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Case Report

Neurofibromatosis type I with large head and neurofibromas cause spinal cord compression

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Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder which exhibits variable clinical expression. The birth incidence of NF1 is 1 in 3000 that making NF1 becomes one of the most common genetic disorders. Genetic testing can be performed to confirm the prenatal diagnosis of NF1, but it could not predict the severity of the disease. Pregnant woman who diagnose NF1 has increased morbidity of hypertension and cerebrovascular complications. We report a case of who had family history of NF1 that born with large head and neurofibromas cause spinal cord compression.

Keywords: pregnancy; neurofibromatosis type 1; large head; neurofibroma

Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder with variable clinical presentation. The birth incidence of NF1 is 1 in 3000, making it becomes one of the most common genetic disorders. Pregnant women with NF1 are at increased risk of hypertension and cerebrovascular complications. Genetic testing can be helpful for prenatal diagnosis of NF1 but not for predicting severity of disease. [1,2]

According to the criteria, the diagnosis of NF1 is largely based on clinical expressions, therefore, NF1-related children should be screened more frequent to protect their function. [4]

We report a case with a family history of NF1 born with large head and neurofibromas causing spinal cord compression.

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Case report

A 34-year-old G3P2SA1 (P2 was preterm, born at 20 weeks' gestation) pregnant woman had regular antenatal care at our obstetrics clinic since 2nd trimester. She has family history of NF1 (Figure 1) and clinical features of multiple café-au-lait spots and cutaneous neurofibromas all over her body were noted. Although she experienced

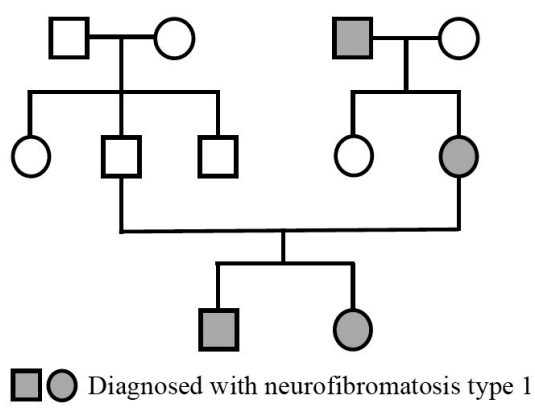

Fig. 1 Genogram of maternal family

flaring up of lesions during pregnancy, she denied having any headaches, visual changes, or hearing loss. She also had no history of hypertension. Her blood pressure and laboratory test results were all normal throughout her pregnancy. The fetus was in breech presentation and found to be large-for-gestational age in the third trimester. Biparietal diameter became larger that compared with abdominal circumference and femur length in subsequent antepartum sonographic measurement shown in Table 1. Polyhydramnios was noted with amniotic fluid index of 31.1 cm in the 34th week of pregnancy. Placental function was normal.

Table 1. Fetal anatomical measurements

GA	BPD	AC	FL
28+	7.8 cm (30 wks)	25.7 cm (30 wks)	5.4 cm (29 wks)
30+	8.4 cm (32 wks)	27.2 cm (31 wks)	5.9 cm (31 wks)
32+	9.0 cm (35 wks)	30.4 cm (34 wks)	6.4 cm (34 wks)
34+	9.9 cm (40 wks)	31.8 cm (36 wks)	6.6 cm (35 wks)

