our two-stage surgical procedure. She was

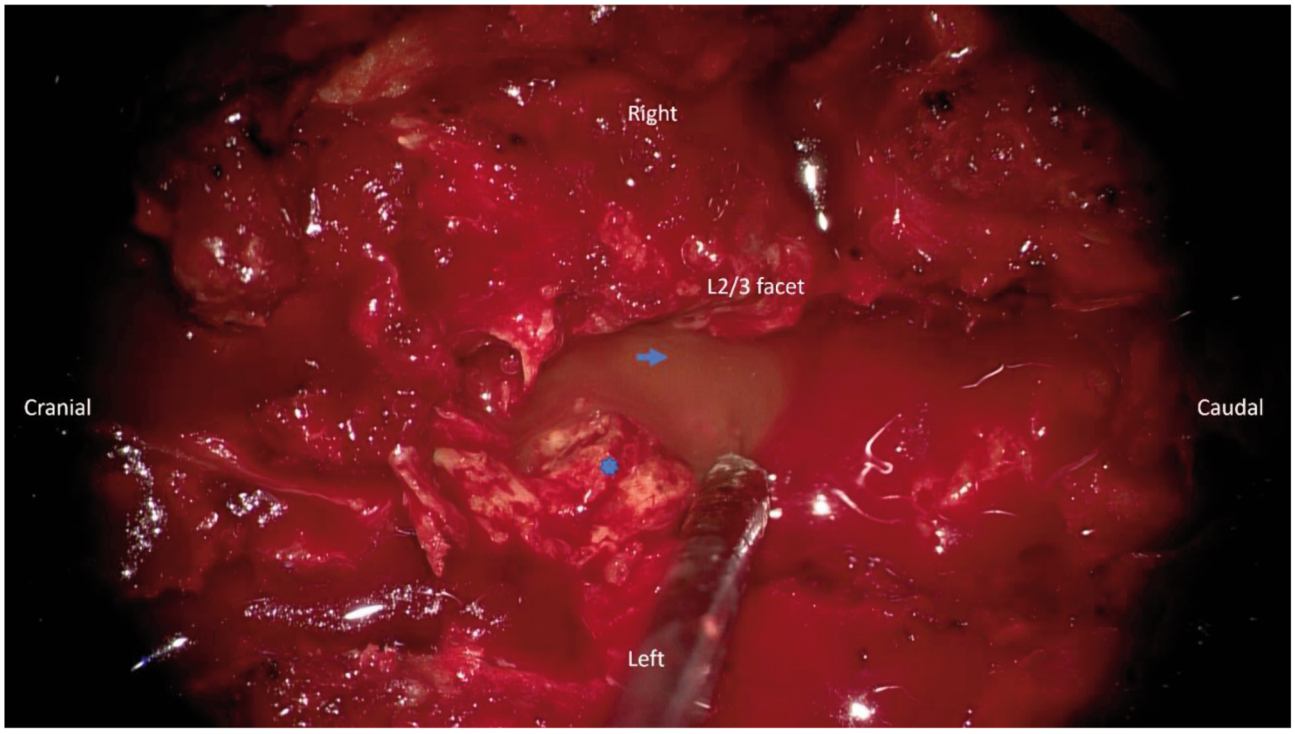

Figure 3. *An organized hematoma was found instead of malignant peripheral nerve sheath tumor. After T12-L3 laminectomy, soft, brownish, cakey epidural organized hematoma and solid, soft, adhesive to dura mass lesion were noted (blue asterisk). Intracystic dark-tan fluid was drained out from right L2 foramen (blue arrow).*

