

Radiology Appearance of Malignant Peripheral Nerve Sheath Tumor: a Case Report

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ABSTRACT

Malignant peripheral nerve sheath tumor (MPNST) is a rare soft tissue sarcoma. This tumor included up to 10% of 1-2 of 100,000 population/year soft tissue sarcoma. This paper presents a MPNST case at superficial body, such as frontal, temporal and parietal head, neck, trunk, left arm, and visceral organs likes brain, lung, liver, right kidney, left intraabdominal, and without associated with Neurofibromatosis type 1 (NF1) and no history of post radiation therapy. Computed tomography (CT) scan of the brain was identified soft tissue mass at frontal and parietal sub cutaneously, hypodensity lesion at frontal obes that enhanced peripherally after contrast administration, suggestive malignancy. Patient complained pain in nodule at his back. Chest roentgenogram and lung CT scan was founded multiple nodules. There are also heterogeneous mass at left lobe of liver. Histological examination confirmed the diagnosis of MPNST. This patient was planned for palliative treatment.

Key words: Radiology, MPNST, sarcoma

ABSTRAK

Malignant peripheral nerve sheath tumor (MPNST) merupakan sarkoma jaringan lunak yang jarang. Tumor ini meliputi MPNST sampai 10% dari 1-2 per 100.000 populasi/tahun kasus sarkoma jaringan lunak. Makalah ini memaparkan kasus MPNST yang ditemukan di permukaan tubuh, yaitu kepala bagian frontal, temporal, parietal kanan, leher, lengan kiri, torso, dan di organ-organ dalam yaitu otak, paru-paru, hepar, ginjal kanan, intraabdomen kiri, dan tanpa terkait dengan neurofibromatosis tipe 1 (NF1) serta tanpa riwayat terapi radiasi. Pasien hanya mengeluh sakit pada benjolan di punggung. Gambaran *computed tomography* (CT) otak ditemukan massa jaringan lunak di subkutis frontal dan parietal, serta lesi hipodens di serebri frontal yang menyangat di perifer setelah pemberian kontras dicurigai ke arah keganasan. Pada foto toraks dan CT paru ditemukan nodul multipel. Tampak pula massa pada ginjal kanan dan massa intraabdomen kiri. Massa heterogen pada hepar lobus kiri ditemukan pada ultrasonografi abdomen. Pemeriksaan histologi memastikan diagnosis MPNST. Pasien ini direncanakan untuk perawatan paliatif.

Kata Kunci: Radiologi, MPNST, sarkoma

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INTRODUCTION

We present a rare case of a patient with malignant peripheral nerve sheath tumor (MPNST) arising in multiple site of the body, from superficial body to visceral organ without known the primary origins. In superficial body, masses located in the frontal, temporal and parietal head, neck, trunk, left arm, and visceral organs likes brain, lung, left lobe liver, right kidney, left intraabdominal. These highly aggressive tumors in the past literature are variously termed malignant schwannoma, neurogenic sarcoma, and neurofibrosarcoma. The current term used by the World Health Organization is MPNST because the originating cell is not clearly

understood.^{1,2} MPNSTs may arise de novo, from transformation plexiform neurofibromas and therefore are strongly associated with neurofibromatosis type 1 (NF1) or von Recklinghausen's disease, and associated secondary to radiation therapy.^{2,3,4} The annual incidence of soft tissue sarcomas is 1-2/100,000 population and MPNSTs account for up to 10% from all soft tissue sarcomas.^{1,2,5,6}

CASE REPORT

The patient, a 38-year-old male, had complained cough with white sputum for about one month. He felt

epigastric pain and dysphagia. No fever, dyspnea and neurologic symptoms were found. Eight months prior to admission, a nodule growth on frontal head with no pain. Three months later nodules appear in other part of the head, neck, trunk, and extremity (Fig. 1). He admitted weight loss for 5 kilogram since the first nodule appeared. He had done a resection of a tumor of his left thigh three years previously in the local hospital without any further information about histological examination of the resected tumor. In physical examination, the nodules were tender and immobile. The largest nodule measured 8 cm in diameter and located in the right frontal head. No other skin lesions could be identified beside those

