MALIGNANT SCHWANNOMA IN NEUROFIBROMATOSIS 1

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ABSTRACT

Malignant peripheral nerve sheath neoplasms are serious complications of Neurofibromatosis. The incidence of which reported in literatures is between 2% and 29%. Once it occurs, the prognosis is poor. We reviewed 2 cases of malignant schwannoma in the vicinity of Neurofibromatosis-1 at Siriraj Hospital in the points of view of radiographic findings with histopathological correlations. One had lesion at chest wall and the other at sacral area. Both CT and MRI provided good structural delineation and tumor extension but malignant or benign lesions can not be distinguished with certainty. Because of its aggressiveness, biopsy with histological diagnosis should be performed in those Neurofibromatosis patients who have peripheral nerve sheath tumors before surgical planning.

Malignant degeneration of peripheral nerve sheath tumors is problematic in NF-1 patients. Its incidence has been estimated to be 2-29 %.[1] or 10 to 10,000 times more than general population.[2] Spontaneous sarcomatous change in patients without von Recklinghausen 's disease is very rare.[3] It has poor prognosis[1,4-9] and causes high morbidity and mortality. Early recognition of this change brings about early treatment and greater awareness. But they are difficult to be differentiated from benign neoplasm.[10] Because they can produce no symptom, either, mild or aggressive symptoms.[3,10]

There is no imaging criteria for differentiation malignant from benign tumor.[10] This study was performed retrospectively to determine if CT scans and MR imaging would be any useful for distinguishing malignant from benign neoplasms. Pathological findings and correlation between pathology and radiology were also analyzed.

MATERIALS AND METHODS

Retrospective medical records of 2 patients at Siriraj Hospital from the period of 1998-1999 who had been diagnosed to be NF-1 according to diagnostic criteria were reviewed. They had sarcomatous degeneration which had been proved by histology. CT scan and MR imaging were reviewed by 1 experienced radiologist. After surgical resections were performed, the histologic sections were reviewed by 1 experienced pathologist. Radiographic findings from CT scan and

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MR imaging were analyzed from the following point of views :

1. size
2. homogeneity
3. margins
4. pattern of enhancement and
5. extension .

CT scans of the lesions at the chest and pelvis were performed with 10 mm. interval slice thickness in both pre and post contrast enhancement. One hundred millilitres of Angiografin was given intravenously. All images were filmed at suitable window widths and level for demonstrating both soft tissue and bone detail. Multisection turbo spin-echo (TSE) imaging was done with a superconducting magnet (ASC II, Phillips Medical System, Best, Netherland) operated at 1.5 T. A body coil with a 50 cm field of view was used routinely. Data were acquired with a 152-203x256 matrix and were displayed with 256x256 matrix. The pixel size was about 1.5x1.5 mm for body coil. TSE pulse sequence was used with T1weighted (TR = 500-729 ms. TE = 12-15ms.) and T2 weighted (TR = 2400 ms. TE = 120-150 ms.) images. T1 weighted with Gd enhancement was also performed. Continuous 8-10 mm. sections were obtained and seperated by 0.8-1.2 mm. gaps.

Pathologic findings were also analyzed about gross pathology , diagnostic histologic criterias of schwannoma and sarcomatous changes and correlation between histology and radiology.

RESULTS

The first patient was 33 years old, a single female who presented with progressively enlarged mass at Rt. anterior chest wall for 4 months. Physical examination revealed a large mass at Rt. Anterior chest wall which was measured about 12x10 cm. It had hard consistency and was fixed to the chest wall with slight tenderness and smooth surface. She also had cafe- au- lait spots more than 6 lesions which each one was larger than 5mm. in diameter. Axillary region freckling was seen. Immediate CXR- PA and CT scans of the chest were performed.

The CXR-PA revealed a large soft tissue mass at Rt. anterior chest wall with rib destruction (fig 1).

CT scans showed heterogeneous density of soft tissue mass. It had smooth border and located at Rt. anterior chest wall. Its size was about 4.53x4.50 cm. This mass destroyed Rt. 6th to 9th ribs and extended into thoracic cavity with invasion of the lung. It has peripheral enhancement (fig 2).

Incisional biopsy was done about 2 weeks later and histologic section was malignant peripheral nerve sheath tumor. Then the patient received a wide excision with RML segmentectomy. The operative findings discovered compression of the liver from the tumor mass without invasion. It extended through the diaphragm and also invaded the Rt. Middle lobe. Serosanguinous pleural effusion about 300 ml. was seen.

