

The abortive form of Bourneville-Pringle syndrome

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Abstract. – *Background/Methods:* To present a 26-year-old woman affected by the abortive form of Bourneville-Pringle syndrome. To our knowledge, this disease is unusual since only very few cases have been reported in the scientific literature at this time.

Results/Conclusions: Visual acuity was 20/20 in both eyes. No relevant ocular abnormalities were observed excepting two retinal hamartomas, a smaller one in the nasal midperiphery of the right eye and a larger one located along the super-temporal retinal vessels of the left eye. Classical signs of Bourneville-Pringle disease, such as mental retardation and epilepsy, were absent whereas a slight facial adenoma sebaceum and renal cysts represented the solely systemic manifestations of the disease. This case report confirms that retinal phakomata are a typical manifestation of Tuberous Sclerosis, even in the absence of a detected involvement of the brain.

Key Words:

Bourneville-Pringle disease, Phakomatosis, Retina, Retinal hamartomas, Tuberous sclerosis.

heart; angiomyolipomas and cysts in the kidney, liver, adrenals and pancreas; fibromas at the side of toenails and along the hairline and astrocytomas in the brain. The characteristic facial lesions is called adenoma sebaceum, although facial angiofibroma would be more correct².

Even though a pathognomonic clinical triad has been described (mental retardation, epilepsy and adenoma sebaceum), it is not always diagnosed in its entirety and atypical forms may be observed. However, since involvement of the central nervous system is very common (over 80% of subjects), some abortive cases of TS, without mental retardation and epileptic seizures, have already been described as unusual forms some years ago⁴⁻⁸.

In this paper, we present a 26-year-old woman affected by the abortive form of BPD, an interesting and unusual variety of TS. An updated review of this syndrome has also been done.

Introduction

The terms Bourneville-Pringle Disease (BPD) and Tuberous Sclerosis (TS) (McK 191100)¹ are often used interchangeably to describe an inherited disorder of early embryogenesis leading, in its most typical form, to the formation of: hard areas of gliotic tissue (tubers) in the cerebral cortex, subependymal glial nodules projecting into the lateral and third ventricles resembling candle drippings, and, more rarely, subependymal giant cell tumors². Various other tumors may occur in different organs: retinal hamartomas³; rhabdomyomas in the

Case Report

I.B., a 26-year-old female affected by BPD-TS, came to our attention for a routine eye examination. The diagnosis of BPD-TS had already been genetically confirmed in the past by linkage to the TSC2 gene region (16p13.3), although family history was negative for TS and for any type of inherited diseases. Computerized Tomography (CT) scanning and Magnetic Resonance Imaging (MRI) didn't show any lesion in the brain whereas a slight facial adenoma sebaceum and renal cysts represented the solely systemic manifestations of the disease. Mental deficiency, epilepsy as well as renal or cardiac tumors were absent. The subject was affected

by hypertension, probably determined by the polycystic kidney, and was taking ACE inhibitors at low doses.

Best corrected visual acuity was 20/20 in both eyes (OU) with $-3.50\text{sf} = -0.75\text{cil}$ (90°). Slit lamp examination of the anterior segment demonstrated no relevant abnormalities. The intraocular pressure was normal (13 mmHg) and the lens and the vitreous were transparent in OU. Fundus examination confirmed the clinical diagnosis of BPD-TS, showing two typical retinal hamartomas, a smaller one in the nasal midperiphery of the right eye and a larger one located along the super-temporal retinal vessels of the left eye (Figure 1). No signs of hypertensive retinopathy were present.

Discussion

The prevalence of BPD-TS is reported to be 1 in 10,000 but milder varieties of the disease are often unrecognized. The condition is

two or three times more common in males than in females and is dominantly inherited with variable penetrance, influenced by modifier genes. Isolated and sporadic cases are frequent, comprising as many as 80% or 90% of index cases. Many of them probably represent new mutations while others are transmitted by gene carriers with trivial manifestations. Genetic heterogeneity has now been established, with separate loci on chromosomes 9q34 (TSC1 – McK 605284: encodes 1164-amino-acid protein, hamartin) and 16p13.3 (TSC2 – McK 191092: encodes 1807-amino-acid protein, tuberin). Both hamartin and tuberin interact in a pathway related to cytosolic G protein regulation. Mutations of TSC2 account for the majority of cases and are more likely to be associated with mental retardation and polycystic kidneys. Other translocations have been identified, such as $t(3;12)(p26.3;q23.3)$ (TSC3 – McK 191091) and $t(11q23.3;22q11.1)$ (TSC4 – McK 191090), but their relevance in the genetic determination of the clinically evident disease remains to be clarified^{1,2}.

