

1 Retinal astrocytoma: a supportive finding in Tuberous sclerosis.

2 **Ranju Kharel(Sitaula) MD^{1*}, Barsha Suwal MBBS¹, Nabin Paudel B**
3 **Optm², Jeevan Kumar Shrestha FRCOph¹.**

4
5 ¹Department of Ophthalmology, B.P.Koirala Lions Centre for Ophthalmic Studies, Institute
6 of Medicine, Tribhuvan University Teaching Hospital, Maharajgunj, Kathmandu, Nepal.

7 ²Department of Optometry and Vision Science, University of Auckland, Auckland, New
8 Zealand.

9
10
11

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, seizures and a variety of cysts and tumors of other organs.

Presentation of case: Herein we report the cases of 2 children with the history of infantile seizure with angiofibromatosis lesions over the face and multiple ash-leaf lesions over the abdomen; who had retinal astrocytic hamartomas in the fundus that aided in the diagnosis of tuberous sclerosis.

Conclusion: It is important to be cognizant of the likely presence of systemic and ocular pathology in a child of mental retardation with skin lesions. Ocular evaluation in any suspected case of Tuberous sclerosis is **essential** to detect retinal phakomatosis which **can aid** in the establishment of the disease.

12
13
14
15

Keywords: [Astrocytoma; hamartoma; tuberous sclerosis]

16 INTRODUCTION

17 Tuberous sclerosis (TS) is a complex disorder characterized by a variety of hamartomas,
18 including congenital ash-leaf macules, facial angiofibromas, intracranial paraventricular or
19 subependymal astrocytoma, cardiac rhabdomyoma, renal angiomyolipoma and retinal
20 astrocytic hamartomas.

* Tel.: 0977-9841314495(mobile), 0977-01-4486950(landline) Fax No: 0977-01-4720142

E-mail address: -helloranju50@yahoo.com, -helloranju50@gmail.com

21 Bourneville in 1880 was the first to identify the disease. In 1908, Vogt described the classic
22 triad of epilepsy, mental retardation, and adenoma sebaceum. Later in 1920, Van der Hoeve
23 described the retinal tumors of tuberous sclerosis.[1] Its prevalence is approximately
24 1:10,000 to 1:15,000.[2]

25 Though the classical triad of TS is Salaam seizures, facial angiofibromas and developmental
26 delay, approximately one half of all patients affected by TS develop at least one retinal
27 astrocytoma in one eye. And multiple lesions in both eyes occur in 40-50% of cases.[3]

28 These astrocytoma are the lesion in the retinal nerve fiber layer(RNFL) arising from
29 undifferentiated glioneurocytes during the embryological development of the retina
30 commonly in the posterior pole and can be of 3 morphological types.[4] Histologically, a
31 typical retinal astrocytoma consists of a mass of interlacing spindle-shaped fibrous
32 astrocytes that contain small bland elongated oval nuclei and have indistinct wavy
33 cytoplasmic borders with or without foci of calcification.

34 Besides TS, this retinal astrocytoma can be present in neurofibromatosis and sometimes in
35 healthy individuals too hence detailed systemic workup is essential to curtail the diagnosis.

36 Non-retinal findings of TS are less frequent and include angiofibromas of the eyelids,
37 coloboma of the iris, lens and choroid, strabismus, poliosis of eyelashes, papilloedema and
38 sectoral iris depigmentation.[5]

39 Usually astrocytic retinal hamartomas do not affect vision and require no treatment. Rarely,
40 may lead to vitreous hemorrhage and serous retinal detachment. Vitreous hemorrhage as a
41 complication of retinal hamartomas may resolve spontaneously, but pars plana vitrectomy
42 represents a successful therapeutic strategy in cases of persistent and recurrent vitreous

43 hemorrhage. The life expectancy of individuals with TS is reduced substantially compared
44 with normal population.[6]

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

48 **PRESENTATION OF CASES**

49 **Case-1**

50 A 14 years boy with facial eruptions and episodic seizures was referred from pediatric

51 department for ocular evaluation. Though he had an uneventful birth history; his

52 development of milestones was abnormal with delayed speech and walking. Due to his

53 subnormal IQ level and poor memory power, he had aborted school.

54 However he had no ocular complaints and the vision in both eyes were 20/20. The anterior

55 segment findings were normal. Upon dilated fundus evaluation, there were yellow-white

56 elevated intraretinal astrocytic hamartomas with mulberry appearance in both the eyes. The

57 right eye had 3 retinal hamartomas ranging from half disc diameter to more than one disc

58 diameter [Figure 1] and the left eye had single hamartoma. All the hamartomas were

59 calcified and vascular. The retinoscopy reading and intraocular pressures in both the eyes

60 was normal. The axial length in right eye was 23.4mm and in left eye was 23.76mm. B scan

61 showed calcified retinal astrocytomas with focal strong intralesional reflections and orbital

62 shadowing by the mass.