Gross pathologic examination showed a lobulated mass with rib and lung involvement (fig 3). Microscopic examination demonstrated spindle cell tumor which has hypercellularity, increased N/C ratio, hyperchromatic nucleus, abundant mitosis, pleomorphism and necrosis. The special staining was performed with S-100 protein that was positive in this specimen which confirmed MPNST (fig 4). Heterogeneous density in the mass was necrotic area.

MPNST = Malignant peipheral nerve sheath tumor

The patient was free of disease for 2 months. Local recurrence of tumor had occurred with multiple varying in sizes of soft tissue masses adjacent to old surgical scar at Rt. Anterior chest wall. So MR imaging of the chest was done. It showed heterogeneous hyposignal intensity in T1WI (fig 5), heterogeneous hypersignal intensity in T2WI , irregular border with invasion to the lung and liver moderate enhancement (fig 6). The patient obtained symptomatic treatment and external radiation because surgery and chemotherapy played no roles.The patient expired about 3 months later.

The second patient was 34 years old and single female who presented with Rt. Sciatica pain for 4 months. Physical examination revealed loss of sensation at L5 to S2 nerve root levels of Rt. leg. Motor power of Rt. EHL was grade 3 and SLRT was positive about 45° of Rt. leg. She had cafe-au-lait spots more than 6 lesions. Each one had more than 5mm. in diameter. Axillary flecklings were also seen.Prompt plain film pelvis - AP and CT scans of lower abdomen were done. MR imaging of LS spines was accomplished in 3 weeks.

Plain film pelvis- AP revealed soft tissue mass at Rt. side of pelvic cavity with sacral erosion (fig 7).

CT findings showed a large heterogeneous density of soft tissue mass located at Rt. side of pelvic cavity (fig 8). It had smooth margin, lobulated shape, well-defined capsule, protrusion via greater sciatic notch and hrterogeneous enhancement (fig 9). Sacral erosion was noted in bone window (fig 10).

MR imaging demonstrated heterorogeneous signal intensity in T1WI, heterogeneous hypersignal intensity with peripheral hypersignal intensity in T2WI and peripheral enhancement (fig 11 and 12). Afterthat intrapelvic biopsy was performed and histologic section was malignant peripheral nerve sheath tumor. The patient underwent Rt. hemisacrectomy with tumor resection and partial resection of iliac crest about 3 weeks later. Operative findings revealed sacral nerve root involvement at S2 to S4 levels. The mass also compressed and blended to sciatic nerve. Tumor extended beyond sciatic notch. Mass was removed by blunt dissection. Sciatic nerve which attached to the mass was resected. Post operative infection had occured but finally it could be got rid off.

Gross pathologic examination showed lobulated mass covered with capsule (fig. 13).

Microscopic examination demonstrated the ame histologic findings as the first case (fig. 14). But there was a larger area of necrosis. Capsule of the mass on imaging findings consisted of compact surrounding fibrous tissue. Hence it was pseudocapsule. Heterogeneous density in the mass were necrotic areas.

The patient lost follow up and expired 15 months later from lung metastasis.

EHL = Extensor Hallucis Longus
SLRT = Straight Leg Raising Test

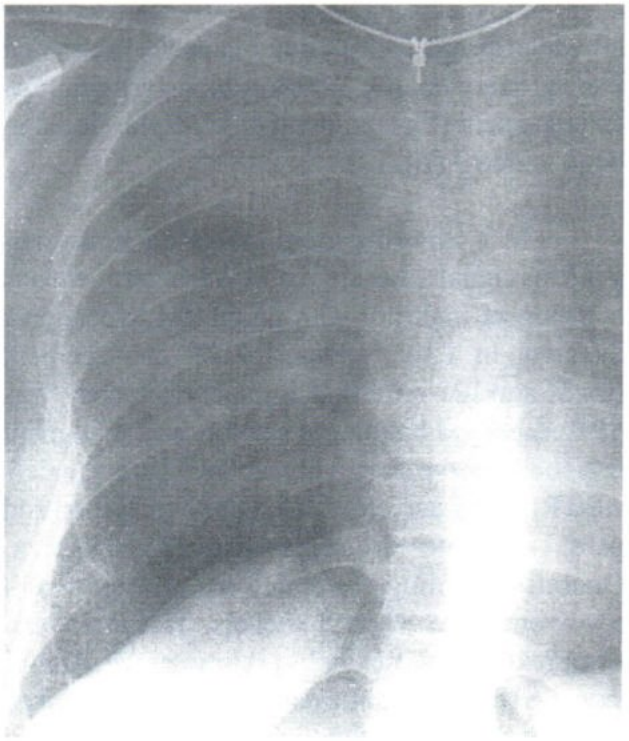


Fig. 1. CXR-PA demonstrated soft tissue mass at right chest wall with adjacent multiple rib destruction.

