American Journal of Cancer Case Reports

Cancer Case Reports
http://ivyunion.org/index.php/ajccr/
Vol. 1, Article ID 201300076, 9 pages

Case Report

Undifferentiated High-grade Pleomorphic Sarcoma (Malignant Fibrous Histiocytoma) Occurring in the Nerve Root: A Rare Case Report and Review of the Literature

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Abstract

Introduction: undifferentiated pleomorphic sarcoma (UPS) represents a group of pleomorphic mesenchymal neoplasms without any defined cell differentiation, occurs more commonly in the extremities. However, we report a rare case of UPS, not malignant peripheral nerve sheath tumor (MPNST) in which the nerve root of the forth cervical vertebrae and adjacent tissues were involved.

Presentation of Case: Histopathologically, this tumor was composed of highly atypical spindle cells, pleomorphic cells and multinucleated giant cells. Nuclear mitoses were frequently observed. Immunohistochemistrical results showed that the tumor cells stained positively for vimentin but negatively for all the other immunomarkers.

Conclusion: We here reported an extremely rare case of UPS arising from the nerve root of the forth cervical vertebrae and proposed a hypothesis “tumors without any expression of neural markers should be diagnosed as UPSs, not MPNSTs, even though which may arise from peripheral nerve branches”.

Keywords: Undifferentiated pleomorphic sarcoma; Malignant fibrous histiocytoma; Nerve root

Peer Reviewers: Abhijit M. Godbole, MD, PhD, Internal Medicine, St Barnabas Hospital, United States; Chien-Feng Li, ND, PhD, Department of Pathology, Chi Mei Medical Center, Taiwan

Received: December 22, 2012; **Accepted**: March 26, 2013; **Published:** May 2, 2013

Competing Interests: The authors have declared that no competing interests exist.

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Introduction

Undifferentiated pleomorphic sarcoma (UPS) which previously was known as pleomorphic malignant fibrous histiocytoma (MFH), has been defined as an entity in the WHO classification of soft tissue tumors since 2002 [1, 2]. Cases without definite differentiation were commonly used to be diagnosed as malignant fibrous histiocytoma (MFH), a term that has been kept as being synonymous with UPS. In the past, MFH was considered to be the most common type of sarcoma [3], composing 40% of the malignant sarcomas; however, with the new classification the UPS accounts for only about 5% of all soft tissue sarcomas in adults [2]. UPS/MFH represents a group of high-grade pleomorphic sarcomas, occurs more frequently in the extremities, mainly lower limbs of patients during the 5th and 7th decades of life [2].

As we know, tumors arising from the nerve root without any definite cell line of differentiation were always diagnosed as malignant peripheral nerve sheath tumors (MPNSTs) according to the WHO classification of nervous system tumors [4], contrary to the definition of UPS nominated by the WHO classification of soft tissue tumors [1]. We here reported an extremely rare case of UPS arising from the nerve root of the forth cervical vertebrae and proposed a hypothesis "tumors without any expression of neural markers should be diagnosed as UPSs, not MPNSTs, even though which may arise from peripheral nerve branches".

Case Presentation

A 56-year-old woman was admitted to Xijing Hospital, the Forth Military Medical University, with a history of intermittent pain in the left neck and shoulder for a half and two years. Physical examination revealed a well-appearance woman with tenderness and slight fever in the spinous process of the forth cervical vertebrae and its adjacent tissues on the left. Eighteen years ago, this patient was resected her uterus, bilateral fallopian tube and ovary for leiomyoma of the uterus. Other medical and family histories, such as NF-1 or radiation exposure, were unremarkable. Magnetic resonance imaging (MRI) (Figure1) showed that an extramedullary tumor arised from vertebral canal of the third and forth cervical vertebrae (C3 and C4), and extended to the adjacent tissues along the intervertebral foramina. Operative findings were as follows: C4 nerve root were thickened to 1cm, forming a focal mass enclosed with pseudocapsule; This mass passed through intervertebral foramina and squeezed adjacent vertebrae.

