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Research Article

LISCH NODULES, ONE OF THE HALLMARK MANIFESTATIONS OF NEUROFIBROMATOSIS TYPE 1

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Abstract

Von Recklinghausen disease or neurofibromatosis type I (NF1) is the most common phacomatosis. Inherited forms are transmitted in an autosomal dominant fashion. Lisch nodules are the most common ophthalmological manifestation of NF1, reported in 73-95% of cases. We report the case of a 49-year-old female patient, referred to ophthalmology for a systematic ocular check-up in view of the following cutaneous signs: café-au-lait spots and multiple neurofibromas.

Keywords: Neurofibromatosis type 1, Lisch nodules, Von Recklinghausen desease, Case report.

INTRODUCTION

Neurofibromatosis type 1 (NF1) is a genetic disease caused by a defect in a single gene encoding neurofibromin, a cytoplasmic protein involved in cell cycle control. The eye is frequently affected in neurofibromatosis, and consequently ocular manifestations play a major role in the diagnosis of NF (1). This rare clinical case highlights the importance of ophthalmic examination in these patients, describing the ocular manifestations found in neurofibromatosis.

Case presentation

We report the case of an 18-year-old man followed for 5 years for neurofibromatosis type1. Questioning revealed no first-degree consanguinity of the parents and no similar family history. Generally speaking, the patient was in good health, with a single plexiform neurofibroma on the thorax and "café au lait" pigmented patches on the trunk (Fig. 1). Ophthalmologically, visual acuity was 10/10 P2 in both eyes. Slit-lamp examination of the anterior segment showed a few Lisch nodules on both irises. These were scattered over the iris surface and varied in size (figure 2). The rest of the examination was unremarkable, with intraocular pressure of 15 mmhg. Orbito-cerebral CT scan revealed no associated lesions.

Neurofibromatosis type 1 (NF1), or von Recklinghausen disease, is one of the most common of the so-called "phacomatoses" (2). Named after Friedrich von Recklinghausen, the anatomist and pathologist who described its characteristics in 1882(3). It results from mutations or deletions in the NF1 gene (17q11.22), a tumor suppressor gene; in around 50% of cases, these are neomutations, so no family history is found. It results in generalized neuroectodermal and mesodermal dysplasia, progressively and polymorphically affecting the dermis, nervous system, skeleton and vascular system (4). The expression of the disease is variable and depends on the patient's age.

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Plexiform neurofibromas of the upper eyelid should be looked for on inspection of the child, as they cause an S-shaped deformity of the upper eyelid, which may lead to occlusion of the visual axis and require surgery. It is often associated with strong homolateral myopia (5). Ophthalmological manifestations include sphenoid dysplasia, responsible for orbital dystopia and/or exophthalmos, which may be pulsatile in severe forms (6).

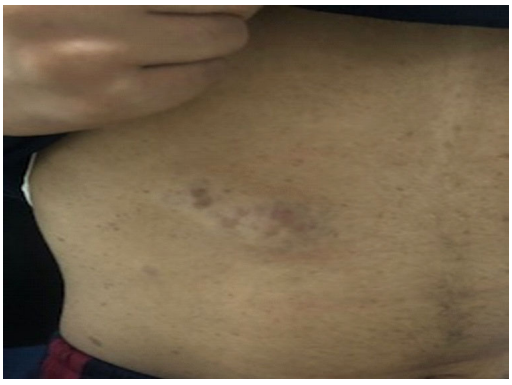

Figure 1. Showing Café-au-lait spots and thoracic plexiform neurofibroma (arrow)

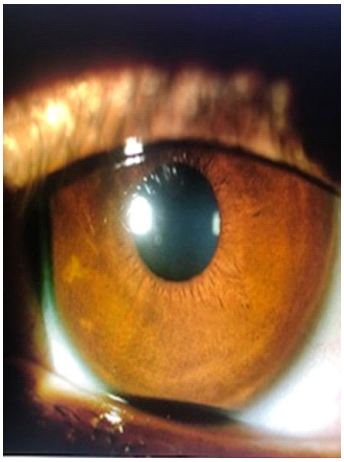

Figure 2. Lisch Nodules (Arrows) on the Iris of our Patient with Neurofibromatosis 1

Lisch nodules are melanocytic hamartomas, benign lesions found in the iris, first described by Lisch in 1937. Histologically, they contain irregular collections of spindle-shaped cells. They are more common in familial cases (93%), compared to sporadic cases (54%), and are more frequently observed on the inferior half of the iris, appearing in childhood in over 75% of NF1 patients. They are characteristic of the disease, but have no clinical repercussions. They appear as small iris elevations with slightly downy margins. Their color varies according to that of the iris, generally being lighter than the iris pigmentation. They are clearly visible with a slit lamp. They should be carefully sought out, and not confused with trivial small flat pigmentations; the differential diagnosis includes iris nipples, iris nevi, iris melanoma, iris granulomatous nodules. In contrast to cutaneous signs, several Lisch nodules are considered specific to NF1. These nodules may appear early in childhood, and their prevalence and number increase with age. They are present in 30% of children by the age of 6, and 95% of adults.

Ectropion of the posterior layer of the iris results from endothelialization of the iridocorneal angle, with centrifugal traction of the outer layer. When present, it is therefore a risk factor for glaucoma, and intraocular pressure and RNFL should be monitored as soon as possible, particularly in these patients. Anterior displacement of the ciliary processes and the presence of uveal neurofibromas probably also contribute to its development (7). Buphthalmia without glaucoma is a rare and generally unilateral occurrence: the eye is clinically buphthalmic, with increased corneal diameter and sometimes considerable axial myopia. It is often associated with a plexiform neurofibroma of the homolateral upper eyelid. This must be a diagnosis of elimination, given the increased frequency of congenital glaucoma in children with NF1. This non-glaucoma buphthalmia is part of orbital gigantism, which affects not only the eye but the entire orbit. It requires strict follow-up, due to the complications of high myopia and the differential diagnosis of glaucoma. Retinal vascular anomalies. Retinal vascular corkscrew tortuosities affect small second- or third-order venules in a third of patients. Much more rarely, telangiectasia or retinal ischemia may be observed. Hyperreflective spots on infrared images, recently described, are not a criterion for NF1, although their sensitivity and specificity are high. They often appear before Lisch nodules, and can be easily detected from an early age. One of the most potentially disabling complications of the disease is confined to children: optic tract glioma, which occurs in 15% of affected children, is a benign tumour that is often asymptomatic, but sometimes causes profound visual impairment. The disease also leads to neurological, skin and orthopedic complications (8,9). Thus, periodic ophthalmological examinations in suspected individuals can help in the early clinical diagnosis of NF1. The treatment of NF is multidisciplinary, and surgery is the mainstay of treatment for Plexiform Neurofibrosis.

Conclusion

Neurofibromatosis can affect the eye and ocular adnexa in a variety of ways. Lisch nodules are almost pathognomonic of neurofibromatosis, and their discovery is therefore an important diagnostic adjunct. It is important to recognize ocular involvement in these patients to facilitate earlier diagnosis of treatable conditions that may threaten vision. The role of ophthalmologists can be seen throughout the NF1 patient journey: at the diagnostic stage, during paediatric follow-up, and finally in the event of the development of visual complications of the disease.

Conflict of Interests: The authors have no conflict of interests to declare.

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