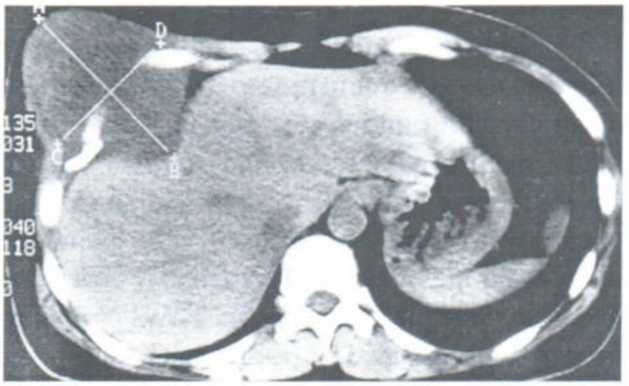


Fig. 2. NECT of the chest included upper abdomen reveals heterogenous hypo-density soft tissue mass at right anterior chest wall with multiple rib destruction.

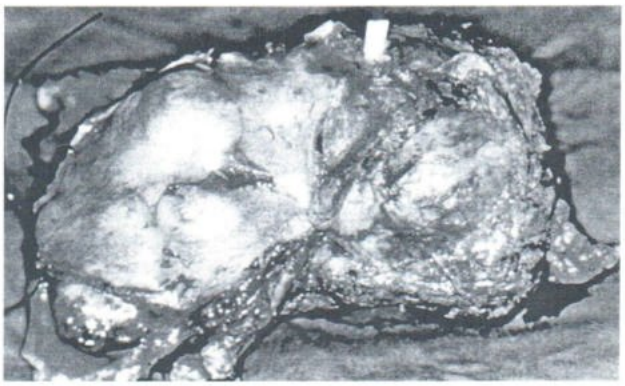


Fig. 3. Gross features of the resected tumor showed the attachment of diaphragm and some ribs.

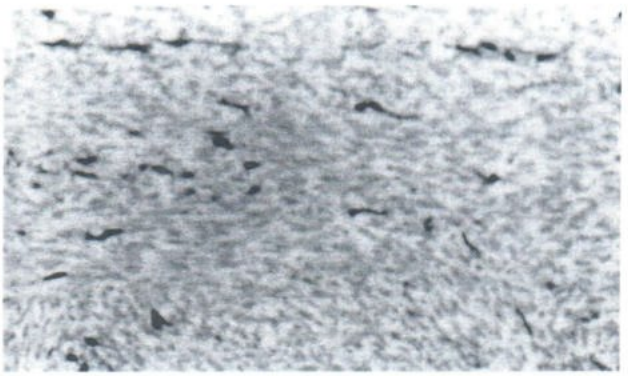


Fig. 4. Special stain by S-100 protein discovered MPNST.

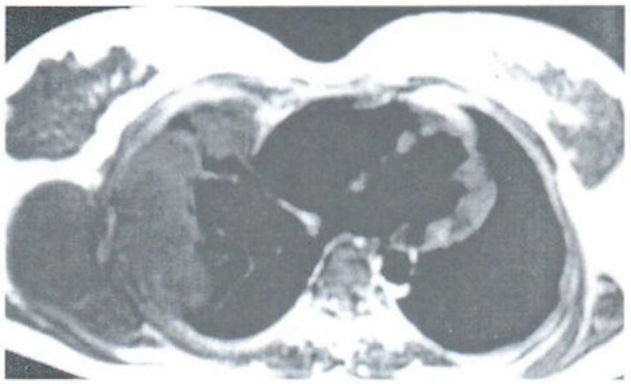


Fig. 5. Axial MRI of the chest in T1W revealed hyposignal intensity soft tissue mass at right anterior chest wall with irregular border and invasion into thoracic cages.