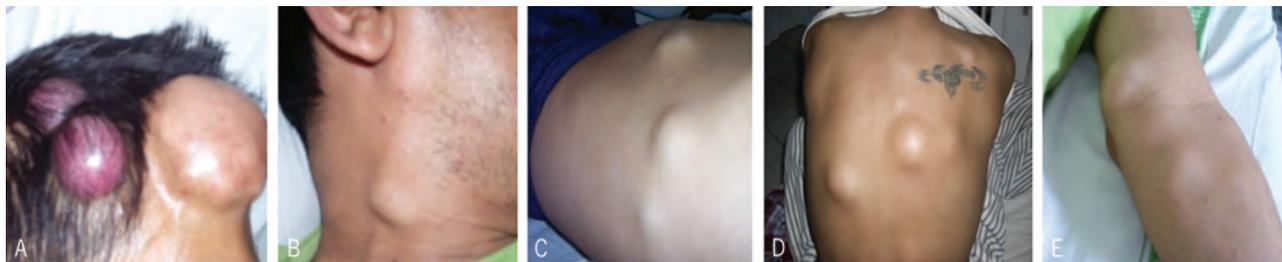


Fig. 1: Multiple soft tissue masses at frontal and parietal of the head (A), neck (B), abdomen (C), back (D), and left arm (E).

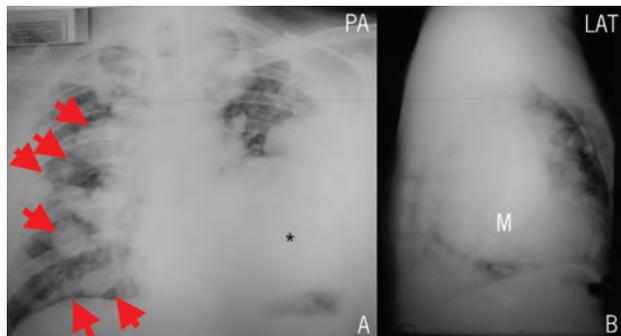


Fig. 2. A: CXR: well-defined multiple right lung nodules (red arrows) and left lower mass (*). Fig. 2. B: from lateral CXR, the mass located at posterior of the lung (M).

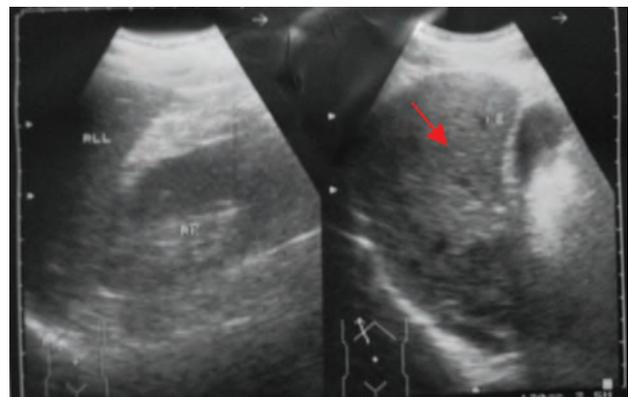


Fig. 4: Ultrasound: Hyperechoic round mass in the left liver lobe (red arrow).

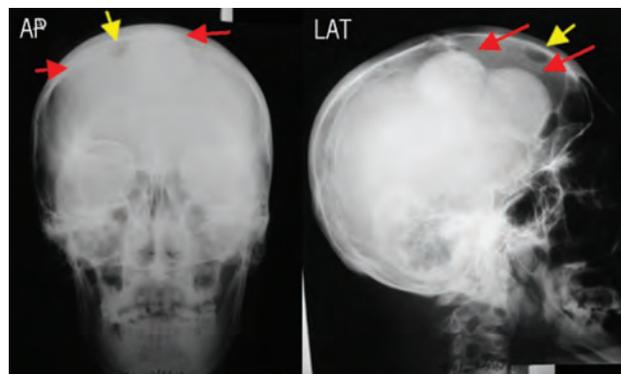


Fig. 3: Skull radiograph: multiple soft tissue masses at the frontal and parietal area (red arrow), with small lytic lesion at the right frontal area (yellow arrow).

multiple nodules. Chest examination found asymmetrical chest, stem fremitus of the left lung are dull. Ronchi was heard in both of the lung, respectively.