63 Systemic evaluation revealed the presence of adenoma sebaceum in face sparing the

64 eyelids [Figure 2], multiple hypo pigmented macular ash-leaf lesions over the abdomen and

65 shagreen patches over the lumbosacral regions [Figure 3]. The brain MRI revealed multiple
66 subependymal nodules, white matter lesions and **nodules** in foramen of monro probably
67 **subependymal periventricular nodules** [Figure 4]. Presence of renal and cardiac
68 cysts/tumors was ruled out by ultrasound of abdomen and echocardiography respectively.
69 Based on the skin lesions, intracranial manifestations and retinal astrocytic hamartomas, the
70 final diagnosis of TS was established. We counseled the patient and his parents about the
71 disease and advised for regular follow to observe the progression or regression of the retinal
72 astrocytoma. The dermatologist advised the patient to undergo carbon dioxide laser therapy
73 for the facial lesions and the neurosurgeons advised for excision of astrocytic lesion over
74 foramen of monro only if it produced the features of obstructive hydrocephalus.
75 The fundus of the patient was reevaluated after 3 months and the findings were static.

76 **Case -2**

77 A 3 years female with the history of infantile seizure was referred by the pediatrician for
78 ocular examination. The mother had uneventful pregnancy but the child developed multiple
79 episodes of tonic –clonic seizures from 3 months of age which was followed by skin lesions
80 over the face and abdomen and lumbosacral region. Though the facial lesions resolved over
81 time, other lesions persisted. There was delay in development of milestones of the child and
82 till the date the child was unable to speak, stand and walk. The intelligence level of the child
83 was subnormal.
84 On ocular examination, the visual acuity could not be recorded but the child could follow and
85 fixate the light. The anterior segment findings were normal. Upon dilated fundus
86 examination, the right eye was normal but the left eye had a single flat **noncalcified,**

87 translucent lesion of 1disc diameter just inferio-temporal to the disc [Figure 5] with smooth
88 surface. The retinoscopic reading was grossly normal. B-scan ultrasonography showed ill-
89 defined lesions having reflectivity similar to that of normal retina. Systemic evaluation
90 revealed the presence of ash leaf spot over the abdomen of 5 x 2cm [Figure 6]. The
91 ultrasonography of abdomen ruled out the presence of renal angiofibromatosis. The MRI
92 brain showed multiple subependymal nodules and white matter lesions in the brain. No facial
93 lesions were present at the time of ocular evaluation. The child was under treatment of
94 clonazepam 0.5mg daily regularly.

95 Only after the ocular evaluation the diagnosis of tuberous sclerosis was confirmed. We
96 advised the parents for regular follow up to evaluate the progression or regression of the
97 retinal phakoma and the lesion was found to be static in size and appearance after 4 months
98 of follow up.

99 **DISCUSSION**

100 Ocular evaluation in any child with the history of seizure and skin lesions should be paid
101 attention. The principle ophthalmic manifestations of TS are astrocytic hamartoma of the
102 retina, which rarely interfere with visual functions. Recognized risk factors for development of
103 an astrocytoma of the retina include tuberous sclerosis and possibly neurofibromatosis. But
104 detailed systemic examination and radio imaging ruled out other differential diagnosis of
105 retinal astrocytoma in our cases.

106 As retina and the optic nerve are derived from the central nervous system; intracranial
107 paraventricular or subependymal astrocytoma may be associated with retinal astrocytoma.

108 There is no correlation between age and the predominant type of lesion [4] and all three
109 types of retinal hamartomas may be found in young children. Our cases had type 2 and type
110 1 retinal astrocytic lesion respectively. Most retinal lesions remain stable and change little
111 with time. Spontaneous symptomatic progression of these lesions have been reported in 11
112 cases in the world literature.[7] In rare instances, the retinal astrocytic hamartoma can show
113 progressive growth and cause severe local complications. Moderate progression of retinal
114 hamartoma from a flat to a more elevated lesion without symptomatic changes may occur.
115 Marked enlargement of retinal astrocytic tumors eventually causing total retinal detachment
116 and neovascular glaucoma that required enucleation of the affected blind painful eye have
117 also been reported in the literature.[8]

118 **CONCLUSION**

119 Emphasis on eye evaluation should be given by the clinicians and parents in a child of seizure
120 and skin lesions. The presence of retinal phakoma in form of astrocytic hamartomas can aid
121 in the diagnosis of the disease as it is one of the 11 major diagnostic criterias. Examination
122 of family members to look for a familial pattern is also appropriate for which genetic testing is
123 of great value but it was not possible to perform genetic studies in our patients due to
124 unavailability in Nepal.