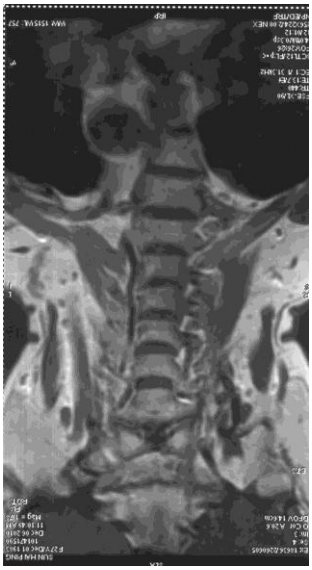

Figure 1 Magnetic resonance imaging (MRI) presented that this tumor arised from vertebral canal of the third and forth cervical vertebrae (C3 and C4), and extended to the adjacent tissues along the intervertebral foramina.

Materials and Methods

The specimen was fixed with 10% buffered neutral formalin. After routine series of dehydration, transparency, oozing wax, and embedding, paraffin-embedded blocks were obtained, and then were cut in 5-μm sections for H&E (Hematoxylin & Eosin) and immunohistochemical staining.

According to manufacturer's standardized

protocols, slides were stained immunohistoc--hemically using the Dako EnVision 2-step system. Primary antibodies included epithelial membrane antigen, CK7, CK20, 34βE12, thyroid transcription factor-1, glial fibrillary acidic protein, S-100 protein, synaptophysin, neurofilament, CD56 (Leu-7), neuron specific enolase, myelin basic protein, CD31, CD34, vimentin, leukocyte common antigen, CD20, CD79α, CD3, CD163, CD138, plasma cell, desmin and myoglobin. Appropriate positive and negative controls were used in all reactions. To evaluate the cell proliferation index, Ki-67 expression was also analyzed.

After the process of dewaxing and dehydration, formalin-fixed tissue was fixed in 2.5% glutaraldehyde with 0.1mol sodium cacodylate buffer and postfixed in 1% osmium tetroxide for electron microscopic examination. Tissues were stained en bloc with 2.5% uranylacetate, dehydrated in graded alcohol solutions, and embedded in epoxy resin. Sections were cut and poststained with 5% uranyl acetate and lead citrate. Thin sections were examined under an electron microscope.

Results

Grossly, the biopsy specimen showed gray-white soft masses measuring 2cm × 1 cm × 0.5cm, with presence of an incompletely fibrous pseudocapsule. The cut surface examination confirmed that the tumor was a solid lesion with scattered foci of hemorrhage and necrosis.

Histologically, with a sarcoma-like appearance, the primary tumor showed a mixture of highly atypical spindle cells, pleomorphic cells and multinucleated giant cells (Figure2). The cytoplasm of the tumor cells was homogeneous, scanty and basophilic containing irregular and vacuolated nuclei. Some tumor cells with a high degree of mitotic activity were loosely arranged in a myxomatous background (Figure3), while others densely in a storiform or whorl pattern. Areas of hemorrhage and necrosis were present (Figure 4).

