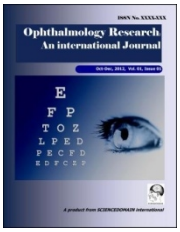

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Retinal Astrocytoma: A Supportive Finding in Tuberous Sclerosis – An Experience from Nepal

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Authors' contributions

This work was carried out in collaboration between all authors. Authors RKS and BS were involved in evaluation and management of the patients. Authors RKS, NP and JKS were involved in literature review, conception, design and preparation of manuscript draft. Author JKS critically reviewed and provided important intellectual contents. All the authors read and approved the final manuscript.

Case Study

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ABSTRACT

Aims: Tuberous sclerosis is a multiorgan tumor syndrome that is characterized by retinal astrocytic hamartomas, astrocytic tumors of the CNS, several unusual cutaneous lesions, mental retardation, spasms and a variety of cysts and tumors of other organs.
Presentation of Case: Herein we report the cases of 2 children with a history of infantile spasm with angiofibromatosis lesions over the face, multiple ash-leaf lesions over the abdomen and retinal astrocytic hamartomas in the retina.
Conclusion: It is important to be cognizant of the likely presence of systemic and ocular pathology in a child with mental retardation and skin lesions. Identification of retinal phakomatosis during ocular evaluation in any suspected case of Tuberous sclerosis can aid in the establishment of the diagnosis of the disease.

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Keywords: Astrocytoma; hamartoma; tuberous sclerosis.

1. INTRODUCTION

Tuberous sclerosis (TS) is a complex disorder characterized by a variety of hamartomas, including congenital ash-leaf macules, facial angiofibromas, subependymal nodules, cardiac rhabdomyomas, renal angiomyolipomas and retinal astrocytomas caused by mutations in either of two genes, TSC1 and TSC2.

Bourneville in 1880 was the first to identify the disease. In 1908, Vogt described the classical triad of TS having epilepsy, mental retardation and adenoma sebaceum. Later in 1920, Van der Hoeve described the retinal tumors in tuberous sclerosis [1]. Its prevalence is approximately 1:5,000 to 10, 000 [2].

Though the classical triad of TS includes infantile spasms, facial angiofibromas and developmental delay, approximately one half of all patients affected by TS develop at least one retinal astrocytoma in one eye. And 40-50% of all cases have been reported to develop multiple lesions in both eyes [3]. These astrocytomas are lesions in the retinal nerve fiber layer (RNFL), arising from undifferentiated glioneurocytes during the embryological development of the retina, especially the posterior pole, and can be of 3 morphological types [4]. Histologically, a typical retinal astrocytoma consists of a mass of interlacing spindle-shaped fibrous astrocytes that contain small bland elongated oval nuclei and have indistinct wavy cytoplasmic borders with or without foci of calcification.

Non-retinal ophthalmic findings of TS are less frequent and include angiofibromas of the eyelids, coloboma of the iris, the lens and the choroid; strabismus, poliosis of eyelashes, sectoral iris depigmentation and papilledema [4].

Usually retinal astrocytic hamartomas do not affect vision, therefore, require no treatment with the rare exception of growing lesions, where photodynamic therapy can be effective but regular examination should be done to monitor the growth [5].

Besides TS, this retinal astrocytoma can be present in neurofibromatosis and sometimes in otherwise healthy individuals. Hence an exhaustive systemic workup is essential to arrive at the diagnosis.

Herein, we report the cases of two children with infantile spasms and skin lesions whose definitive diagnosis of tuberous sclerosis was established after the identification of the concomitant presence of retinal astrocytoma.

2. PRESENTATION OF CASES

2.1 Case -1

A 14 years old boy with facial eruptions and episodic spasms was referred from the pediatric department for ocular evaluation. Inspite of his uneventful birth history, he showed signs of abnormal developmental milestones-delayed speech and walking. Due to his subnormal IQ level and poor memory, he left school.