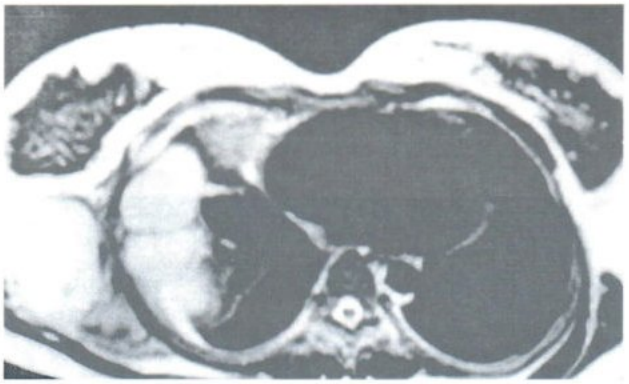


Fig. 6. Axial MRI of the chest in T1W with Gd enhancement disclosed markedly homogenous enhanced mass.

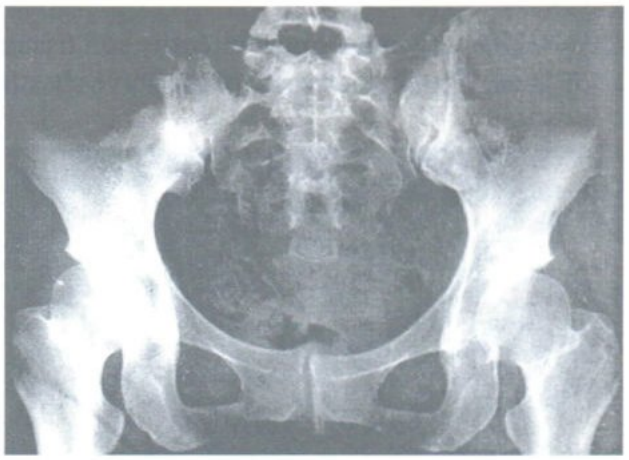


Fig. 7. Plain film pelvis AP showed soft tissue mass at right side of pelvis and erosion of sacrum.

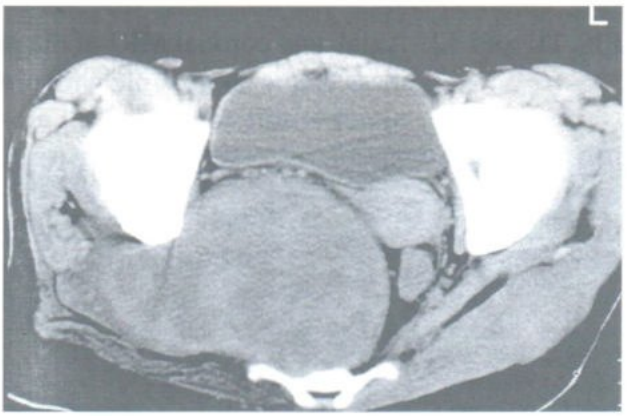


Fig. 8. NECT of the pelvis showed a large heterogenous soft tissue mass extended via greater sciatic notch which is typically seen in nerve sheath tumor.