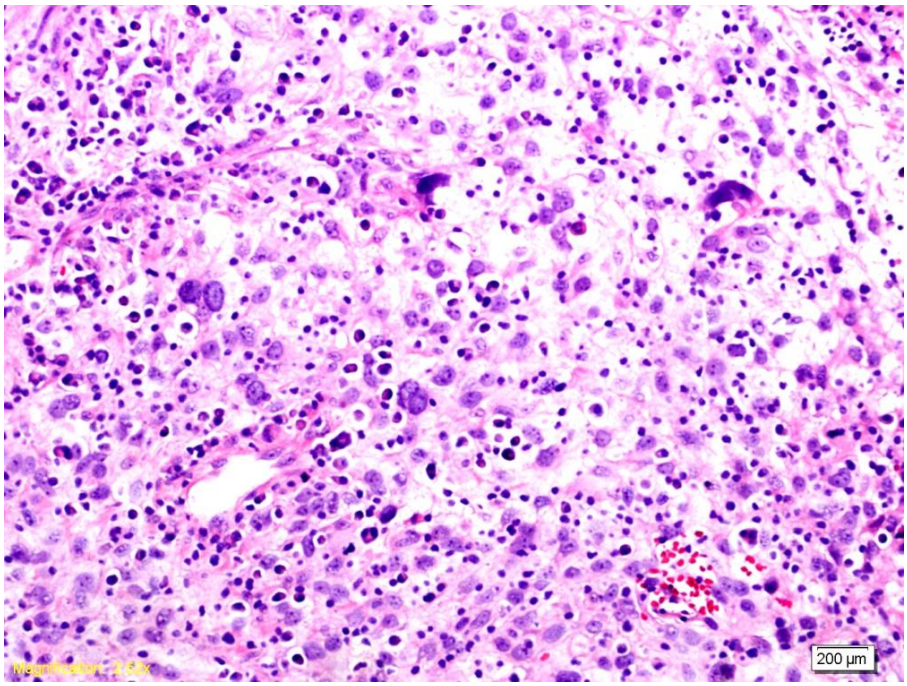

Figure 2 Some areas showed pleomorphic cells and bizarre multinucleated large cells within a myxoid stroma (HE×200).

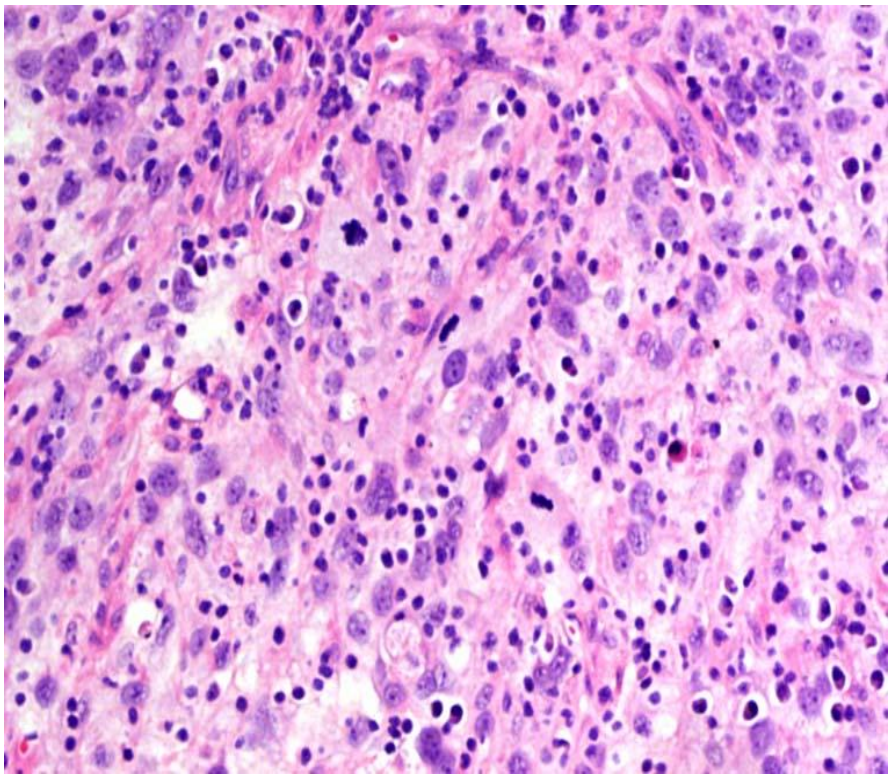

Figure 3 Tumor cells showed pleomorphism with frequent atypical mitoses (HE×200).