From Laboratory finding, he had a white blood cell count of $13.1 \times 10^3/\text{mm}^3$, erythrocyte sedimentation rate of 100 mm/hour, total protein level of 9.2 g/dL, albumin level of 2.8 g/dL, globulin level of 6.4 g/dL, SGOT level of 70 U/L, SGPT level of 79 U/L, and urea level of 53 mg/dL.

The chest radiograph (CXR) showed well-defined multiple right lung nodules and left lower lung nodule. (Fig. 2. A). Lateral CXR was identified the mass located at posterior of the lung. Skull radiograph showed multiple soft tissue masses at frontal and parietal area with small

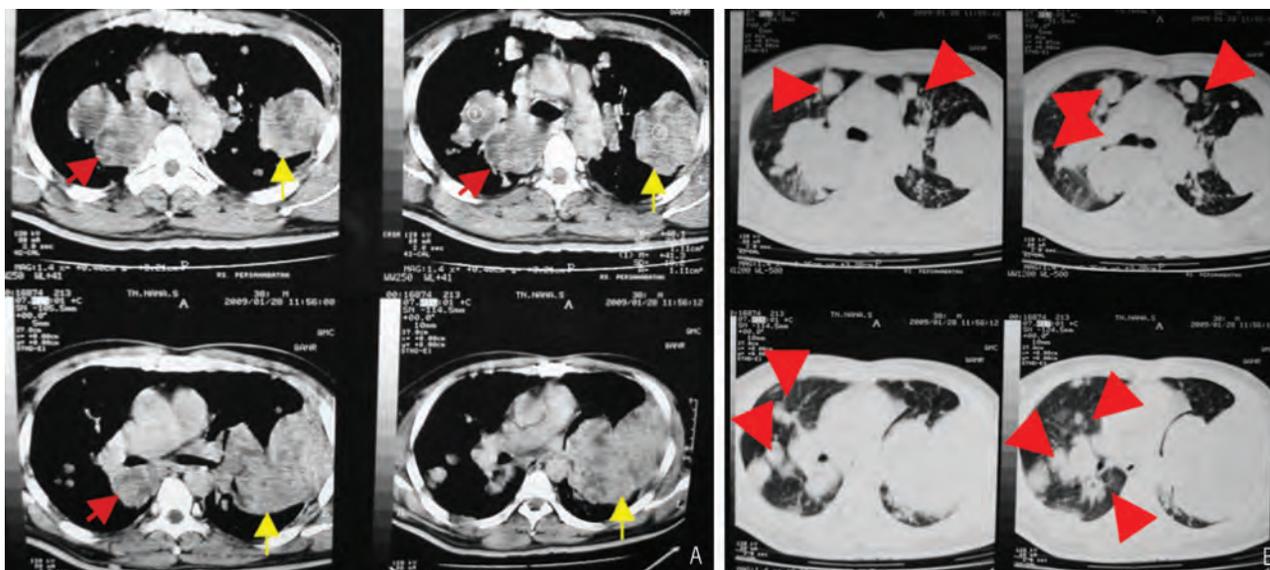


Fig. 5. A: Mediastinal window: contrast enhanced CT of the chest at the level of the carina showed right lobulated central mass with heterogen density that attach to thoracic vertebral body (red arrow) and left round peripheral mass and with no interface with parietal pleura (yellow arrow). Lymphadenopathy in the para arcus aorta. **Fig 5. B.** Lung window: there are multiple nodules and masses in both of the lungs (red arrow head).

