

The recurrent plexiform neurofibroma of the scalp in neurofibromatosis type 1: illustrative case

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BACKGROUND Plexiform neurofibroma is a benign tumor of the peripheral nerves. It is an unusual variant of neurofibroma originating from all parts of the nerve. Plexiform neurofibroma is primarily pathognomonic and exhibits an unusual variant from neurofibromatosis type 1 (NF1). The possibility of malignancy and recurrence are the main reasons for long-term, close follow-up.

OBSERVATIONS The authors report a case of a 14-year-old girl with a recurrent plexiform neurofibroma derived from the peripheral nerves, which also presented with a typical sign of NF1 disease. The aim of the tumor resection is symptomatic relief.

LESSONS Accomplishing a good outcome can be related to good perioperative planning and a precise operative procedure. The result of anatomical pathology determines the prognosis of the patient. Clinical examination and radiological studies are needed to evaluate the recurrence of complications after surgical procedures.

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KEYWORDS plexiform neurofibroma; neurofibromatosis type 1; recurrent; tumor resection

Neurofibroma is a benign tumor of the peripheral nerve sheath. It arises due to the abnormal proliferation of Schwann cells, perineural cells, and endoneurial fibroblasts. Several types of pathology are identified, including localized, plexiform, and diffuse types.^{1,2} Neurofibromatosis type 1 (NF1) is a neurocutaneous, autosomal dominant disorder.³ NF1 affects approximately 1/2700 newborns, with variable presentation and disease severity.³ The disease manifestations are café-au-lait macules (CALMs), neurofibromas, skin-folding freckling, iris hamartomas (Lisch's nodules), optic pathway gliomas, and skeletal deformities.^{1,3} Plexiform neurofibroma is a benign tumor of the peripheral nerves (World Health Organization grade I) and an unusual variant of neurofibroma that arises from a proliferation of all parts of the nerve. Plexiform neurofibroma is essentially pathognomonic of NF1.^{2,4-6} This tumor has a significant risk of eventual malignant transformation.⁷ The possibilities of malignancy and recurrence are the main reasons for long-term, close follow-up.⁸⁻¹³ Plexiform neurofibromas are an uncommon type of NF1 developed from multiple nerves as bulging and deforming masses that also involve connective tissue and skin folds, also known as "bags of worms."¹³⁻¹⁷ We report a case of

recurrent plexiform neurofibroma, originating from the peripheral nerves, which also presented with typical signs of NF1 disease.

Illustrative Case

History and Examination

A 14-year-old girl presented with a recurrent tumor mass in the posterior scalp, right parietooccipital region. She complained of pain in the tumor region that eased with morphine medication. She had been diagnosed with NF1 at age 10 years based on the clinical signs of numerous CALMs, pseudoarthrosis, cutaneous neurofibroma, and one plexiform neurofibroma. She underwent brain magnetic resonance (MR) imaging examination, which demonstrated a mass in the posterior scalp, right parietooccipital region. There was T2 signal abnormality extending in the right parietooccipital region with increased signal intensity. There was no abnormality in the brain and along the optic nerve. We distinguished healthy tissues and tumors by the different hair colors. The tumor region had more white hair color than black hair color, as in healthy tissues (Fig. 1). At 6 years of age, she had undergone orthopedic surgery procedures for pseudoarthrosis in the right tibia.

ABBREVIATIONS CALM = café-au-lait macule; MR = magnetic resonance; NF1 = neurofibromatosis type 1.

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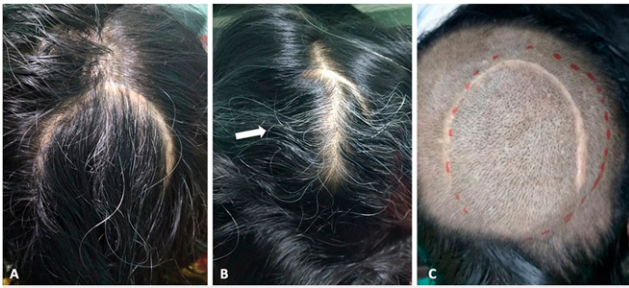


FIG. 1. A 14-year-old girl patient presented with a recurrent soft tissue mass (dotted line) in the parietooccipital region after resection had been performed (C). We could differentiate healthy tissues and tumors by the difference in the hair colors (A and B). Tumor areas were revealed by whiter hair color (arrow) than healthy tissues.