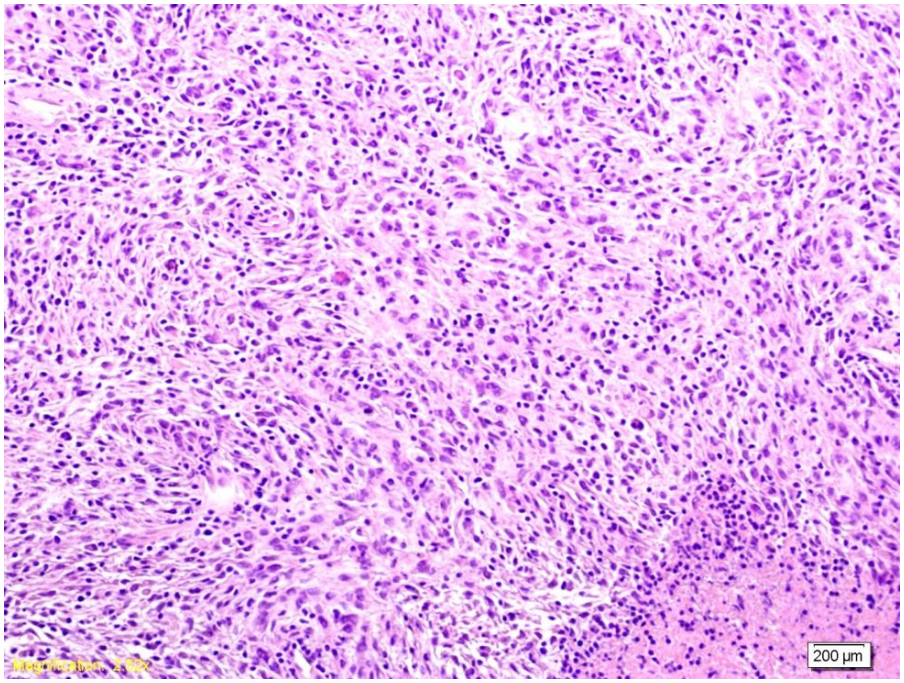

Figure 4 Pleomorphic spindle-shaped cells arranged in a storiform pattern around focal lesion of necrosis (HE×100).

A battery of immunohistochemical tests showed that the tumor cells stained positively for vimentin (Figure5) but negatively for all the other

immunomarkers illuminated on the preceding. The labeling index of Ki-67 to the tumor cells was 41%, declaring that the proliferative activity of this tumor was very high (Figure 6).

Ultrastructural observation showed that most tumor cells were autolyzed, and only vacuoles existed in cytoplasm. Besides that, incomplete rough endoplasmic reticulum and lysosome were founded in some few cells (Figure 7). In conclusion, results of electron microscope could not certify the definite differentiation of this tumor.

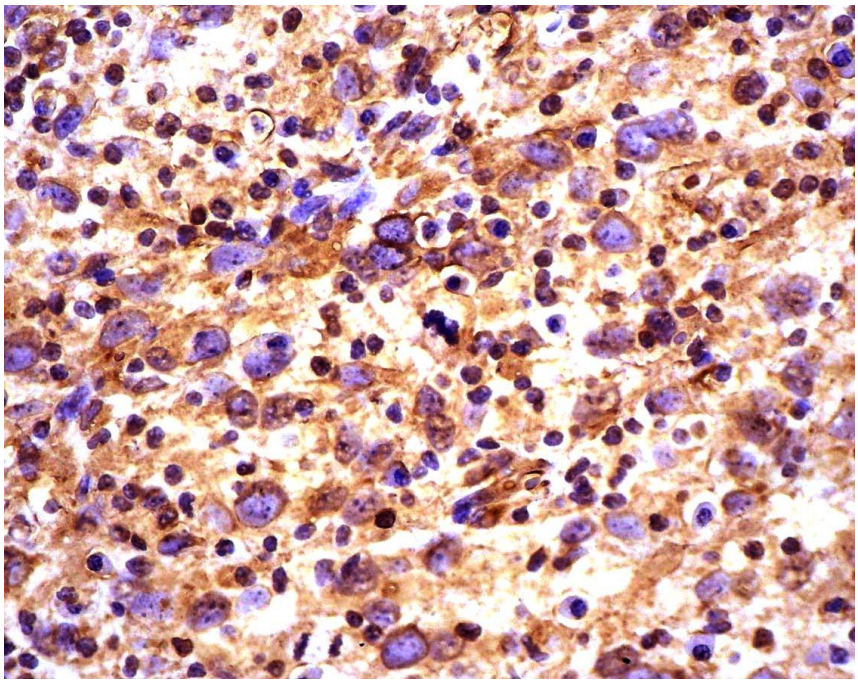

Figure 5 Tumor cells showed strong positivity for vimentin (HE ×200)