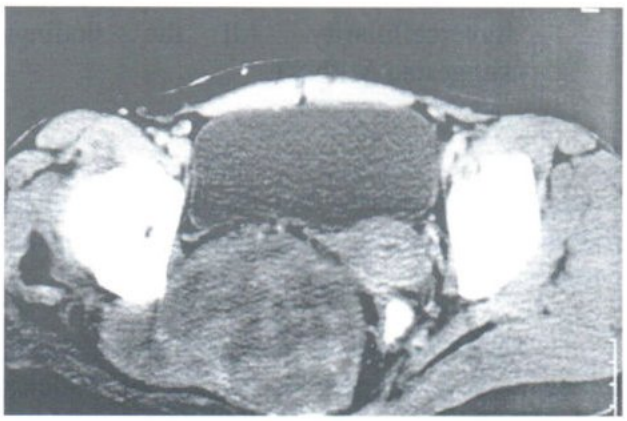


Fig. 9. CECT of the pelvis reveals heterogenous enhanced mass at the same level

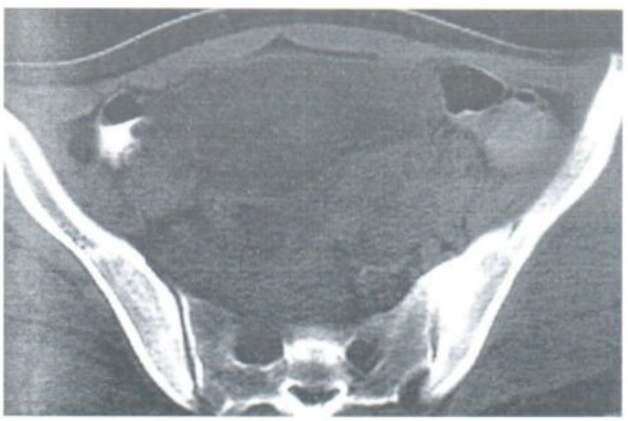
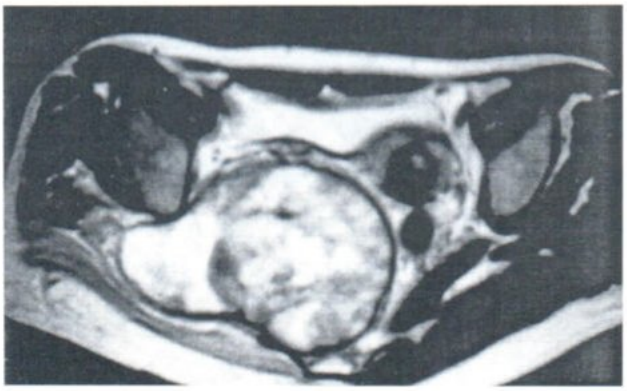


Fig. 10. Bone window of the pelvis demonstrated widening and erosion of the foramen.



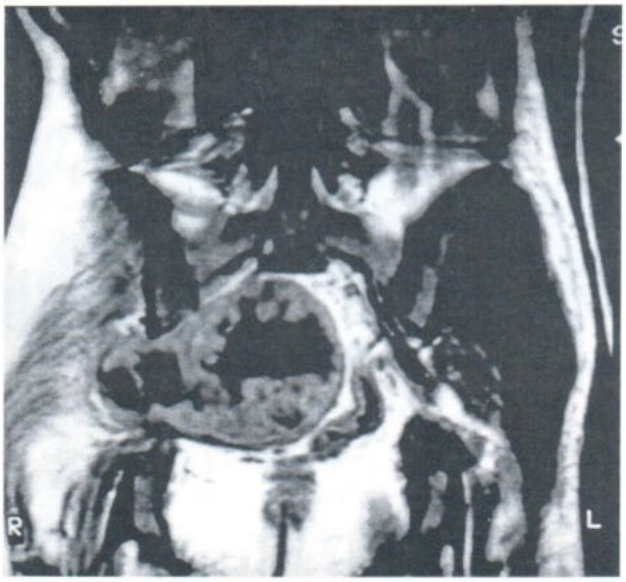


Fig. 11. and 12. Axial and coronal MRI of the pelvis showed heterogenous signal intensity soft tissue mass that is compatible with previous CT scan. The characteristic of the nerve sheath tumor is still noted.

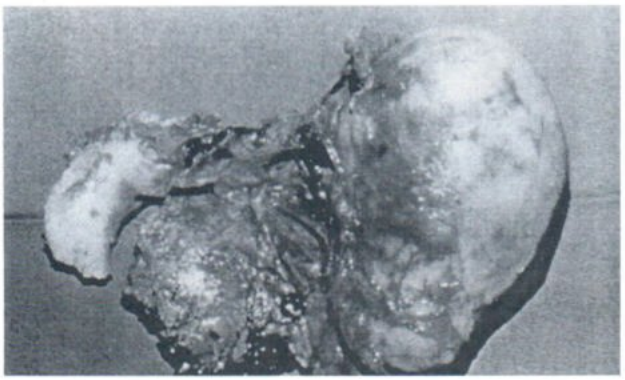


Fig. 13. Gross specimen revealed smooth round encapsulated mass with some part of resected pelvic bone.

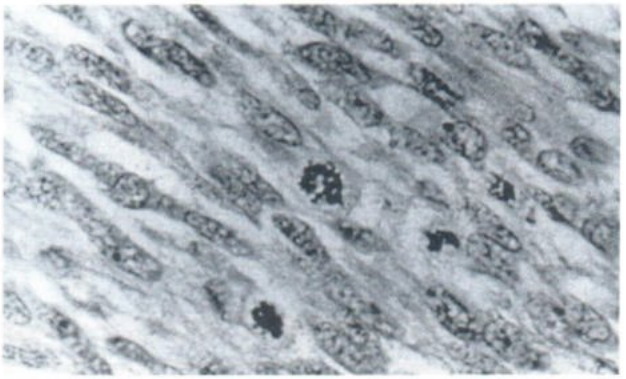


Fig. 14. Microscopic examination disclosed abundant mitosis, pleomorphism and hypercellularity. All the findings suggested MPNST.