litic lesion at the right frontal bone area (Fig. 3). Ultrasound found hyperechoic round mass in the left liver lobe (Fig. 4). Contrast enhanced CT of the chest at the level of the carina showed right lobulated central mass with heterogen density that attach to vertebral body and left round peripheral mass and no interface with parietal pleura. Lymphadenopathy in the para arcus aorta has found (Fig. 5. A). In the Lung window, there are multiple nodules and masses both of the lung (Fig. 5. B). Contrasted enhanced CT at the level of kidney, there is a round solid mass arise in the posterior of the right kidney and round mass with low area density in the center at the anterior tail of the pancreas (Fig. 6). Unenhanced CT of the brain showed hypodensity lesion in the right parietal lobe and multiple soft tissue masses at the right frontal and parietal area (Fig. 7. A). An enhanced CT of the brain show enhancement of the lesion (Fig. 7. B). Bone window setting: frontal bone destruction (Fig. 7. C). The histopathologic diagnosis was high grade sarcoma, MPNST (Fig. 8). Palliative treatment was planned for this patient.

DISCUSSION

MPNSTs are locally very invasive malignant sarcomas, multiple recurrences are frequent and eventual metastatic spread.³ Ducatman et al. reported that multifocal occurrence MPNST is rare, one of their study subject developed a second primary MPNST after 30 months and the other one after 13 years.⁴ MPNSTs arise from neurofibromatosis I (NF1) between 40-60% and there is 4% chance of malignant transformation of NF1 after latent periods of 10-20 years.^{1,2,7,8} Patients with NF1 is 4600

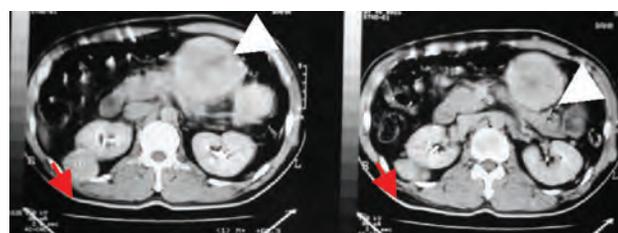


Fig. 6: Contrasted enhanced CT at the level of kidney, there is a round solid mass arise in the posterior of the right kidney (red arrow) and round mass with low area density in the center at the anterior tail of the pancreas (arrow head).

times greater for developing MPNST than general population.¹ There is 11% of MPNST follow to radiation therapy with range 5-29 years latent periods.^{4,7} MPNSTs impinge on young to middle-aged. The mean age patients with NF1 are 28.7 years and without NF1 are 39.7 years, respectively.^{4,7} Overall, the range age at diagnosis between 20-50 years with an approximately equal sex distribution.⁹ The origin cell of MPNSTs still not known, Schwann cell is the most evidence than fibroblast or perineural cells.⁷

Clinically, usually the peripheral nerve tumor do not cause symptoms.⁷ Pain is the classic presenting symptoms if any because of compression of intercostals nerves or major airways.^{2,4,6,7} MPNSTs that are located in the head and neck are rare, only 10% of all MPNSTs, mostly are affected trunk and extremities.^{1,4,7} The most common nerve affected is the sciatic nerve, followed by brachial plexus and sacral plexus.^{1,2,9} Okada et al.

