Acta Scientific Neurology (ISSN: 2582-1121)

Volume 4 Issue 3 March 2021

Case Report

Bourneville Disease (Tuberous Sclerosis), Case Report

Randrianjafisamindrakotroka Ony[1]*, Rakotoarisoa Rivo Tahiry Rabetafika[2], Tongavelona Adrianna[3], Raobela Léa[1] and Randrianjafisamindrakotroka Nantenaina Soa[3]

[1]Ophtalmology Care, Training and Research Units of Joseph Ravoahangy Andrianavalona University Hospital Center, Antananarivo, Madagascar

[2]Ophtalmology Care, Training and Research Units of Anosiala University Hospital Center, Antananarivo, Madagascar

[3]Surgical and Cytopathology Laboratory of Joseph Ravoahangy Andrianavalona University Hospital Center, Antananarivo, Madagascar

***Corresponding Author:** Randrianjafisamindrakotroka Ony, Ophtalmology Care, Training and Research Units of Joseph Ravoahangy Andrianavalona University Hospital Center, Antananarivo, Madagascar.

Received: September 11, 2020

Published: October 07, 2020

Abstract

Introduction: Bourneville disease or tuberous sclerosis complex (TSC) is an autosomal dominant disease with variable penetrance. It is classically described in the literature as a triad of seizures, intellectual disability and adenoma sebaceum. Rare disease, it concerns 1/10000 live births. Retinal phages are present in almost 50% of patients. These are glial hamartomas characteristic of the affection.

Case Report: We report the case of a 9 years-old boy referred to the Ophthalmology Department This patient was followed in Rheumato-Dermatology clinic for tuberous sclerosis for about 4 years and there was an evolving of his cutaneous lesions. Dermatologists wanted to find out whether there was ocular manifestations. The interview revealed no history of epilepsy, nor intellectual retardation no similar case in the family neither. The patient had angiofibromas on his face, the rest of the somatic examination was normal. On ophthalmic examination his visual acuity was 10/10 P2 for both eyes. Biomicroscopic examination was normal. The fundus showed a peripapillary retinal phages in the right eye consisting of two yellowish, multinodular raised lesions of tapioca granules, one of which was the same size as the papilla in diameter and the other one was smaller. These corresponded to retinal phage type 2 and papillary pseudo-edema on both eyes.

Conclusion: Bourneville disease or tuberous sclerosis presents a notorious variability of expressivity. Retinal astrocytic hamartoma confirms the diagnosis of this rare disease.

Keywords: Bourneville Disease; Hamartoma; Retina; Tuberous Sclerosis

Introduction

The term "tuberous sclerosis" was given by the French neurologist Bourneville in 1880, to define a rare form of multiple cerebral sclerosis. "Tuberous" because the brain lesions were comparable to potato tubers. It is an autosomal dominant disease with variable penetrance. It is classically described in the literature as a triad of seizures, intellectual disability and adenoma sebaceum. It is a rare condition, concerning 1/10000 live births. Retinal phages are present in almost 50% of patients. These are glial hamartomas characteristic of the affection.

Case Report

We report a case of tuberous sclerosis complex (TSC) in a 9-years-old boy, patient of the Dermatology Department for about 4 years. This patient was referred to the Ophthalmology Department following an evolving of his cutaneous lesions. The interview revealed no history of epilepsy, intellectual retardation, nor similar cases in the family. The patient had symmetrically distributed angiofibromas in the nasolabial folds, around the cheeks and around the mouth, in characteristic butterfly pattern (Figure 1). These angiofibromas consisted of small protruding firm nodules. In the right lumbar region, firm, elastic, bumpy, orange peel skin plaques were found (Figure 2). The rest of the somatic examination was normal with no cardiac nor renal manifestations.

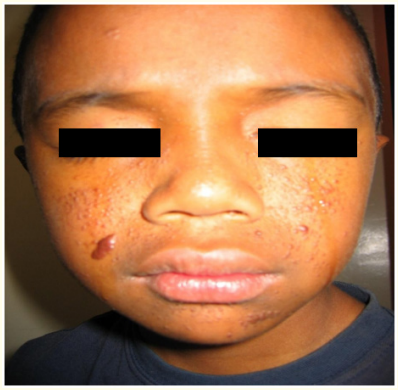

Figure 1: Symmetrically distributed angiofibroma appearance in nasolabial folds, on the cheeks and around the mouth, in butterfly pattern.

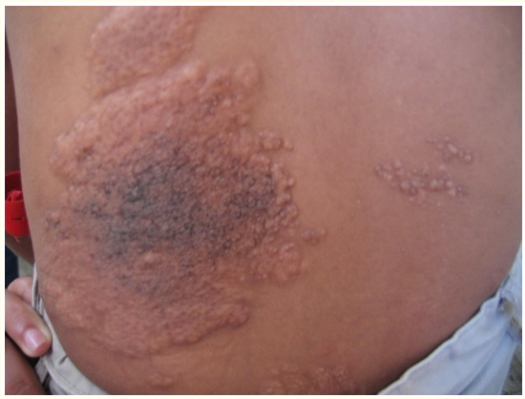

Figure 2: Skin of soreness plate in the right lumbar region made of thick, firm, elastic, bumpy, "orange peel" surfaces.