However, he had no ocular complaints and unaided visual acuity was 20/20 in each eyes. The slit-lamp examination of the anterior segment revealed normal findings. Upon dilated fundus examination, there were yellow-white elevated intraretinal astrocytic hamartomas with a mulberry appearance in both eyes. The right eye had 4 retinal hamartomas ranging from ½ disc diameter to more than 1 disc diameter [Fig. 1a] and the left eye had a single hamartoma. All the hamartomas were calcified and vascular. The retinoscopy reading and intraocular pressure in both eyes were normal. The axial length in right eye was 23.4 mm and in left eye was 23.76 mm. B-scan showed calcified retinal astrocytomas with focal strong intralesional reflections and orbital shadowing by the mass.

Systemic evaluation revealed the presence of adenoma sebaceum on the face, sparing the eyelids [Fig. 2] and multiple hypopigmented macular ash-leaf lesions over the abdomen and shagreen patches over the lumbosacral regions [Fig. 3a]. The MRI scan of the brain revealed multiple subependymal nodules, white matter lesions and nodules at the foramen of Monro consistent with subependymal periventricular nodules [Fig. 4]. Presence of renal and cardiac cysts/tumors was ruled out by ultrasound of abdomen and echocardiography respectively.

Based on the skin lesions, intracranial manifestations and retinal astrocytomas, the final diagnosis of TS was established. We counseled the patient and his parents about the disease and advised following up regularly with the view to observing the progression or regression of the retinal astrocytoma. The dermatologist advised the patient to undergo carbon dioxide laser therapy for the facial lesions and the neurosurgeons advised for excision of astrocytic lesions at foramen of Monro only if the former produced the features of obstructive hydrocephalus.

The fundus of the patient was reevaluated at three months following the initial examination and the findings obtained were static.

2.2 Case -2

A 3 years old girl with the history of infantile spasms was referred by the pediatrician for ocular examination. Though the mother had an uneventful pregnancy, the child developed multiple episodes of tonic–clonic spasms at age 3 months. Spasms were followed by skin lesions over the face, the abdomen and the lumbosacral region. Though the facial lesions resolved over time, other lesions persisted. There was delay in the development of milestones of the child and till date the child had not been able to speak, stand and walk. The intelligence level of the child was subnormal.

On ocular examination, the visual acuity in both eyes could be only recorded as ‘fixates and follows light’ and could not be quantified. Slit lamp examination of the anterior segment revealed normal findings. Upon dilated fundus examination, the right eye was normal but the left eye had a single flat noncalcified translucent lesion, 1disc diameter in size just inferotemporal to the disc [Fig. 1b] with a smooth surface. The retinoscopy reading and intraocular pressure in both eyes were normal. B-scan ultrasonography showed ill-defined lesions having reflectivity similar to that of the normal retina. Systemic evaluation revealed the presence of ash-leaf spot over the abdomen measuring 5 x 2 cm [Fig. 3b]. The ultrasonography of the abdomen ruled out the presence of renal angiofibromatosis and echocardiography was normal. The MRI scan of the brain showed multiple subependymal nodules and white matter lesions in the brain.

Based on the ocular and systemic findings, the diagnosis of TS was established. The fundus of the patient was reevaluated at four months following the initial examination and the findings obtained were static.

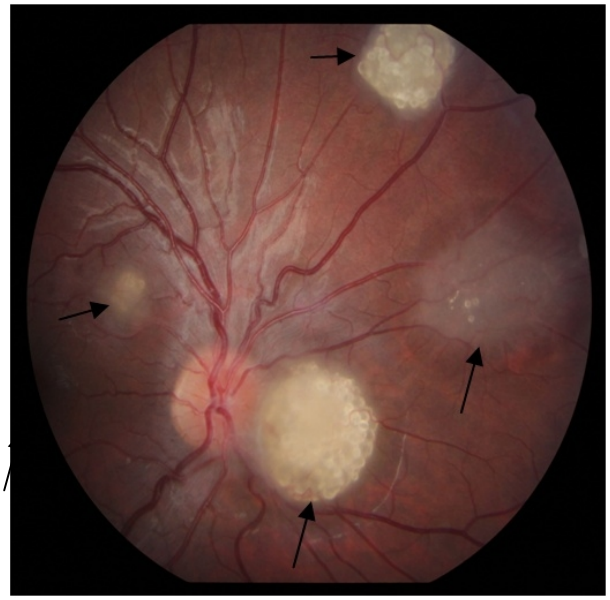

Fig. 1a. Fundus of right eye showing multiple calcified astrocytic lesions in the retina in case 1