DISCUSSION

Neurofibromatosis is neurocutaneous syndrome that is inherited as an autosomal dominant that which virtually 100% penetrance.[11] Mainly sarcomatous degeneration complicated neurofibromatosis are of nerve trunk origin and uniform composition. The other type of sarcoma which is lessly occured attributed to multipotentiated neurilemmal cells. They can produce fat, striated muscle, cartilage and osteoid by metaplasia and finally they will be rhabdomyosarcoma, liposarcoma or osteosarcoma.[1,11]

About malignant peripheral nerve sheath tumor, it is developed in 2-29% of patients with NF-1.[1] The latent period is vary from weeks to 18 years.[12] The causes are still unknown and the hypothesis that trauma and surgery

predispose to sarcomatous degeneration remains unsubstantiated.[1,13] They usually arise in deep structures[10] so early detection can not be performed until symptoms are appeared. The disease has poor prognosis.[1,2,4,5,7-9] Location and histology do not seem to affect the prognosis.[12] But some studies comment that deep location do.[14] Several diagnostic tools are established, CT scan, MR imaging and Ga-67 scanning for examples, but histologic section is still necessary for definite diagnosis. These lesions have tendency to grow slowly, local recurrence after excision and metastasis via blood stream especially to the lungs.[4]

Either CT scans or MR imaging were analyzed about size, homogeneity, margin, pattern of enhancement and extension of the masses. Both patients had a huge mass at Rt. anterior chest wall and pelvic cavity respectively but the size did not give an indication of the likelihood of malignancy.[10] Neoplasm inhomogeneities on CT scan and MR imaging were seen in both patients. Low density component usually resulted from hemorrhage or necrosis[10,13,14,16,17] Benign neoplasms also mimic malignancy by inhomogeneity. Both patients have smooth border of masses, One had rib destruction and RML involvement. The other had sacral bone erosion. But MR imaging of the chest showed irregular border of recurrent tumor. So malignant tumors had either aggressive behavior such as an irregular, infiltrative border, bone destruction and RML involvement or non aggressive behavior such as smooth edge without surrounding extension. Benign tumor also had the former feature but it is less obvious.

Malignant tumors demonstrated peripheral and moderate enhancement. Extension could not predict malignant potential because one looked well capsulated without breaking through its margin. It showed extension from pelvic cavity to outside via greater sciatic notch which was suggestive of nerve sheath tumor. The other extended outward from its margin and invaded surrounding structures. RML involvement and rib erosion were occured. In conclusion, there are no definite imaging criterias suggesting malignancy by CT scans or MR imaging. Although inhomogeneity, infiltrative margin or irregular bone destruction are more common in malignant neural neoplasm.[10] Finally they are still overlapped. But CT scans and MR imaging provide better structural delineation of the mass and its relationship to adjacent structures for surgical planning. The gross pathology of Rt. anterior chest wall mass is lobulated mass with invasion to Rt. hemidiaphragm, RML and rib. Pelvic mass is characteristic by lobulation with pseudocapsule.

Neurofibroma in general population rarely changes into malignant schwannoma. NF-1 patients who have neurofibroma tend to occur sarcomatous degeneration so histologic diagnosis of MPNST is related to clinical manifestation such as NF-1 patient and mass that arise in close contact with a peripheral nerve. Microscopic appearance of MPNST is hypercellularity, increased nuclear cytoplasmic ratio, hyperchromatic nucleus, abundant mitosis, pleomorphism and necrosis of spindle cells. Malignant spindle cell tumors include MPNST, fibrosarcoma, leiomyosarcoma and synovial sarcoma which can be differentiated from each other by immunohistochemical stains such as S-100 protein. S-100 protein is an antigen that present in the cytoplasm of schwann cells. So this comfirmation is MPNST. Both patients have spindle cell tumors with positive staining for S-100 protein and microscopic appearance of MPNST as mentioned. Well capsulated pelvic mass is surrounding fibrous tissue which is looked like capsule from compression. Hence it is pseudocapsule. Heterogeneous areas in both mases are resulted from necrosis which are more obviously seen in the pelvic mass.

The treatment of choice is surgical removal of the tumors but local recurrence and distant metastasis are still presented.

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