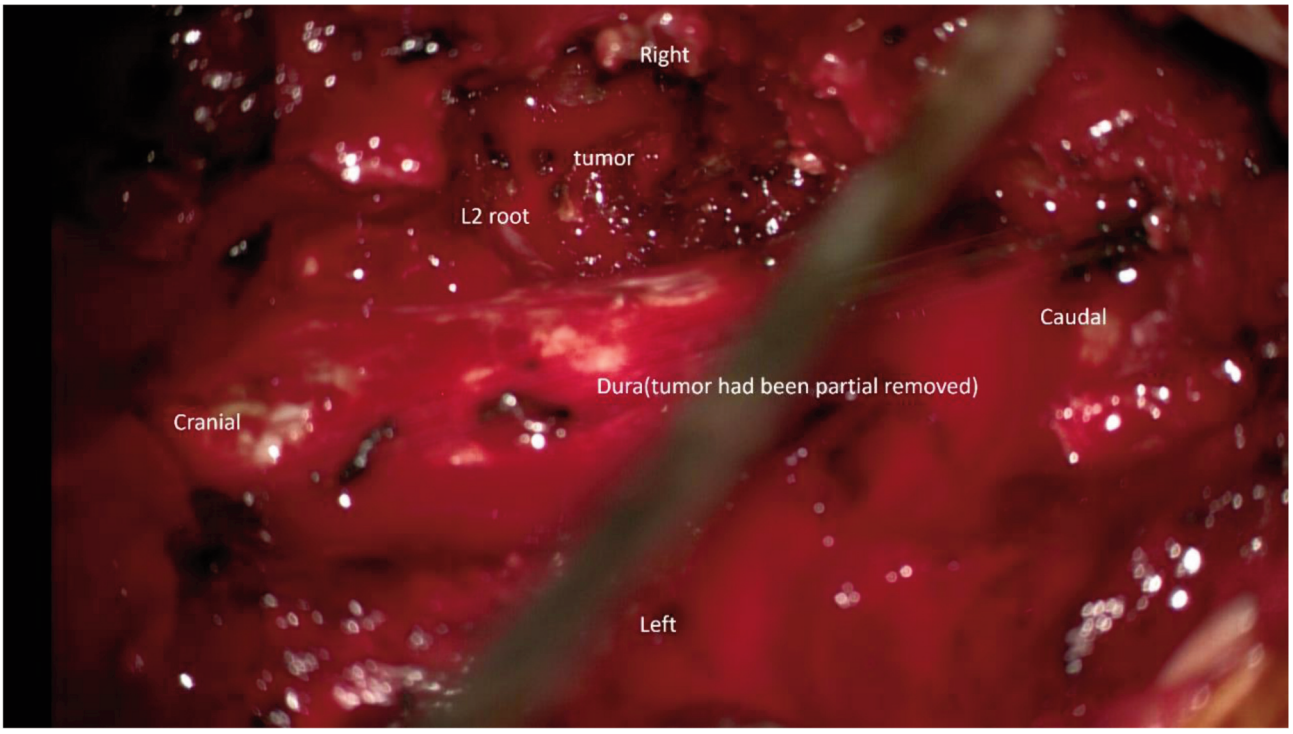

Figure 4. *Image after the foraminectomy. A severe adhesive, fibrotic mass lesion which compressed L2 and L3 nerve root and extended to retroperitoneum and L1-L3 epidural space was shown.*