On ophthalmic examination his visual acuity was 10/10 P2 with +0.25 diopters correction for both eyes. The eyelids were normal as well as ocular motility. There was no squint.

Biomicroscopic examination was normal, without depigmentation nor coloboma of the iris and the anterior chamber was calm.

The fundus examination revealed peripapillary retinal phages in the right eye consisting of two yellowish, multinodular, tapioca-shaped raised lesions, one of which was the same size as the papilla in diameter and the other one was smaller. These corresponded to retinal phages type 2 (Figure 3). Papillary pseudo oedema of both eyes was also noted.

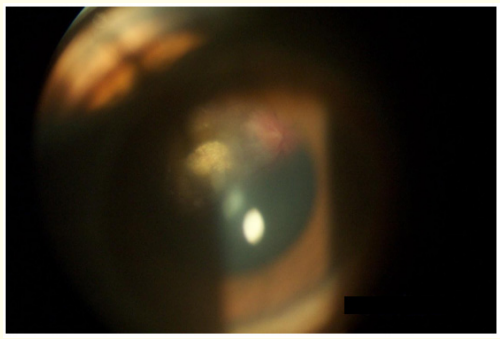

Figure 3: Fundus examination showing the peripapillary retinal phages type 2.

Discussion

TSC belongs to the group of phacomatosis which refers to hereditary diseases characterized by the presence of congenital anomalies more or less diffuse and multiple development. Manifestations include malformations, tumors or hamartomas. In TSC, lesions consist in benign tumors with astrocytic hamartomas. Those lesions can have multiple locations, such as the skin, the brain, the kidney, the heart and the eye [1,10].

STB is due to the mutation of tumor suppressor genes during embryonic life in 60% of cases [7]. Two genes are involved: TSC1 coding for hamartin, which is on chromosome 9 long arm, and TSC2, which produces a protein called tuberin, located on the short arm of chromosome 16 [7].

It is inherited in 40% of the cases. TSC is an autosomal dominant disease and affects boys as well as girls. Clinical manifestations remain the same in both cases [5,6]. Unfortunately we could

not have performed genetic testing on our case report. But given the absence of a family history, it is assumed that it is a spontaneous mutation.

The revised international criteria 2012 for the diagnosis of STB are [5]:

- **Genetic criteria:** The identification of either a TSC1 or TSC2 pathogenic mutation in DNA from normal tissue is sufficient to make a definite diagnosis of tuberous sclerosis complex (TSC). A pathogenic mutation is defined as a mutation that clearly inactivates the function of the TSC1 or TSC2 proteins (e.g. out-of-frame indel or nonsense mutation), prevents protein synthesis (e.g. large genomic deletion), or is a missense mutation whose effect on protein function has been established by functional assessment. Other TSC1 or TSC2 variants whose effect on function is less certain do not meet these criteria and are not sufficient to make a definite diagnosis of TSC. Note that 10% to 25% of TSC patients have no mutation identified by conventional genetic testing, and a normal result does not exclude TSC, or have any effect on the use of clinical diagnostic criteria to diagnose TSC [5].
- **Clinical diagnostic criteria:** The clinical diagnostic criteria were revised in 2012 according to table 1 [5].

In our case, three major criteria are present: facial angiofibromas, lumbar soreness skin and nodular retinal hamartomas found in the right eye fundus. Based on the revised diagnostic criteria in 2012, we have a definitive diagnosis of TSC.

Although literature describes the disease as a triad of seizures, intellectual disability and adenoma sebaceum, it should be noted that nearly 40% of the affected subjects have neither seizures nor intellectual disability [5,6]. Our patient followed normal schooling for his age, but with some difficulties in memorization.

Ophthalmologic manifestations of STB may be of extra-retinal or retinal localization. The first, less frequent, consist of depigmentations or coloboma of the iris, angiofibromas of the eyelid or nonparalytic strabismus [5] and more recently hamartomas of the iris and the ciliary body histopathological diagnosis have been described [3,5]. We did not find any extra-retinal localization in our patient.

