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A 63-Year-Old Man with Neurofibromatosis Type 1 and Intracerebral Astrocytoma: A Case Report

Iman Hakim Wicaksana^{1*}, Geizar Arsika Ramadhana²

¹Resident of Surgery, Faculty of Medicine, Universitas Sebelas Maret/Dr. Moewardi General Hospital, Surakarta, Indonesia

²Consultant, Department of Neurosurgery, Faculty of Medicine, Universitas Sebelas Maret/Dr. Moewardi General Hospital, Surakarta, Indonesia

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*Corresponding author:

Iman Hakim Wicaksana

E-mail address:

hakimwicaksana@gmail.com

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ABSTRACT

Background: Neurofibromatosis type 1 (NF-1) is one of the hereditary neurocutaneous disorders. Neurofibromatosis type 1 has broad clinical manifestations that can occur in the skin, bones, eyes, and nervous system. In progressive cases, NF-1 can malign and cause intracerebral tumor lesions. Astrocytoma, especially pilocytic astrocytoma, is one of the tumor classes that patients with NF-1 can develop with far-reaching disease progression. This case report presents a case of NF-1 with intracerebral astrocytoma. **Case presentation:** A 63-year-old man with whole body lumps since childhood presented with weakness in the right limbs 1 month ago. 3 months earlier, the patient also had a full-body seizure for 1 minute twice. The patient then underwent a magnetic resonance imaging (MRI) examination of the brain and found a mass in the left centrum semiovale, left corona radiata, left insular, left external capsule, and left frontotemporoparietal lobe with a size of 7.2 x 5.3 x 6.2 cm. The patient then underwent a VP shunt followed by tumor resection. The tumor was successfully evacuated, and histopathological examination with hematoxylin & eosin (HE) staining revealed glioblastoma multiformis. The patient also underwent histopathologic examination with Ki-67 immunohistochemistry (IHC) staining and showed pilocytic astrocytoma. **Conclusion:** Craniotomy of tumor excision is the definitive therapy in neurofibromatosis patients accompanied by intracerebral astrocytoma.

1. Introduction

Neurofibromatosis type 1 (NF-1), or Von Recklinghausen disease, is a heritable neurocutaneous disorder that also carries a risk of bone abnormalities, vasculopathy, and cognitive impairment.¹ Neurofibromatosis type 1 is an inherited disorder that is predominantly autosomal.² In addition, NF-1 is also the most common hamartoma neoplastic syndrome, such as tuberous sclerosis, Gardner, and Cowden syndromes.³ Other types of neurofibromatosis are neurofibromatosis type 2 (NF-2) and schwannomatosis. Cafe-au-lait macules and neurofibromas are characteristic of NF-1. Lesions in NF-2 can have skin manifestations similar to NF1.

Typical manifestations of NF-2 include schwannoma, meningioma, and ependymoma.⁴ This case report presents a case of NF-1 with intracerebral astrocytoma.

2. Case Presentation

A 63-year-old man came to the surgical clinic with the main complaint of right side weakness since 1 month ago. Three months previously, the patient also experienced whole-body seizures for 1 minute twice. The patient has a history of lumps all over his body since elementary school, but the patient has never had the lumps checked on his body previously. The patient was then taken to the regional hospital and treated by

a neurologist and psychiatrist. The patient underwent a CT scan at Sukarno Hospital and found a tumor in the brain and excess fluid in the ventricles of the brain. The patient was then referred to a referral hospital for further examination and treatment.

Physical examination showed that the patient appeared moderately ill, *compos mentis*, and vital

signs were within normal limits. There were solitary, multiple, rubbery, skin-colored papules and nodules (Figure 1). Chest and abdominal examinations were within normal limits. Extremity examination revealed weakness in the right superior extremity.



Figure 1. Clinical manifestations of the patient.

Routine blood and clinical chemistry examinations showed a Hb level of 16.1 g/dL, hematocrit level of 48%, monocytes 11.40% (normal 0.0-6.0%), creatinine 0.7 mg/dL, urea 21 mg/dL, blood sodium 135 mmol/L. Chest X-ray examination was within normal limits. The patient then underwent an examination of magnetic resonance imaging (MRI) of the brain, which showed a mass in the left centrum semiovale, left corona radiata, left insular, left external capsule, and left frontotemporoparietal lobe measuring 7.2 x 5.3 x 6.2 cm (Figure 2). The patient then underwent a VP procedures hunt followed by tumor resection. The

tumor was successfully evacuated, and the results of histopathological examination with staining hematoxylin & eosin (HE) and a picture of glioblastoma multiforme were obtained (Figure 3). Patients also underwent histopathological examination with staining immunohistochemistry Ki-67 and were shown the picture of pilocytic astrocytoma (Figure 4). Examination of the skin lesion revealed features of neurofibroma. The patient was diagnosed with neurofibromatosis type 1 with pilocytic astrocytoma. This patient was treated with a tumor excision craniotomy.