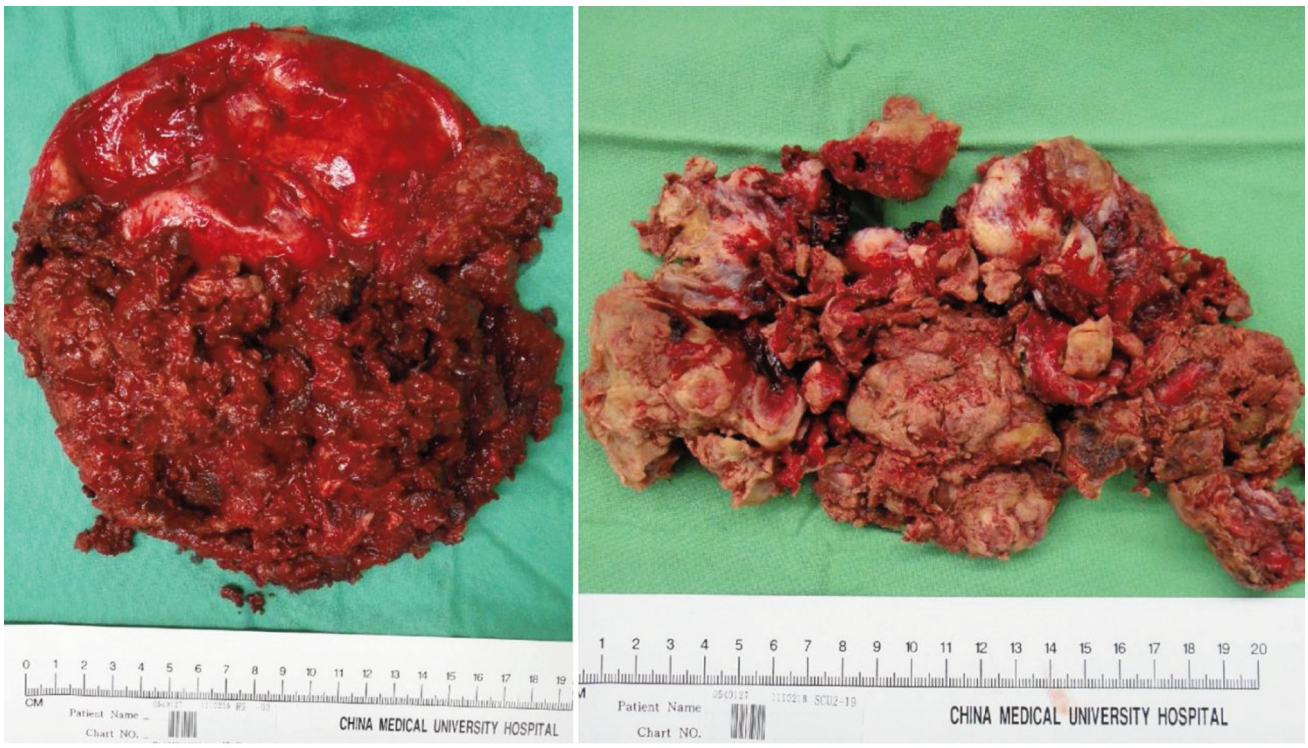

Figure 5. *The huge cystic mass excised was shown in the figure with an elastic capsule and solid components. The turbid fluid inside the cyst was aspirated during surgery.*

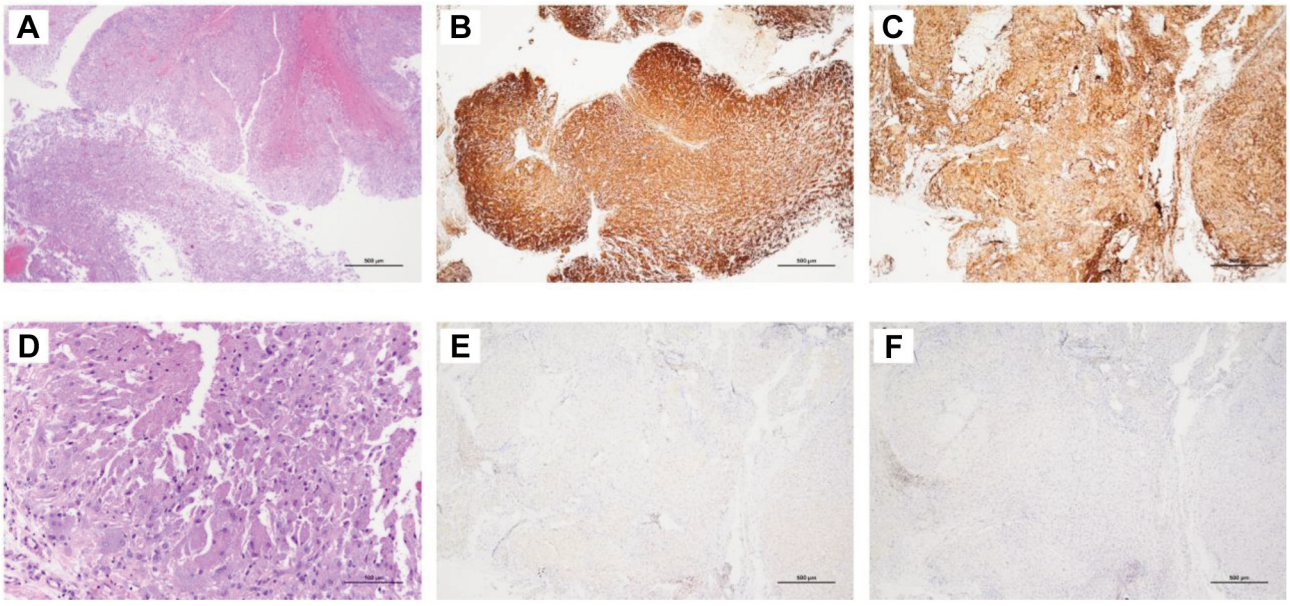

Figure 6. *Pathological examination confirmed a diagnosis of reactive histiocytosis. (A) Eosinophilic and granular contents in the cytoplasm of the foamy cells. (B) CD-68 with strong positive staining. (C) CD-163 with strong positive staining. (D) The organization of foamy cells. (E) CD-1a with negative staining. (F) S-100 with negative staining.*