Majors features	Minors features
1. Hypomelanotic macules (≥3, at least 5-mm diameter) 2. Angiofibromas (≥3) or fibrous cephalic plaque 3. Ungual fibromas (≥2) 4. Shagreen patch 5. Multiple retinal hamartomas 6. Cortical dysplasias* 7. Subependymal nodules 8. Subependymal giant cell astrocytoma 9. Cardiac rhabdomyoma 10. Lymphangioleiomyomatosis (LAM) ** 11. Angiomyolipomas (≥2) **	1. "Confetti" skin lesions 2. Dental enamel pits (>3) 3. Intraoral fibromas (≥2) 4. Retinal achromic patch 5. Multiple renal cysts 6. Nonrenal hamartomas
* Includes tubers and cerebral white matter radial migration lines. **A combination of the two major clinical features (LAM and angiomyolipomas) without other features does not meet criteria for a definite diagnosis. Definite diagnosis: Two major features or one major feature with ≥ 2 minor features Possible diagnosis: Either one major feature or ≥ 2 minor features	

Table 1: Clinical diagnostic criteria revised in 2012.1

The retinal astrocytic hamartoma is the most recovered ophthalmological manifestation. Its prevalence is nearly 53% in the STB [1,4,5] but it can also be found in the normal subject. The location can be bilateral or unilateral on equal parts, single or multiple, around the disc [8]. There are 3 types of retinal astrocytic hamartomas [1,3,9]:

- Type I, the most frequently found (57 to 70% of cases), is a woolly nodule, flat or slightly salient, of 1/4 to 2 papillary diameters, not calcified, greyish and translucent;
- Type II, represents 50 to 55% of retinal astrocytic hamartomas is a multi-nodular tumor like tapioca granules, calcified, opaque, yellowish, more posterior seat and a size of 1/4 to 4 papillary diameters. This is the case of our patient.
- Type III, transitional between the two types I and II, is found in 9 to 12% of cases. In our case, it is an astrocytic hamartoma type II.

There is no correlation between the patient's age and the observed retinal lesion [5,9].

According to most of authors, retinal hamartomas are not very progressive and the visual function is preserved for a long time except for foveal location or complications [1,8].

Complications occur with no consideration of age and can be: retinal serous detachment with exudates, vitreous hemorrhage, vitreous swarming, retinal necrosis, neovascular glaucoma, or even anatomical and/or functional loss of the eye [1]. In our case, we found only unilateral peri- papillary localization. Our patient had no complications yet. Moreover, his visual acuity is preserved.

In addition, astrocytic hamartomas may have cardiac, renal or pulmonary localizations. We did not find any cardiac or renal manifestations in our patient.

Cutaneous involvement, as in our case, is found in all patients with STB. It is about angiofibromas: small projecting of firm nodules. They are located at the level of the face in a symmetrical distribution in the nasolabial folds, the cheeks and in the perioral region [4,10].

The other type of cutaneous lesion also found in our patient is the skin of lumbar sorrow. They are thick, firm, elastic, bumpy, with "orange peel" surfaces [4].

Currently, Rapamycin, Everolimus and Sirolimus derivatives are considered as a causal treatment for STB. Indeed, these drugs offer targeted therapy by binding to and inhibiting mTORC1 [2].

Conclusion

The STB has a noticeable variability of expressivity. The retinal astrocytic hamartoma is the most recovered ophthalmologic manifestation. Thus, ophthalmologist plays an important role in the diagnostic confirmation of this rare disease.

Conflicts of Interest

The authors declare no conflict of interest.

Authors Contributions

All authors contributed to this article and read and approved the final version of this manuscript.

Bibliography

1. Benatiya AI., *et al.* "La sclérose tubéreuse de Bourneville, à propos d'un cas". *Journal Française d'Ophtalmologie* 28 (2005): 1121-1125.

2. Curatolo P and Moavero R. "mTOR Inhibitors in Tuberous Sclerosis Complex". *Current Neuropharmacology* 10.4 (2012): 404-415.

3. Eagle RC., *et al.* "Hamartomas of the Iris and Ciliary Epithelium in Tuberous Sclerosis Complex". *Archives of Ophthalmology* 118 (2000): 711-715.

4. Lautier-Frau M., *et al.* "Slérose tubéreuse de Bourneville: étude à propos de 10 cas". *Journal Française d'Opthalmologie* 25 (2002): 86-87.

5. Northrup H and Krueger DA. "Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference". *Pediatric Neurology* 49 (2013): 243-254.

6. O'Callaghan FJ and Osborne JP. "Advances in the understanding of tuberous sclerosis". *Archives of Disease in Childhood* 83 (2000): 140-142.

7. Pirson Yves., *et al.* "Sclérose tubéreuse de Bourneville: poser le diagnostic et traiter à bon escient". *Louvain Médical* 136.1 (2017): 10-15.

8. Prasad S and Kamath GG. "Retinal astrocytic hamartoma". *Journal of Postgraduate Medicine* 77 (2001): 556.

9. Shields JA., *et al.* "Aggressive Retinal Astrocytomas in 4 Patients With Tuberous Sclerosis Complex". *Archives of Ophthalmology* 123 (2005): 856-863.

10. Wolkenstein P. "Neurofibromatose et sclérose tubéreuse de Bourneville". *The Journal of Neuroradiology* 32 (2005): 174-179.