She had undergone surgery for neurofibroma in the right parietooccipital region at age 10 years. The anatomical pathology result was plexiform neurofibroma. She routinely came to the clinic for clinical evaluation. Four years later, she presented with a recurrent tumor mass and pain. The tumor measured approximately $9 \times 11 \times 2$ cm and was solitary, mobile, and not attached to the bone below it. She also had another mass in the lower back, approximately $5 \times 3 \times 2$ cm, solitary, mobile, and not attached to its muscle. She had CALMs all over the body with a maximum diameter of more than 15 mm (Fig. 2). The patient also presented with tibial pseudoarthrosis, and surgery was performed for the orthopedic procedure.

MR imaging evaluation showed that the lesion had reappeared in the same location four years after the initial surgical procedure (Fig. 3).



FIG. 2. Patient presented with CALMs in the back region with a variation of diameters.

MR imaging demonstrated contrast enhancement of the subcutaneous soft tissue mass in the parietooccipital region. The mass was smaller than before with the same imaging intensity on MR imaging. Management options were discussed with the family, including tumor resection with a preserved epidermis layer above the tumor or aggressive tumor resection with a skin flap. The family agreed to a tumor resection with preservation of the epidermis layer above the tumor, considering the risks of the skin flap, such as alopecia in the flap region because of the patient's age and gender.

Pathological Examination

The tumor grossly appeared as a mass with white-gray color and rubbery, dense consistency. The intraoperative cytological preparation showed cells with a mixture of fat tissue and tumor cells between them. Tumor cells consist of proliferative cells with an oval nucleus and partly wavy spindle, smooth chromatin, and elongated cytoplasm. The stroma contains collagen fibers. There was no sign of malignancy or tumor cells infiltration to the epidermis layer (Fig. 4). The pathological studies led to the diagnosis of the plexiform neurofibroma, which was the same as previous results. It was a recurrent tumor without any sign of malignancy.

Operation and Postoperative Course

Resection of the tumor lesion was performed under general anesthesia (Fig. 5). During the operation, the tumor was noted to be highly infiltrative into its epidermis layer. The resection was done by carefully separating the cutaneous and subcutaneous layers. The tumors were located in the subcutaneous layer. It is important to know the border of healthy tissues and tumors. Total resection of the tumor up to the margin of healthy tissue was gently performed. The target of the resection was up to where the hair follicles of the epidermis layer were seen. The patient was evaluated by routine clinical examination in the clinic and MR imaging 3 months postoperatively.

Discussion

NF1 is a condition of rare autosomal dominant genetic mutations of the NF1 gene at chromosome 17q11.2.¹ Clinical manifestations of this abnormality consist of multiple skin alterations such as CALMs and axillary freckling, and by tumoral growth along nerves, called "neurofibromas."^{1,5,18–21} Plexiform neurofibroma is an unusual type of neurofibroma and a benign tumor of the peripheral nerve that possesses a high risk of malignant transformation.^{7,13,16,18,19,22–25} Plexiform neurofibromas are usually diagnosed in early childhood and found in approximately 30% of NF1 cases, most frequently in the cranio-maxillofacial region.^{7,13,26} Malignant transformation occurs in 2% to 16% of cases and is considered the leading cause of mortality.²⁷ NF1 is diagnosed using 2 or more criteria from the National Institutes of Health. Plexiform neurofibromas are diagnosed clinically by the typical manifestations of the disease. Histopathological studies are performed to differentiate malignant changes.^{3,4,11,12,15,17,20,28–30} Our patient had the manifestations of numerous CALMs, pseudoarthrosis, cutaneous neurofibroma, and one plexiform neurofibroma. Surgery remains the treatment of choice in plexiform neurofibromas. Total resection of the tumor mass is performed when malignant transformation occurs, especially in recurrent cases. The incidence of recurrence is 20% of cases, even when the approach was done appropriately.^{31,32} Given this concern and its nature, some authors^{23,33} suggest that neurofibroma should receive a more radical tumor mass resection. Even this tumor recurrence may occur even if completely resected. The tumor resection aims to relieve the symptoms.^{22,23,31,34–36} This patient had undergone total resection of the tumor. Four years later, the patient presented with