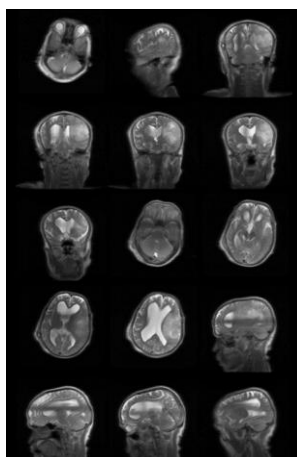


Figure 2. MRI of the head with contrast.

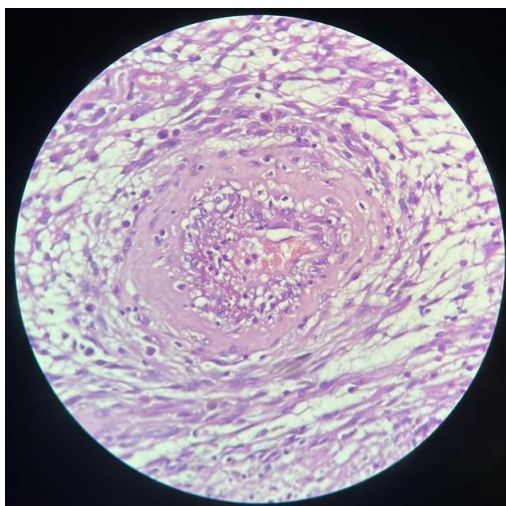


Figure 3. Histopathological examination of the mass in the brain with hematoxylin-eosin staining.

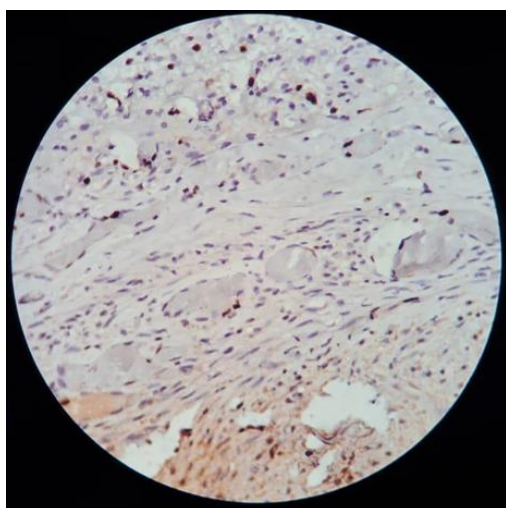


Figure 4. Histopathological description of brain tumor mass with Ki-67 immunohistochemical staining.

3. Discussion

Neurofibromatosis type 1 is an inherited disorder that is predominantly autosomal. The gene for NF-1 is located on chromosome 17 and encodes a gene product called neurofibromin.⁵ The global prevalence of NF-1 was found to be 1/3,000 people.^{6,7} The survival rate of individuals with NF-1 is reduced between 8-21 years, and a relatively high number of deaths occur in younger individuals aged <40 years compared to the general population. The most common cause of premature death in NF-1 is the development of NF-1 into a malignant neoplasm.^{8,9} The cumulative risk of malignancy at age 50 years in individuals with NF-1 is estimated at 20-39% with a

lifetime risk of developing malignant neoplasms of 60%.¹⁰

NF-1 gene mutations cause decreased neurofibromin expression, thereby increasing tumorigenesis. Neurofibromin itself functions as a protein to suppress tumor formation.^{11,12} Neurofibromas develop when both NF-1 alleles are mutated. Neurofibromas include Schwann cells, perineural cells, mast cells, and fibroblasts. Neurofibromas affect the skin originating from peripheral nerves and their supporting structures, including neurilemmal cells. Fibroblasts in neurofibromas originate from factor XIIIa connective tissue cells, which are human leukocyte antigen DR

(HLA-DR) positive in peripheral nerves. Skin fibroblasts secrete hepatocyte growth factor and stem cell factor in large amounts and contribute to increased melanin deposition in the epidermis.⁸ Café-au-lait macules contain giant pigment granules found in epidermal cells and melanocytes. There was a high genotype-phenotype correlation observed in NF1.¹³

The primary treatment for NF-1 is anticipatory management. Genetic counseling and evaluation of first-degree family members are very important things to do. At each doctor's visit, monitoring for macrocephaly, growth failure, precocious puberty, hypertension, developmental delay, learning disabilities, and scoliosis should be performed. At each age, there are a variety of problems that can develop, so focused, age-appropriate evaluations are needed for both children and adults. Annual ophthalmological examinations by an ophthalmologist in NF-1 should be performed until the age of 12 years to screen for the possible presence of optic glioma. Neuroimaging surveillance in asymptomatic patients as a screening test for optic pathway glioma is not recommended. However, loss of vision or other concerning symptoms such as precocious puberty should be performed immediately with magnetic resonance imaging (MRI) of the brain.^{14,15}

4. Conclusion

Tumor excision craniotomy is the definitive therapy in patients with neurofibromatosis accompanied by intracerebral astrocytoma.

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