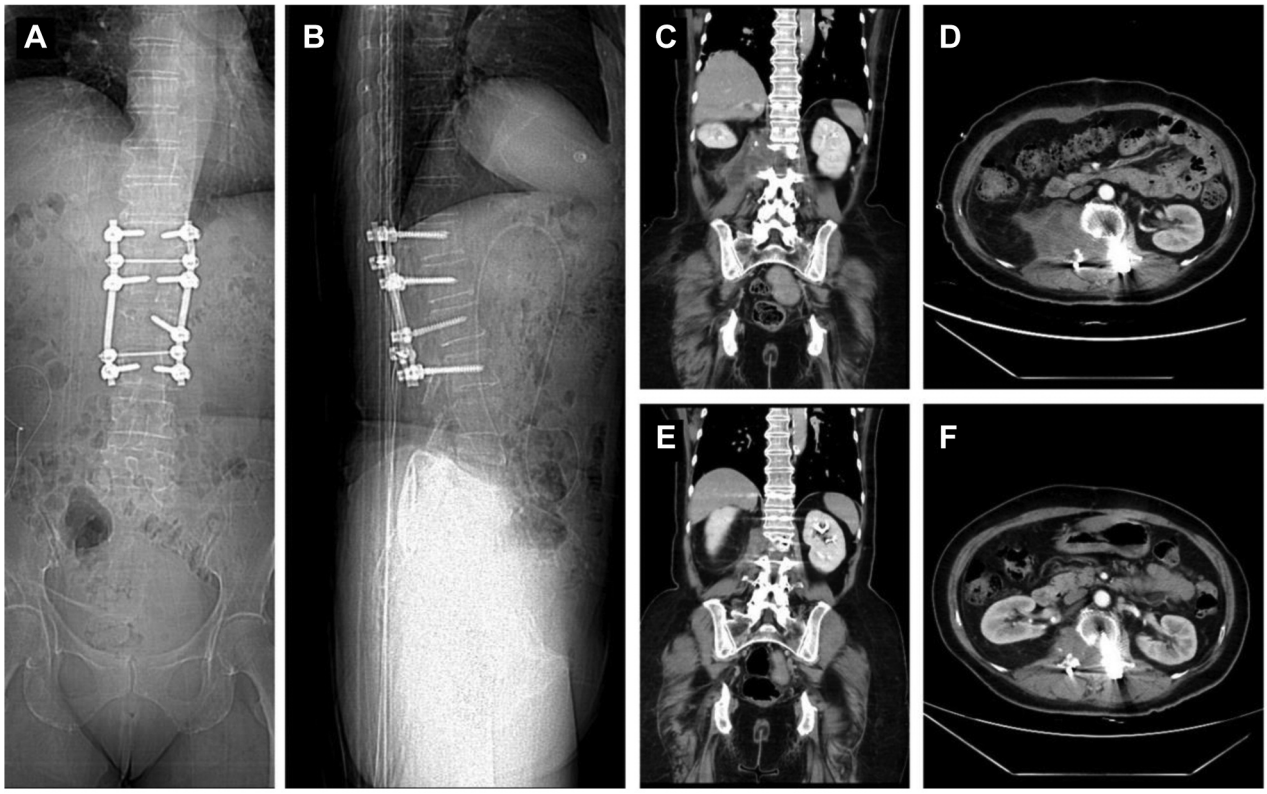

Figure 7. *Post-operative abdominal CT revealed a residual mass lesion with good position of the instrument. (A-D) Post-operative day 7. (E and F) Post-operative 4 months. CT: Computed tomography.*

able to resume work one month following surgery and experienced a satisfactory quality of life.