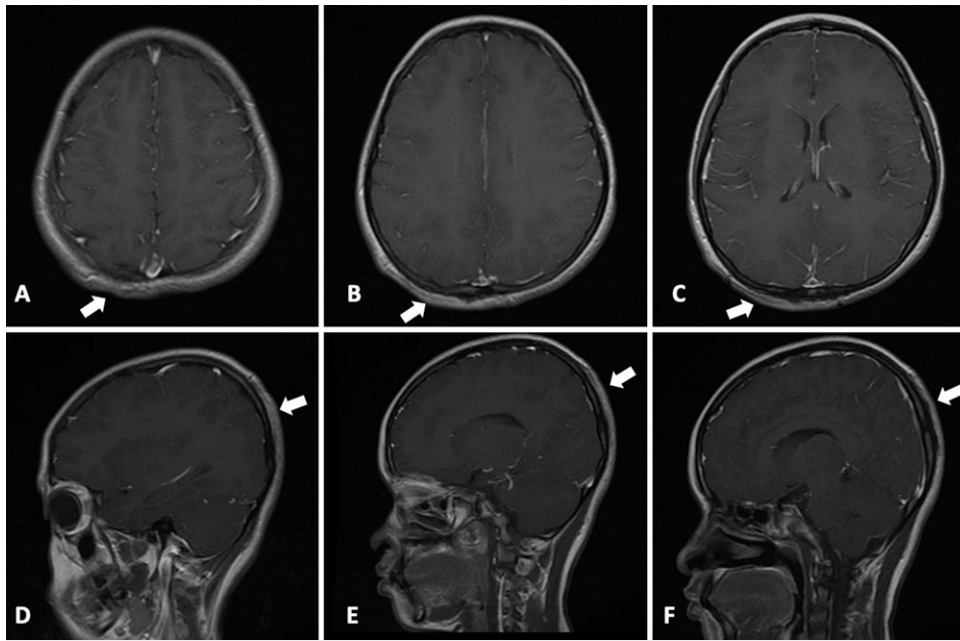


FIG. 3. MR imaging, axial (A–C) and sagittal (D–F) sections, demonstrated contrast enhancement of subcutaneous soft tissues (arrows) in the right parietooccipital region, 4 years after tumor resection.

a recurrent tumor in the same location as previously and a pain that did not subside with nonopioid medication.

Observations

A more aggressive surgery should be performed, especially in the case of recurring symptoms. Surgical tumor mass resection indications in neurofibroma include pain, functional impairment, cosmetics, and malignant transformation.^{27,33,37–39} The procedure should have realistic aims, and the associated risks should be explained to patients and families. We explained the surgical technique and the surgery's goal to the patient and her family, including whether we would perform aggressive tumor resection to the cutaneous epidermis layers above the tumor or tumor resection with preservation of the cutaneous layers

above the tumor. Aggressive resection had the advantages of minimal risk of recurrence and relief of the symptoms. However, we needed to perform a massive surgical flap, which is a complicated surgical procedure and may cause alopecia in the affected skin.^{31,33,34,37,40,41} This surgical approach optimally recovers the appearance and function of the patient. However, neurofibroma usually has diffuse tissue infiltration, which barely allows complete total resection.^{18,33,41,42–44} Tumor resection with preservation means patients can still take care of the cosmetics in the affected skin, but the risk of recurrence is more significant than with the other procedure. This approach depends on how aggressive the resection is and how carefully the healthy tissue is preserved. Total tumor resection up to the margin of healthy tissue is challenging to perform due to extensive involvement with adjacent