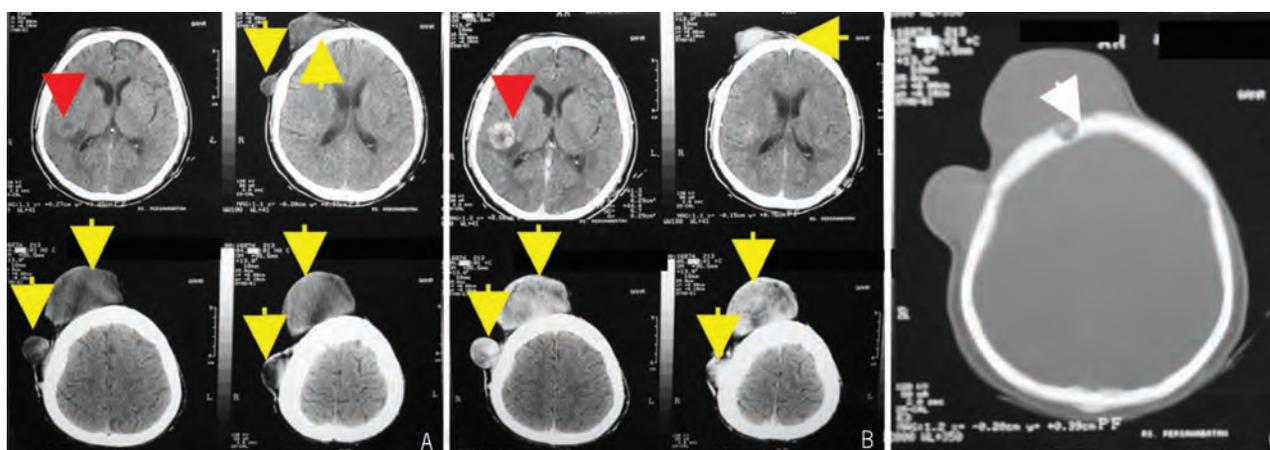


Fig. 7. A: An enhanced CT of the brain showed hypodense lesion in the right parietal lobe (red arrow head) and multiple soft tissue masses at the right frontal and parietal area (yellow arrow). Fig. 7.B. Enhanced CT of the brain show enhancement of the lesion red arrow and yellow arrow). Fig. 7. C. Bone window setting: frontal bone destruction (white arrow).

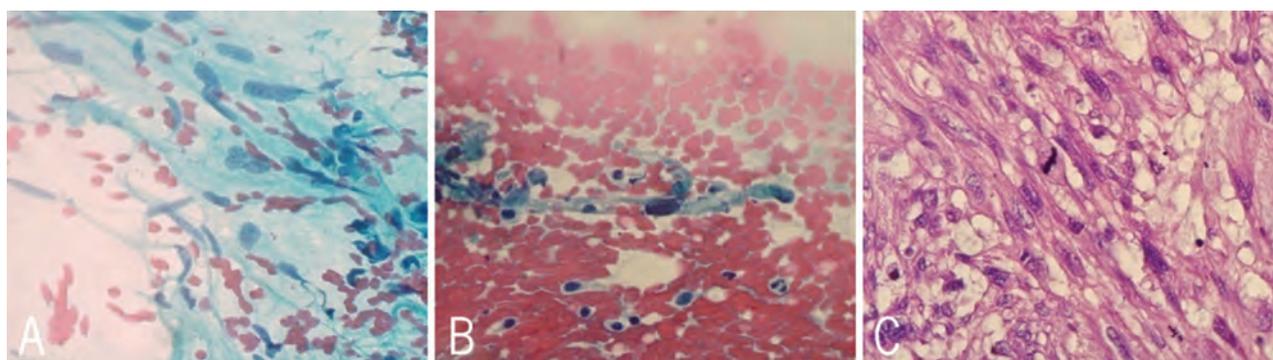


Fig. 8. A: Fine Needle Aspiration Biopsy (FNAB) from left arm nodule, tumor cell with characteristic pleomorphic core in hyperchromatic spindle cell. Fig. 8. B. Trans Thoracic Needle Aspiration (TTNA) found malignancy cell with characteristic pleomorphic core in hyperchromatic round and partly spindle cell. Fig. 8. C. Histopathology from nodule in the head: pleomorphic core in hyperchromatic spindle cell, mitotic activity was founded in the fibrillar and myxoid stroma.

reported from their studied that 46 of 56 MPNSTs located in deeper tissue.¹⁰ Sarcomas arise in the superficial tissues they tend to be less aggressive compared than the deep-seated tumor.^{7,9} Other signs of these tumor include progressive enlargement, tumor size larger than 2-6 cm (frequently exceeds 5 cm in diameter) with irregular border, and increasing neurologic deficit.^{2,6,11} MPNSTs that arise from NF1 should has NF1's signs as seen in table 1.^{2,9,12}

In this case, there were no signs of NF1 and no history of radiation therapy. The tumor resection at his left thigh had been done three years ago. Unfortunately, there was no histological information about the tumor. The multiple nodules growth in his body fit to the characteristic of MPNST as already mentioned above.