Discussion

MPNST arise from the major or minor peripheral nerve branch or sheath of peripheral nerve fibers, and are relatively rare malignant soft tissue tumors. Spinal MPNSTs are even rarer, with a poor prognosis, and an 80% mortality rate when occurring in the spinal column (6). Due to the aggressive nature of the disease, early and accurate diagnosis is crucial. CT and MRI can aid in the differential diagnosis of spinal MPNSTs. Typically, MPNSTs present as large masses, with maximal diameters greater than 50 mm in most cases (10 out of 12), and have a clear boundary and equal or low density on imaging (7, 8). The MRI characteristics of MPNSTs include a clear boundary and complex components. In our case, we observed a central cystic lesion with necrosis, inhomogeneous enhancement under contrast-enhanced scan, and an enlarged intervertebral foramen with a connection to the spinal nerve, which is consistent with the imaging properties of neurogenic tumors (6). Enlarged intervertebral foramen and connection with spinal nerve was also noted (Figure 2C). This is in agreement with the imaging property of neurogenic tumor (9). Bone erosion is commonly observed, while vertebral body compression is rare (6). To sum up, large tumor(s), complex components, inhomogeneous enhancement, abundant blood supply and edema or invasion of surrounding structures could be observed on the images. However, it is still difficult to make the precise and accurate diagnosis with images only, preoperative biopsy was suggested for surgical decision-making and preoperative preparation (10). In our case, proper surgical procedures and expert pathological identification helped imaging findings, to accurately differentiate between MPNST and BRH with hematoma, leading to successful medication.

Histiocytic disorder is characterized by the proliferation of histiocytes, which have two cell lineages: monocytes/macrophage series and Langerhans cell/dendritic cell series. According to the pathology, the disorders are categorized into four diseases: reactive macrophage, malignant macrophage, reactive Langerhans cell, and malignant Langerhans cell disorders. As for imaging methodology

reported in routine radiological studies, for instance, X-ray, CT, and MR imaging, are capable of identifying osseous lesions but have little value in differentiating histiocytic disorders from other osteolytic tumors (11). Besides, histiocytic disorders could be a systemic disease. In order to ensure optimal patient care, it is recommended to conduct a comprehensive whole-body evaluation prior to any medical intervention, particularly surgery. Histological analysis with immunostaining plays a crucial role in the differential diagnosis of various disorders. For example, reactive histiocytic disorders are a group of conditions characterized by localized or systemic proliferation of benign histiocytes. Immunostaining can be used to detect the presence of CD68+ and CD163+, while CD1a- and S100- staining are negative in these disorders (12).

In our case, MRI findings revealed a tumor originating from the right L2/3 foramen, accompanied by erosion of the L2 pedicle, as well as extension into the epidural space and retroperitoneal cavity. The tumor consisted of both solid and cystic parts, with hemorrhagic content and heterogeneously contrast-enhancing features, which are typical characteristics of MPNST. Therefore, extensive surgical resection and reconstruction were initially recommended. However, with the aid of expert pathological identification, intraoperative frozen section biopsy showed no evidence of malignancy. As a result, our surgical approach was adjusted from radical resection to optimal nerve decompression with subtotal tumor resection. Fortunately, the final diagnosis was benign reactive histiocytosis with an organized hematoma.

In this study, we emphasize the importance of utilizing proper surgical procedures and expert pathological identification to differentiate BRH with organized hematoma from MPNST. We strongly recommend conducting a whole-body survey, such as brain imaging, PET scanning, or genetic testing for NF1, before surgery to rule out the possibility of systemic spread. Furthermore, genomic patterns for MPNST have been reported in recent studies and may be used in the future as guidelines for surgeons encountering similar cases (13). Additionally, conducting routine tumor biopsies before surgery may provide valuable information for making informed surgical decisions. These recommendations may help guide surgeons in managing similar cases in the future.

Conclusion

To our knowledge, we described the first case on clinicians can distinguish a BRH with surgical procedures and pathological identification in addition to typical imaging only, from MPNST. Images should be accompanied with proper surgical procedures and expert pathological identification to distinguish the cases of reactive histiocytosis from MPNST.

Conflicts of Interest

The Authors declare no conflicts of interest regarding this study.

Authors' Contributions

Protocol design and originality: Chang CJ, Chen CC and Chen CH; patient and clinical data collection: Chang CJ and Chen CH; imaging and data analysis: Chen CC and Chen CH; article writing: Chen CH and Bau DT; manuscript preparation and discussing: Chang CJ, Chen CC, Chen CH and Bau DT.

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