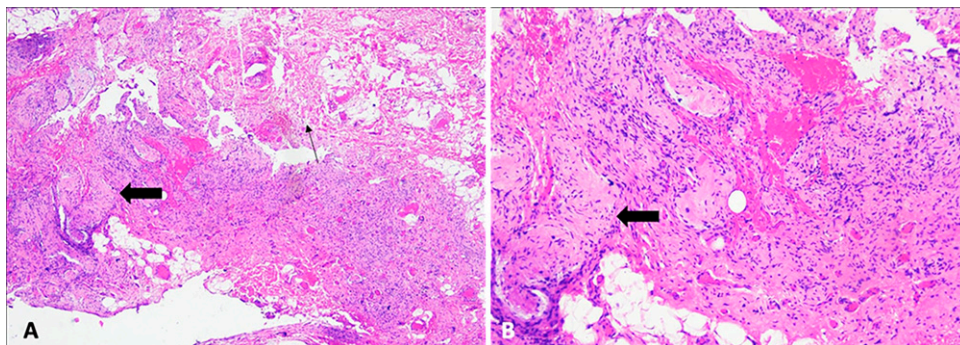


FIG. 4. Pathological anatomy of the plexiform growth pattern showing multiple tumoral nodules, each composed of loose spindle cells with short, elongated, wavy nuclei embedded in a mucinous stroma.¹³ There is no cutaneous infiltration of the tumor (arrows). Hematoxylin-eosin stain, original magnifications $\times 40$ (A) and $\times 100$ (B).

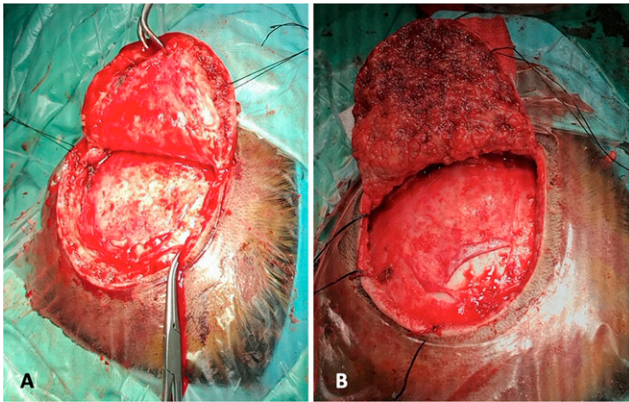


FIG. 5. Aggressive tumor resection with preservation of epidermis layers. Soft tissue mass tumor before tumor resection (A). After tumor resection revealed the hair follicles that showed the healthy tissue (B).

tissues. In our case, we performed aggressive tumor resection with preservation of the epidermis layer up to the healthy tissue border. A pathological study showed no sign of malignancy or tumor cell infiltration to the epidermis cutaneous layer. After the procedure, clinical and radiological evaluations were scheduled to seek another recurrence risk.

Lessons

Plexiform neurofibromas exhibit an unusual type of NF1 with a higher risk of recurrence after surgical procedure. Recurring tumor harbors a high risk for malignant transformation. Accomplishing a good outcome can be related to good perioperative planning and precise operative procedure, without local recurrence complications. Periodic clinical and radiology imaging examinations are essential in the evaluation of the recurrence.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Permana, Parenrengi, Suryaningtyas. Acquisition of data: Permana, Parenrengi. Analysis and interpretation of data: Permana, Parenrengi, Suryaningtyas. Drafting the article: Permana, Parenrengi, Suryaningtyas. Critically revising the article: Parenrengi, Fauziah. Reviewed submitted version of manuscript: Parenrengi, Suryaningtyas, Fauziah. Approved the final version of the manuscript on behalf of all authors: Permana. Statistical analysis: Parenrengi. Administrative/technical/material support: Permana, Parenrengi. Study supervision: Parenrengi. Assisted corresponding author: Azzam.

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