MPNSTs develop distant metastases including soft tissue, lung, liver, pleura, bone, brain, abdominal cavity, retroperitoneum, kidney, adrenal gland, diaphragm, mediastinum, and ovaries.^{4,9,10,12} The lung is the most

common hematogenous metastatic spread.² Intraneural invasion through the nerve bundles is also common.⁷ Perineural spread is a metastatic type through the planes of the neural sheath or along lymphatics of the epineurium and perineurium.^{1,13,14,15}

Radiography findings of MPNSTs usually normal or non specific soft tissue mass.⁹ Usually screening CXR are discovered this tumor.⁷ A sharp border, round, elliptical, or lobulated mass may be seen on plain radiograph.⁷ In rare cases there are a fusiform mass with surrounding fat, calcification and bone involvement.^{7,9} At angiography, characteristic of neurogenic neoplasms is recognition of corkscrew-type vessels at the upper or lower pool of the tumor, which is manifestation hypertrophy of nutrient nerve vasculature. Also there is displacement of major vascular structures because the site of the origin lesion inside the neurovascular bundle.⁹ Bone scintigraphy of MPNSTs are not specific.⁹ Gallium-67 is very helpful for distinguish MPNST from benign lesion.

Table 1: Criteria of NF1*

Six or more
Greater than 5 mm in greatest diameter in prepubertal patients
Greater than 15 mm in greatest diameter in postpubertal patients
Two or more neurofibromas (any type) or one plexiform neurofibromas
Axillary or inguinal freckling
Optic glioma
Two or more Lisch nodules (i.e., iris hamartomas)
Distinctive osseous lesions (e.g., sphenoid dysplasia, pseudoarthrosis)
First-degree relative with NF1, as diagnosed by above criteria

*Two or more of these criteria are required for diagnosis.

Source: Murphey MD, Smith WS, Smith SE, Kransdorf MJ, Temple HT. Imaging of musculoskeletal neurogenic tumors: radiologic-pathologic correlation.⁹

Gallium-67 imaging has shown that MPNSTs have greater uptake compared with benign lesions.^{2,8,9,12} Used of 18-fluorodeoxyglucose positron emission tomography (18-FDG PET) to identification MPNSTs have been reported. MPNST will increase uptake of 18-FDG but some benign plexiform neurofibroma also showed the same activity.¹² MPNSTs can be detecting by either CT or MRI although some medical literature reported MRI is superior to CT.^{1,9} Several imaging characteristics are listed in table 3.⁹

At CT, the most characteristic feature of malignancy is round or linear low-density areas in central or peripheral within higher density mass after contrast administration. The low-density area is due to hemorrhage and necrosis.^{6,16} Other imaging features of MPNSTs are irregular and infiltrative of tumor border; bone destruction with irregular margins.⁸ A sudden increase in size or development of heterogeneous attenuation at CT should be suggestive of malignant degeneration of a benign neurogenic tumor to MPNST.^{16,17} MPNSTs are usually of variable signal intensity on T1WI and T2WI magnetic resonance imaging (MRI).^{5,17} Nerve sheath tumors have slightly greater signal intensity than muscle on T1WI and markedly increased signal intensity than fat on T2WI or contrast-enhanced images.^{7,9} The pathognomonic sign of neurogenic tumor is seen as fusiform shape with the nerve entering and exiting mass. In small nerves or those in the subcutaneous and retroperitoneum, these sign is not always seen.⁵ On T2WI MRI, a central hypointensity surrounded by peripheral hyperintensity is called target sign and mostly benign characteristic.^{5,17,18} Target appearance caused by the more vascular fibrous tissue seen centrally and less cellular and vascular myxoid tissue peripherally.² Target sign can be seen on CT not well as MRI.^{7,9,18} Multiple small ring-like structures with peripheral higher signal

intensity on T2WI or proton density MRI occasionally (fascicular sign) can be seen in MRI.^{5,9}