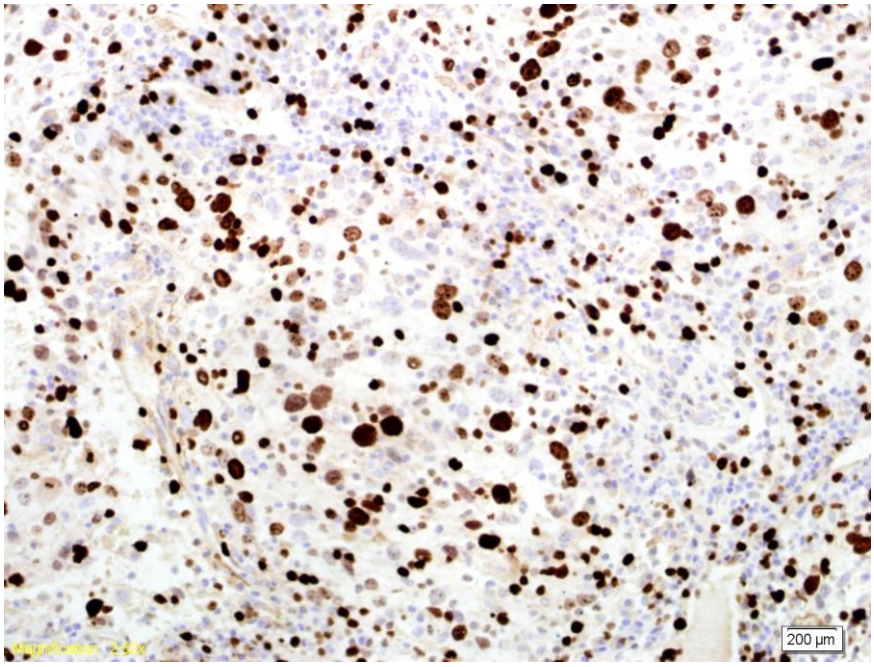

Figure 6 Tumor cells showed positivity for Ki-67 (HE ×200).

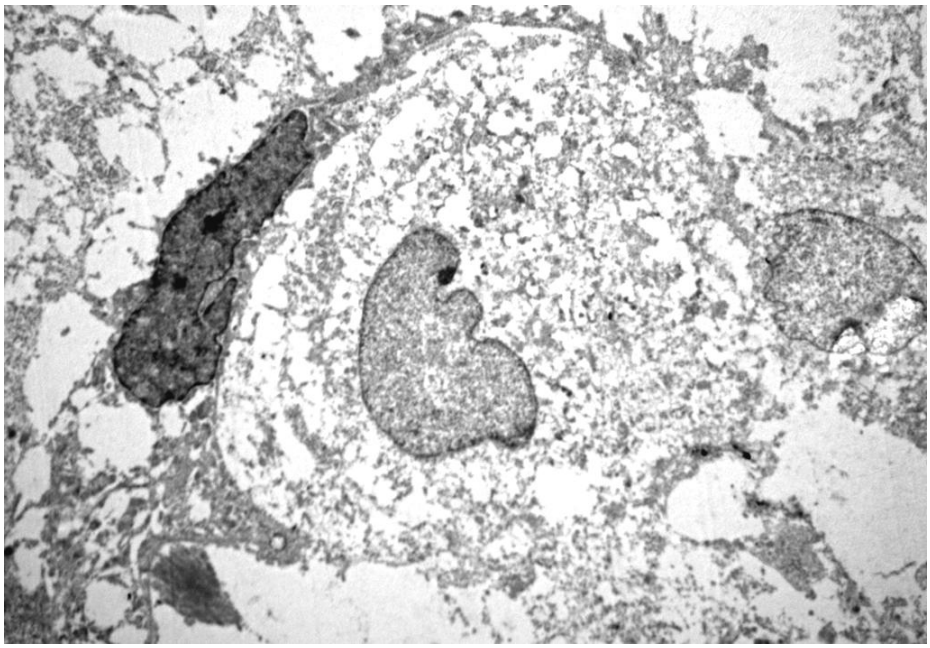

Figure 7 Most tumor cells were autolyzed, with vacuoles and incomplete rough endoplasmic reticulum existing in some few cells.

Discussion

UPSs or MFHs are a group of high-grade pleomorphic sarcomas. MFHs were primarily defined as pleomorphic spindle cell sarcomas with fibroblastic nature and facultative histiocytic differentiation in morphology [5-7]. It was divided into 4 main subtypes by Weiss and Goldblum, such as storiform pleomorphic, myxoid, giant cell, and inflammatory [7]. However, many tumors previously diagnosed as pleomorphic malignant fibrous histiocytoma were later confirmed as pleomorphic leiomyosarcomas, rhabdomyosarcomas, liposarcomas, osteosarcomas, malignant nerve sheath tumor, melanomas, lymphomas, and carcinomas by being applied more advanced diagnostic techniques, i.e., immunohistochemistry, electron microscopy and molecular genetics [5-7]. Besides that, recent evidence also demonstrates that this tumor does not present true histiocytic differentiation [5-7]. Therefore, the current WHO classification published in 2002 proposed this denomination UPS, which was synonymous with MFH. It represents a group of pleomorphic mesenchymal neoplasms without any defined cell differentiation, so this tumor "UPS/MFH" becomes a diagnosis of exclusion [8].