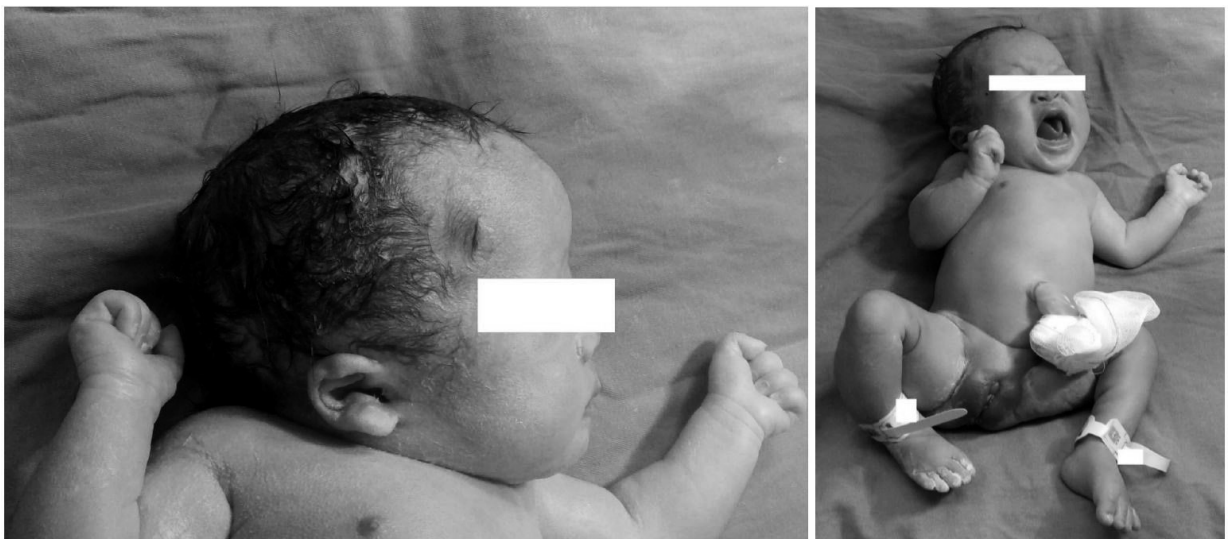

Fig. 2 Large head and appearance of newborn.

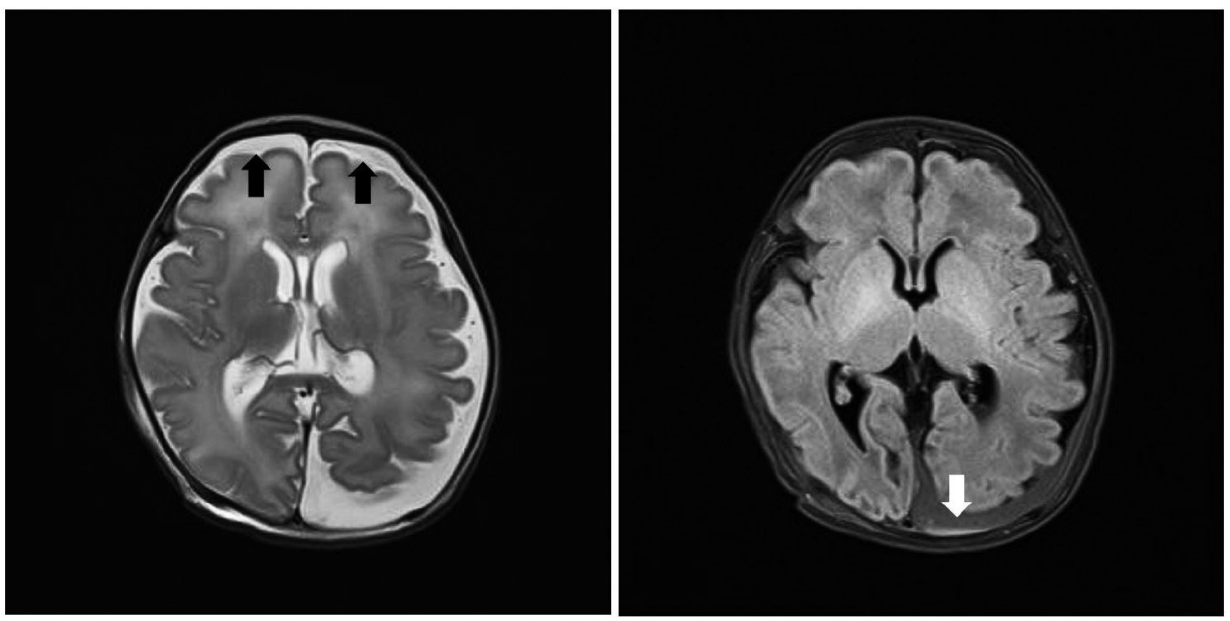

Fig. 3 MRI of the brain reveals enlarged subarachnoid spaces without ventricular enlargement (black arrows) and fluid in bilateral subdural spaces that more in left parietooccipital region (white arrow).