In this case, radiology appearances lead to malignancy without any information type of the tumor. Patient has founded multifocal mass with multiple lung mass and nodules that identified at the beginning of the case. This patient was not examined under MRI, angiography and Gallium-67 scintigraphy because those modalities are not provided in our hospital. The patient's skull radiograph showed the multiple soft tissue masses. CXR clearly, described multiple nodules in both over the lung. CT of the chest showed one mass that attach to thoracic vertebral body at the level of carina is suspected origin from spinal nerve. There was no neurologic deficit though there is metastatic mass in his parietal lobe of the brain.

MPNST grow inside the nerve sheath, adopting a spindle or globular appearance, and though most of them present fusiform, a shape caused by nerve roots entering and exiting the nerve.^{1,9} Microscopically, MPNSTs are usually more hypercellular with hyperchromatic spindle cell proliferation, irregular and pleomorphism nuclei, cyst formation, and mitotic activity.^{2,7,19} Immunohistochemical demonstrate focal S-100 protein positivity (50%-90%), though 30% may be negative.^{1,2,3} These tumors may reactivity for Leu-7 or myelin basic protein, but they are negative for cytokeratins. Occassionally, they are positive for the melanocytic marker HMB-45.¹ This patient have FNAB from nodule of the left arm, TTNA, and biopsy examination from nodule of the head. All of this examination positively diagnosed MPNST. Very aggressive multifocal MPNSTs possibly happened in this case. Yet, in this patient we cannot confirm the primary of the tumor.

First choice of treatment is surgical; with wide en bloc resection.^{1,2,7} Local recurrence rate different between 40-68%.^{2,7} Postoperative radiations and chemotherapy has benefit to reduce local recurrence significantly.^{1,7} In contrast, most reports emphasize that

Table 2: Imaging Signs of Neurogenic Neoplasms

Sign	Modality Depicting the Sign
Fusiform	MR (less well seen with CT, US)
Entering and exiting nerve	MR (less well seen with CT, US)
Low attenuation	Unenhanced CT
Target sign	T2-weighted MR (less well seen with CT)
Fascicular sign	T2-and proton density-weighted MR
Split-fat sign	T1-weighted MR (less well seen with CT)
Associated muscle atrophy	T1-weighted MR

Source: Murphey MD, Smith WS, Smith SE, Kransdorf MJ, Temple HT. Imaging of musculoskeletal neurogenic tumors: radiologic-pathologic correlation.⁹

radiation and chemotherapy not effective in the treatment of MPNSTs.^{7,19,20} Palliative treatment was planned for this patient.

Patients with and without NF1 have 10%-16% and 50%-53% five years survival rate, respectively.^{1,2,7,12} Factors that influence prognosis of patient are patient's age (age > 30 yo has better prognosis), tumor location, size (tumor < 10 cm in diameter has better prognosis), histological subtype, tumor grade, molecular genetics, completeness of resection, recurrence, metastasis, and presence of NF1.^{1,7} Okada et al. reported only large tumor size and metastatic at presentation were independent prognostic factors.¹⁰ High histological grade were related with poor prognostic although an independency of histological grade of MPNST still obscure.¹⁰

CONCLUSION

This is a rare case of MPNST in Indonesia with multifocal mass which was not associated of NF1 and no history of radiation therapy. In this case the primary origins of the tumor difficult to explained because patient has came with respiratory complain and swelling in the head, with history of tumor resection in the left thigh 3 years before without histological information of the tumor. This soft tissue sarcoma is not always symptomatic especially in early stage. The diagnosis of this case have been made based on clinical finding, CXR, chest CT, head CT and ultrasound of the abdomen and proven by histological examination. v

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