Longitudinal changes in choroidal abnormalities in patients with neurofibromatosis type 1

Shinji Makino

Department of Ophthalmology, Jichi Medical University, Shimotsuke, Tochigi, Japan

*Corresponding author
Shinji Makino

Email: maki-chan@jichi.ac.jp

Abstract: We present two cases of neurofibromatosis type 1 (NF1) with near-infrared reflectance (NIR) findings to analyze if the number of choroidal abnormalities increases over time. During a 3-year follow-up period, NIR findings showed no change in the choroidal lesions in one patient, while those in the second patient increased. Our findings may contribute to a better understanding of the natural course of NF1.

Keywords: neurofibromatosis type 1, near-infrared reflectance, choroidal abnormality, longitudinal study.

INTRODUCTION

Neurofibromatosis type 1 (NF1), an autosomal dominant disorder with a high mutation rate, is a neurocristopathy characterized by hamartomatous proliferations of neural crest-derived tissues. A minimum of two of the following criteria are required for diagnosis: six or more café-au-lait spots, two or more cutaneous neurofibromas, one or more plexiform neurofibromas, axillary or groin freckling, optic glioma, two or more Lisch nodules, distinctive bony lesions, and a first-degree relative with NF1 [1]. Lisch nodules, in particular, are frequently observed, and are a recognized feature of the disorder. Retinal and choroidal lesions were, however, until recently, considered unusual in eyes with this disease.

In 2000, Yasunari et al.; [2] demonstrated that choroidal abnormalities were easily detectable by infrared light examination with a scanning laser ophthalmoscope in all their NF1 patients. More recently, choroidal abnormalities have been observed as multiple patchy and bright lesions in patients with NF1, using near-infrared reflectance (NIR) [2-13], prompting several authors to propose the detection of choroidal nodules as a new diagnostic criterion for NF1 [2-4, 12-14]. Few reports have evaluated the correlation between choroidal abnormalities and age [3, 4, 11-13]. However, to our knowledge, changes in choroidal abnormalities over time in NF1 patients have never been reported before. Herein, we present two patients with NF1 examined by NIR.

CASE REPORTS

Case 1

A 9-year-old girl with NF1 was referred to our clinic for an ophthalmological examination. An NF1 diagnosis was made on the basis of several café-au-lait spots and cutaneous neurofibromas. She exhibited no visual symptoms. Her best-corrected visual acuity was 1.2 in both eyes. There were at least 6 Lisch nodules in each eye. Conventional ophthalmoscopic findings were unremarkable. However, NIR (Heidelberg Retina Angiograph 2, Heidelberg Engineering, Heidelberg, Germany) revealed multiple bright, patchy lesions in both eyes (Figure 1A and B). During the 3-year follow-up period, the choroidal abnormalities did not change in either eye (Figure 1C and D).

Case 2

A 4-year-old girl with NF1 was referred to us for an ophthalmological examination. An NF1 diagnosis was made based on the presence of several café-au-lait spots and cutaneous neurofibromas. She exhibited no visual symptoms. Her best-corrected visual acuity was 1.0 in both eyes. There were at least 3 Lisch nodules in each eye. Conventional ophthalmoscopic findings were unremarkable. NIR revealed bright, patchy lesions in both eyes (Figure 2A and B). During the 3-year follow-up period, the choroidal abnormalities in the right eye increased (Figure 2C arrow), while those in the left eye showed no change (Figure 2D).
Fig. 1 NIR images of the right (A, C) and left (B, D) eyes.
A, B: initial visit; C, D: 3 years after initial visit.
Choroidal nodules, visualized by NIR, are seen as multiple bright, patchy lesions.
The hyper-reflective point at the center of the image is an optical artifact.

Fig. 2 NIR images of the right (A, C) and left (B, D) eyes.
A, B: initial visit; C, D: 3 years after initial visit.
Choroidal nodules, visualized by NIR, are seen as bright, patchy lesions. Increased choroidal lesions are observed in the right eye (C arrow). The hyper-reflective point at the center of the image is an optical artifact.
DISCUSSION
The number of neurofibromas and Lisch nodules is known to increase with age in patients with NF [15, 16]. Huson et al.; [16] reported that Lisch nodules were present in 95% of their patients (61/64) and were bilateral in 93% (57/61). Among the patients aged <16 years (n = 24), 3 had no Lisch nodules (13%), and 9 (38%) had fewer than 10 nodules per eye, whereas all patients of ages ≥16 years (n = 40) had Lisch nodules, and only 6 (15%) had fewer than 10 nodules per eye, indicating a significant correlation between age and the number of nodules per eye. Viola et al.[3] reported that Lisch nodules were detected in 68 (72%) of 95 NF1 subjects and in 9 (43%) of 21 pediatric NF1 subjects.

The correlation between the increase in choroidal abnormalities and age has also been studied [3, 4, 11-13]. Nakakura et al.; [4] and Goktas et al.; [12] reported that choroidal abnormalities specific to NF1 appear to increase significantly with age. Viola et al.; [3] reported the detection of bright, patchy choroidal nodules by NIR in 79 of 95 (82%) NF1 patients, including 15 pediatric patients (71%), and also recorded a statistically significant correlation between the age of the patients and the number of regions of the fundus involved. The latter observation was corroborated by Vagge et al.; [13] in a similar study, although they reported no significant difference between the ages of NF1 patients with choroidal nodules and those of subjects with none. It has, therefore, been established that the areas of distribution of choroidal abnormalities in the fundus increase with age. However, there have been no studies focusing on the longitudinal changes in choroidal abnormalities in patients with NF1. Case 2, presented here, is the first report of dynamic changes in choroidal abnormalities over time in a patient with NF1. Although our report is based solely on two patients and only a 3-year follow-up period, our observation that choroidal lesions increased over that period in one of the patients may contribute to a better understanding of the natural course of this disease. Long-term follow-up and additional cases are necessary to further characterize the changes in the appearance of choroidal abnormalities in NF1 patients.

REFERENCES