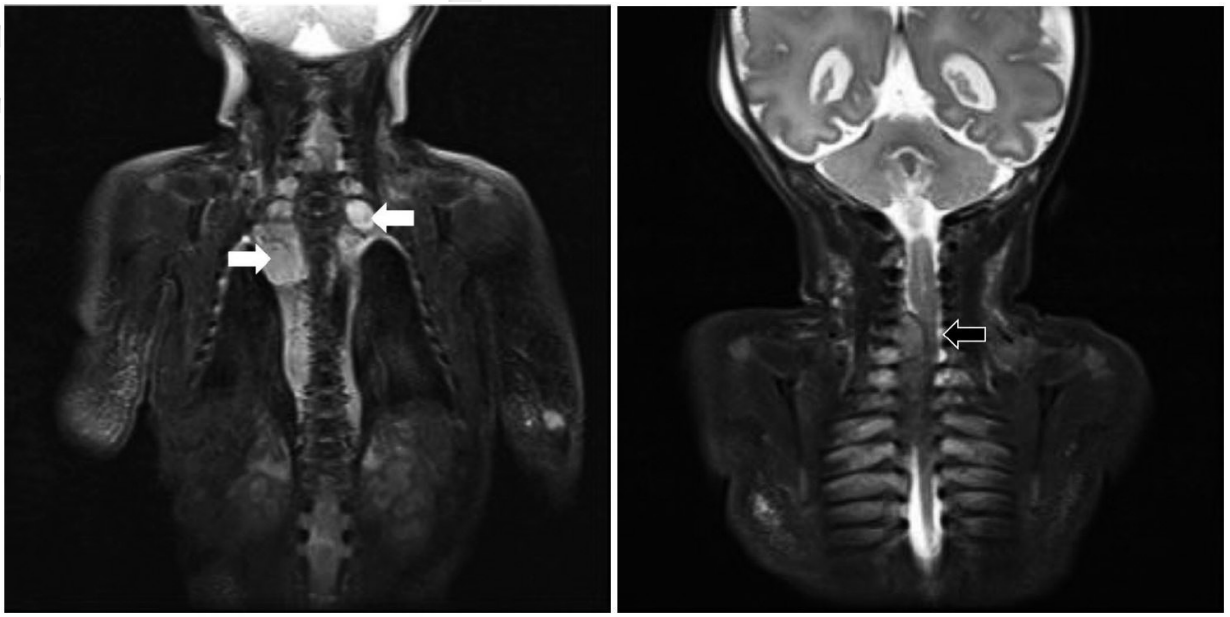

Fig. 4 Image of MRI reveals multiple neurofibromas along bilateral paravertebral regions of neck and mediastinum, and in epigastric region (white arrows). The mass effect of the mentioned lesions with some intraspinal extension on the right side, leading to compression of spinal cord (black arrow).

Amniocentesis was performed and karyotype showed a female chromosome complement.

Due to breech presentation in labor at 35 weeks and 3 days gestational age, she gave birth to a 2930g preterm female live newborn by caesarean section. Apgar score was 9 at one minute after birth and 10 at five minutes after birth. Newborn physical exam showed head circumference of 35.5 cm, which was above the 85th percentile for term newborns (Figure 2). Other physical features were normal. Due to her large head, brain MRI was performed and revealed benign external hydrocephalus, bilateral subdural hematoma or effusion, left cephalohematoma, and multiple neurofibromas in neck, chest, and abdomen with intraspinal extension and spinal cord compression on the right side from C4 to T3 (Figures 3, 4). Chromosome study showed normal female karyotype. The results of bilateral auditory brainstem response were within normal range. Newborn screening tests for inherited metabolic disorders were all negative. Based on National Institutes of Health (NIH) diagnostic criteria for NF1, she manifested at least 2 of 7 criteria for NF1 diagnosis.

Postpartum period of mother was completely normal. She was discharged from the ward five days after birth and provided with adequate advice and recommendations. The newborn was discharged two weeks later and referred to another hospital for conservative surgery due to spinal cord compression.

Discussion

Behavior:

Neurofibromatosis is a genetic disorder in which benign and malignant tumors develop in the central and peripheral nervous systems with variable clinical presentation. There is no definitive medical therapy. [2,3] When neurofibromas become symptomatic tumors that cause neurological impairment, pain, and severe disfigurement, conservative surgical resection is necessary. In this case, we arranged for surgical intervention for spinal cord compression. Neurofibromatosis treatment focuses on healthy growth and development of affected children and early management of complications.