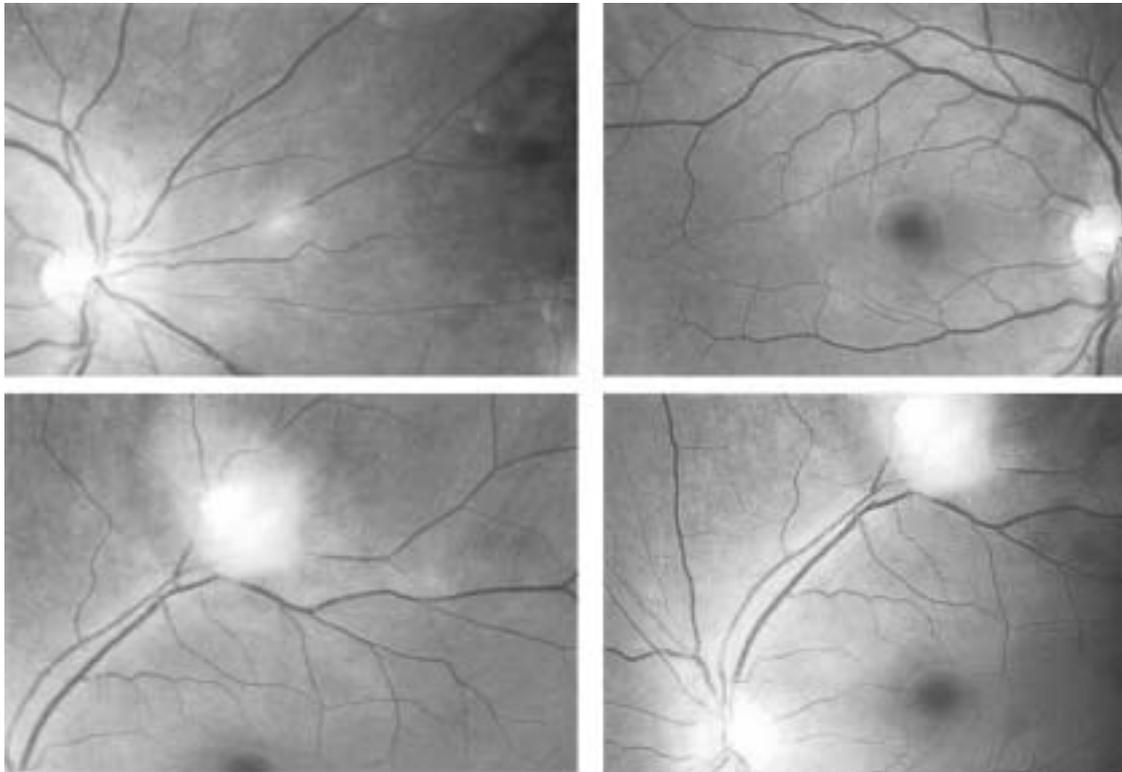


Figure 1. The retinal hamartomas observed in our patient.

The classic diagnostic triad of mental retardation, epilepsy and facial adenoma sebaceum is present in only about 30% of patients and one third of the patients have normal intelligence. Involvement of the central nervous system is very common, since mental retardation ensues in about half the patients whereas seizures occur in more than 80% of the cases. In young children they can take the form of infantile spasms and it is estimated that one third of infants with infantile spasms develop TS2.

The earliest cutaneous lesions are irregular foliate areas of depigmentation over the trunk, readily identified when viewed under ultraviolet illumination using a Woods lamp. By age four, the facial adenoma sebaceum lesions are seen in most patients and present as reddish papules 1 to 3 mm in diameter on the cheeks and around the nose. Other characteristic lesions are the so-called shagreen patches (yellowish thickening of the skin, usually seen after the first decade on the forehead or in the lumbosacral region), depigmented nevi and fibromas along side toenails or eyebrows after puberty. Other tumors include: cardiac rhabdomyomas, which may occur in about 30% of patients; renal angiomyolipomas, which may be silent or may occasionally bleed; renal cysts, which may exert pressure and cause azotemia and hypertension; brain lesions, which may become calcified and may also cause pressure effects, particularly when astrocytomas form near the foramina of Monro. In particular, the renal involvement is common, being angiomyolipomas the most frequent and usually bilateral abnormality. Renal cysts may be present as well and can give an appearance similar to that of autosomal dominant polycystic kidney disease (ADPKD). Moreover, TS may be confused with ADPKD if extrarenal manifestations are minimal².

Corticotropin and corticosteroids may be needed in the treatment of infantile spasms, and various anticonvulsivants may be required for these and other types of seizures. For rhabdomyomas of the heart, medications for dysrhythmia and for improvement of contractility may be helpful, and surgery may be indicated occasionally. Children often need special education and treatment for behavior problems. Brain tumors, status epilepticus, cardiac and renal failure should be an-

ticipated at annual reassessments and treated. Cosmetic surgery, laser therapy or dermoabrasion is available for facial and other skin lesions².

Regarding the ocular involvement, typical retinal hamartomas may be present from birth and may be separated into elevated whitish lesions resembling mulberries, near the optic disc or the retinal vessels, and flat plaques at the periphery³. Visual acuity is generally preserved.

Considering all these previously published reports, the clinical case described here represents an unusual association between ocular and systemic manifestations of BPD-TS in the absence of a clearly detected involvement of the brain. Two small retinal hamartomas, a slight facial adenoma sebaceum and renal cysts – determining hypertension – were the solely clinical features of a genetically confirmed case of BPD-TS.

Abortive forms of BPD-TS, characterized by the absence of mental retardation and epileptic seizures, have already been described in the past⁴⁻⁸. In particular, while the importance of fluorescein angiography in studying the retinal manifestations of the disease was stressed by Orzalesi and Grignolo⁵ and the possibility of false diagnoses was emphasized by Wimmer et al⁶, Ettl et al⁸, reported a case in which retinal phakomata were the solely visible manifestation of BPD.

In conclusion, given the fact that the pathognomonic clinical triad is not always present, the disease might be unrecognized or false diagnosed in some patients. Therefore, we confirm that main attention should be addressed to the search for retinal phakomata, since they may represent a typical manifestation of the disease, even in the absence of a clearly detected involvement of the central nervous system.

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