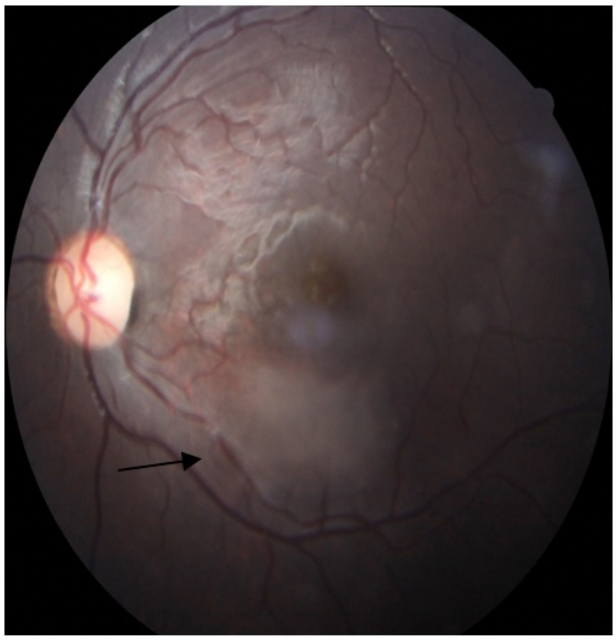

Fig. 1b. Findus of left eye showing single noncalcified astrocytic lesion in the retina in case 2

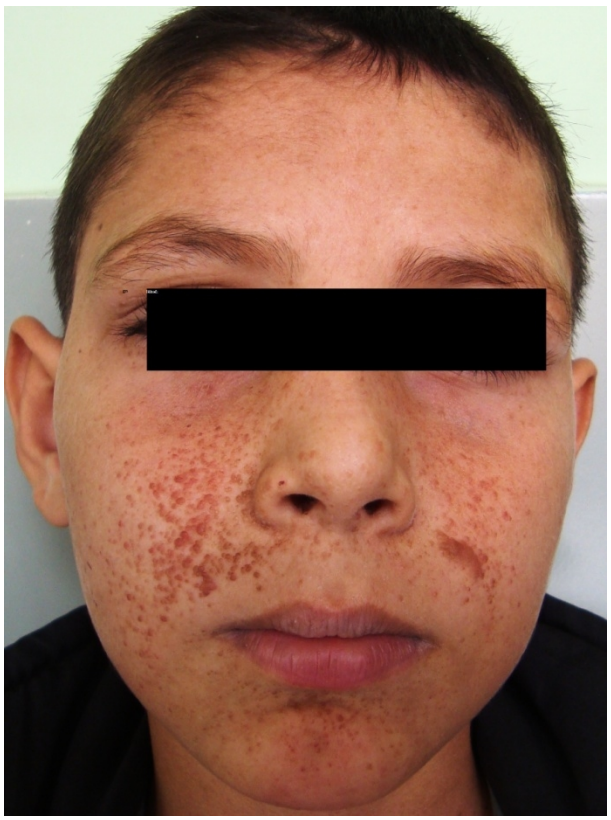

Fig. 2. Clinical photography with adenoma sebaceum over the face sparing the eyelids. (Case 1)