Based on clinical diagnostic criteria, there are three types of neurofibromatosis (neurofibromatosis type 1, neurofibromatosis type 2, and schwannomatosis), each with different signs and symptoms. (Table 2) [2,4] Neurofibromatosis diagnosis is based largely on clinical presentation. However, different clinical

Table 2. Clinical diagnostic criteria for NF1, NF2 and schwannomatosis [2,4]

Neurofibromatosis type 1	Neurofibromatosis type 2	Schwannomatosis
2 or more of the following: 1. ≧6 café-au-lait spots ● ≧1.5 cm in post-pubertal individuals ● ≧0.5 cm in pre-pubertal individuals 2. ≧2 neurofibromas of any type or ≧1 plexiform neurofibroma 3. Freckling in axillary or inguinal regions 4. Optic glioma 5. ≧2 Lisch nodules (iris hamartomas) 6. Bony dysplasia (sphenoid bone dysplasia, long bone cortex dysplasia) 7. A first-degree relative with NF1	Any 1 of the following: 1. Bilateral vestibular schwannomas (VS) 2. Any 2 of the following: meningioma, glioma, schwannoma, cataract, neurofibroma, cerebral calcification ***and*** ● Unilateral VS <30 y/o or ● first-degree family relative with NF2	Age＞30 y/o and all of the following: ● ≧2 nonintradermal schwannomas (at least 1 with histologic confirmation) ● No evidence of vestibular tumor on high-quality MRI scan ● No known constitutional NF2 mutation ● Diagnostic criteria for NF2 not fulfilled ● No first-degree relative with NF2 ***Or*** Age＞30 y/o and 1 pathologically confirmed nonvestibular schwannoma and a first-degree relative who meets above criteria.

features appear at different times, meaning that the diagnosis may be confirmed with age and growth. DeBella et al. studied 1893 NF1 patients under the age of 21. Among them, 30% met only 1 diagnostic criterion at under 1 year of age. Nearly all (97%) and all met the NIH criteria for diagnosis at 8 and 20 years of age, respectively. [5]

NF1 is the most common type of neurofibromatosis and one of the most common autosomal dominant disorders of the nervous system. People with a history of NF1 have a 50% chance of passing this disorder onto their child and both sexes are affected with equal frequency. For patients with mild clinical features for which confirmation of neurofibromatosis diagnosis is needed or who are diagnosed with neurofibromatosis and plan to have a child, genetic testing is suggested. Mutations of NF1 gene are located on chromosome 17 and mutations of NF2 gene are located on chromosome 22. [2,4] All gene mutations can be determined from blood sample of patient or during antenatal care from chorion tissue, amniotic fluid, or fetal umbilical cord blood sample.

Previous studies have shown that pregnancy complications are more common in women with NF1, including gestational hypertension, pre-eclampsia, cerebrovascular disease, intrauterine growth restriction (IUGR), preterm labor, and stillbirth. Increased incidence of caesarian delivery has also been reported. [1,6] Large-for-gestational age was identified in the third trimester in our case. A previous study has shown that NF1 infants have increased weight and head circumference when compared with normal infants. However, length and weight decrease in association with maternal diagnosis of NF1. [7] Thus, it is recommended that in NF1 pregnancies both mother and fetus receive more frequent screenings and the way of delivery should be assessed carefully.

Clinical presentation of NF1 can vary. One of the anatomic signs is an unusually large head due to increased brain volume. [3] External hydrocephalus was observed in our case. Benign enlargement of subarachnoid space with normal ventricles or mild ventriculomegaly is a common cause of macrocephaly in infants in which large head circumference is the only feature. [8] In a previous case report, an infant with external hydrocephalus developed subdural hematoma with minimal or no trauma. [9] A large head, in children with NF1, is not specifically associated with cognitive deficits or lower IQ. [3] However, optic gliomas are clinical features of NF1. [10] Therefore, in the presence of

a large head in children with NF1, with or without neurologic symptoms, MRI is suggested for further evaluation.

Several studies have demonstrated mental retardation (defined as full-scale IQ<70) in 4 to 8% of children with NF1, which is twice as high as in the general population but relatively low when compared with other genetic disorders that affect the central nervous system. (3) The most common NF1-related neuropsychological deficits in children are cognitive dysfunction and learning disabilities. Therefore, affected children should be screened for developmental and behavioral problems and given early support. [3,11]

In conclusion, children with one parent with NF1 are usually diagnosed with NF1 at a young age as they already meet 1 diagnostic criterion, a first-degree relative with NF1. Hence, preconception genetic counseling should be conducted if a NF1 patient plans to have children. Parents should know the risks of passing on this disorder to their offspring and its varied presentation. Moreover, women with NF1 should be made aware of the potential for increased pregnancy complications.

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