MFH was formerly considered to be the most common type of sarcoma in adults, accounting for 40% of the malignant sarcomas; however, using the new WHO-classification the incidence of MFH dropped down to no more than 5% [2]. The UPS occurs most commonly in the extremities of elderly patients, especially the lower limbs. UPS is a group of high-grade sarcoma, showing a heterogeneous pattern with frequent pleomorphism and multiple cellular shapes. Histologically, it often shows pleomorphic cells, sometimes bizarre giant cells and spindle cells. Those tumor cells usually present obvious atypia, with high nuclear/cytoplasm ratio and

irregular hyperchromasia. The quantity of histiocytes was variable, of which cytoplasm may be abundant with foam. In most cases immunohistochemical analysis reveals positive cells only for vimentin[8, 20]. Immunohistochemical markers for histiocytes such as CD68, CD163 and lysozyme have been proved useless for the diagnosis of UPS. Ultrastructurally, the neoplastic cells deficient in the bundles of actin filaments was usually abundant with dilated rough endoplasmatic reticulum.

This tumor was composed of hypo- and hypercellular regions and originated from the nerve root, mimicking the features of malignant peripheral nerve sheath tumors (MPNSTs) [9]. Diagnosis of a MPNST should be combined histopathological features with clinical features, including the status of neurofibromatosis Type-I (NF1), in which approximately 25 to 50% of MPNST arise; clinical or pathological finding of the tumor originating from a major or minor peripheral nerve branches [10] or sheath of peripheral nerve fibers [11,12]; the identification of Schwann cell differentiation by neural markers, including S-100, Leu-7, neuron specific enolase (NSE), myelin basic protein (MBP) and GFAP, which is the most objective and important element to diagnose MPNST [17,18]. Among those markers, S-100 has been certified to be positive in 50-90% of MPNSTs [13-18]. A few parts of UPSs, negative for those neural markers and no relation to special history, were mainly distinguished from other types of sarcomas only by their origin from a nerve trunk [19]. While according to the definition of UPS nominated by the WHO classification of soft tissue tumors since 2002, sarcomas without any definite cell line of differentiation should be classified as UPS, which has not been accepted by the WHO classification of nervous system tumors published in 2007 [4]. So, there was a controversy in the literature. We here suggested those sarcomas, without any expression of nerve sheath markers (S-100 and GFAP i.e.) and relation to NF1 as UPSs, even though which may arise from peripheral nerve branches. Based upon the above hypothesis, we finally diagnosed this case as UPS.

Other high-grade tumors such as leiomyosarcoma, monophasic variant of synovial sarcoma, rhabdomyosarcoma, angiosarcoma, melanoma, spindle cell variant of squamous cell carcinoma and haematopoietic tumors should also be considered in differential diagnosis. While the lack of expression of SMA, keratin, EMA, Myogenin, CD31, CD34, HMB45 and LCA ruled out all the other related tumors [1].

From a clinical standpoint, UPSs are tumors of deep location with a progressive and rapid growth pattern. The prognosis of UPS depends on the area affected, the size and depth of the tumor and the degree of cellular atypia. Approximately 5% of cases already show metastases when the primary tumor is diagnosed [21]. Although UPS is resistant to chemotherapy, the more effective treatment of choice seems to be complete excision combined with appropriate adjuvant radiotherapy [20-23], which contributes to inhibiting more extensive lesions. And a rigorous follow-up is necessary. The prognosis of UPS is poor with a mean 5-year survival rate ranging from 50% to 60% [5-7]. In this case, the patient was submitted to surgical resection associated with adjuvant radiation therapy and had not shown local or distant recurrences after 5 months of the treatment.

Conclusion

We here reported an extremely rare case of UPS arising from the nerve root of the forth cervical vertebrae and proposed a hypothesis "tumors without any expression of neural markers should be diagnosed as UPSs, not MPNSTs, even though which may arise from peripheral nerve branches".

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