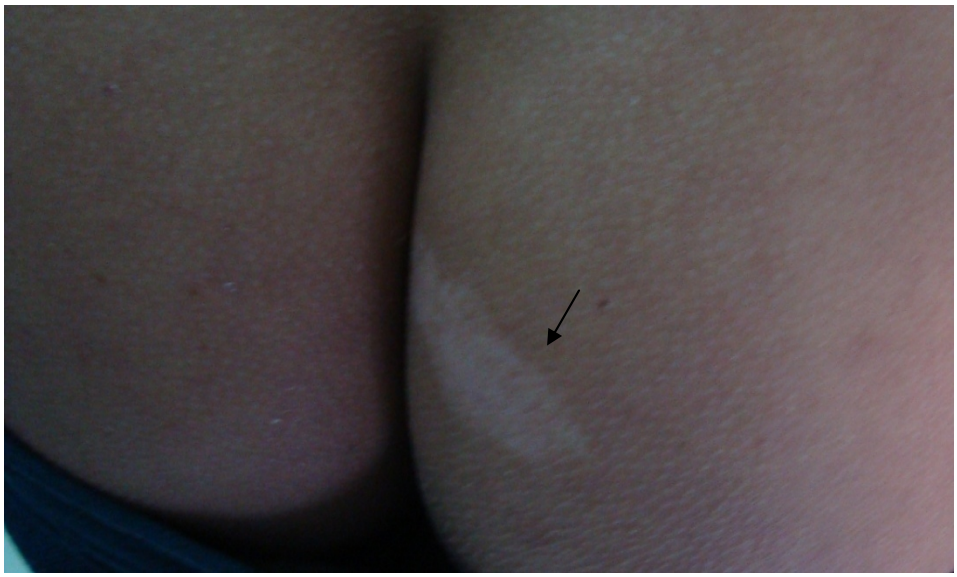

Fig. 3a. Showing shagreen patch over the lumbosacral regions in case 1

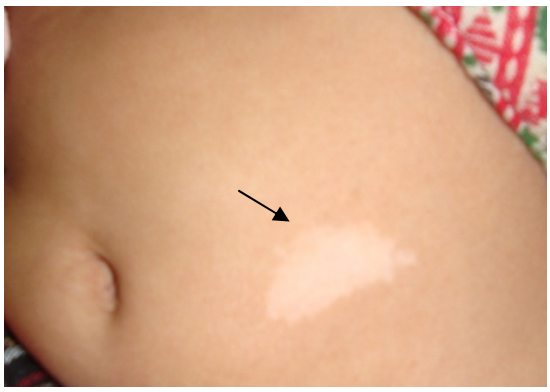

Fig. 3b. Showing ash leaf lesion over the abdomen in case 2

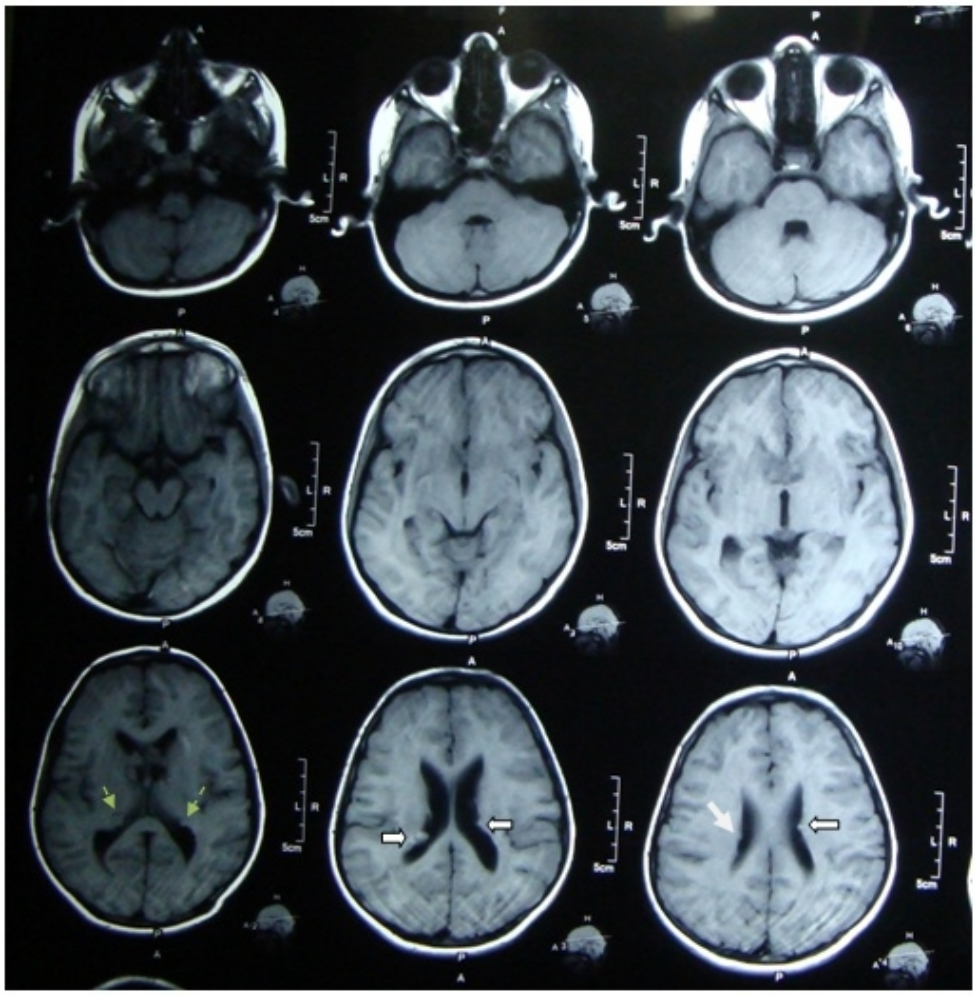

Fig. 4. The MRI scan of the brain showing multiple subependymal nodules, white matter lesions and nodules at foramen of monro. (Case 1)

3. DISCUSSION

Ocular evaluation in any child with a history of spasms and skin lesions should be carried out with meticulous care. The principal ophthalmic manifestations of TS is astrocytic hamartoma of the retina, which rarely interfere with visual function and are detected either on routine or screening fundus examinations in patients with TSC. Recognized risk factors for the development of an astrocytoma of the retina include tuberous sclerosis and possibly neurofibromatosis. But detailed systemic examination and radio imaging ruled out other differential diagnoses of retinal astrocytoma in our cases.

There is no correlation between age and the predominant type of lesion [4] and all 3 types of retinal hamartomas may be found in young children. Our cases had type 2 and type 1 retinal astrocytic lesion respectively. Most retinal lesions remain stable and change little with time. Moderate progression of retinal hamartoma from a flat to a more elevated lesion without symptomatic changes may occur. But spontaneous symptomatic progression of these lesions has also been reported [5]. The progressive growth of retinal astrocytic hamartomas may be associated with vitreous seeds, vitreous hemorrhage and exudative retinal detachment, which can simulate retinoblastoma or choroidal melanoma [6]. Reports of marked enlargement of retinal astrocytic tumors eventually causing a total retinal detachment and neovascular glaucoma that required enucleation of the affected painful blind painful eye, are found in the literature [7]. The life expectancy of individuals with TS is reduced substantially compared to the normal population [8]. Periodic ocular and physical examination and imaging of the CNS and the abdominal-thoracic viscera by CT/MRI are mandatory.

4. CONCLUSION

A greater emphasis should be placed on eye evaluation of a child with spasms and skin lesions by clinicians and parents. The presence of a retinal phakoma in the form of astrocytic hamartomas can aid in the diagnosis of the disease as it is one of the 11 major diagnostic criteria. Examination of family members to look for a familial pattern is also appropriate, for which genetic testing is of great value but nonetheless it was not possible to perform the genetic test in our patients due to its unavailability in Nepal.

Hence, TS is a multidisciplinary medical problem and the ophthalmologist may play an important role in establishing the diagnosis of such a disease where there prevails a diagnostic dilemma. Though a retinal hamartoma is a relatively stationary lesion with extremely limited malignant potential for aggressive behavior, long term observation is warranted to assess the progression thereby, preventing untoward visual loss and amblyopia in a child. In most cases, however, they are associated with normal visual acuity.

CONSENT

Consent was taken from the parents of the children for publication of the case. And approval was taken from the review board of the institute. All authors declare that ‘written informed consent was obtained from the patient and the parents for publication and accompanying images.

ETHICAL APPROVAL

Approval was obtained from the review board of our institute.

COMPLETING INTEREST

Authors have declared that no competing interests exist.

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