125 Hence TS is a multidisciplinary medical problem and ophthalmologist may play an important
126 role in establishing such disease where there is the diagnostic dilemma. Though retinal
127 hamartoma is a relatively stationary lesion with extremely limited malignant potential for
128 aggressive behavior but long term observation is warranted to assess the progression

129 thereby preventing untoward visual loss and amblyopia in a child. In most cases, however,
130 they are associated with normal visual acuity.

131 **COMPLETING INTEREST:** Authors have declared that no competing interests exist.

132 **AUTHORS' CONTRIBUTION:** RKS and BS were involved in evaluation and
133 management of the patients. RKS, NP and JKS were involved in literature review,
134 conception, design and preparation of manuscript draft. JKS critically reviewed and provided
135 important intellectual contents. All the authors read and approved the final manuscript.

136 **CONSENT:** Consent was taken from the parents of the children for publication of the case.

137 And approval was taken from the review board of the institute. All authors declare that
138 written informed consent was obtained from the patient and the parents for publication and
139 accompanying images.

140 **ETHICAL APPROVAL:** Approval was obtained from the review board of our institute.

141
142 **REFERENCES**

- 143 1. David Sami, Anthony Vivian, David Taylor and Dawn Saunders. The
144 Phakomatoses. Duane's Ophthalmology CD-ROM 2006; Volume 5, Chapter
145 36.
- 146 2. Hunt A, Lindenbaum RH: Tuberous sclerosis: a new estimate of prevalence
147 within the Oxford region. J Med Genet. 1984; 21:272.
- 148 3. Roach ES, Smith M, Huttenlocher P et al. Diagnostic criteria: tuberous
149 sclerosis complex. Report of the Diagnostic Criteria Committee of the
150 National Tuberous Sclerosis Association. J Child Neurol. 1992; 7:221-34.

- 151 4. Rowley SA, O'Callaghan FJ, Osborne JP: Ophthalmic manifestations of
152 tuberous sclerosis: a population based study. Br J Ophthalmol. 2001;
153 85:420.
- 154 5. S A Rowleya, F J O'Callaghanb, J P Osborneb. Ophthalmic manifestations
155 of tuberous sclerosis: a population based study. Br J Ophthalmol. 2001;
156 85:420-423.
- 157 6. Sherpherd CW,Gomez MR,Lie JT,Crowson CS. Causes of death in patients
158 with tuberous sclerosis. Mayo Clin Proc.1991;66:792-6.
- 159 7. Stefan Mennel, Carsten H. Meyer, Silvia Peter,Jorg C. Schmidt and Peter
160 Kroll .Current treatment modalities for exudative retinal hamartomas se
161 condary to tuberous sclerosis: review of the literature. Acta Ophthalmol.
162 Scand. 2007: 85: 127–132.
- 163 8. Jerry A. Shields, Ralph C. Eagle, Jr,Carol L. Shields,Brian P. Marr.
164 Aggressive Retinal Astrocytomas in 4 Patients With Tuberous Sclerosis
165 Complex. Arch Ophthalmol. 2005; 123:856-862.

166 **LEGENDS**
167
168



169

170

171

Fig. 1. Fundus of right eye showing multiple astrocytic lesions of various sizes in the retina. (Case 1)

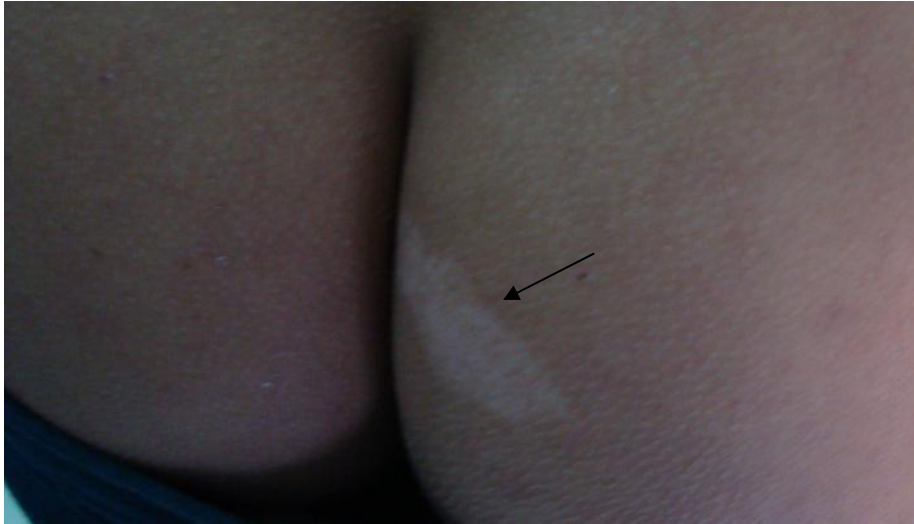


172

173

174

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



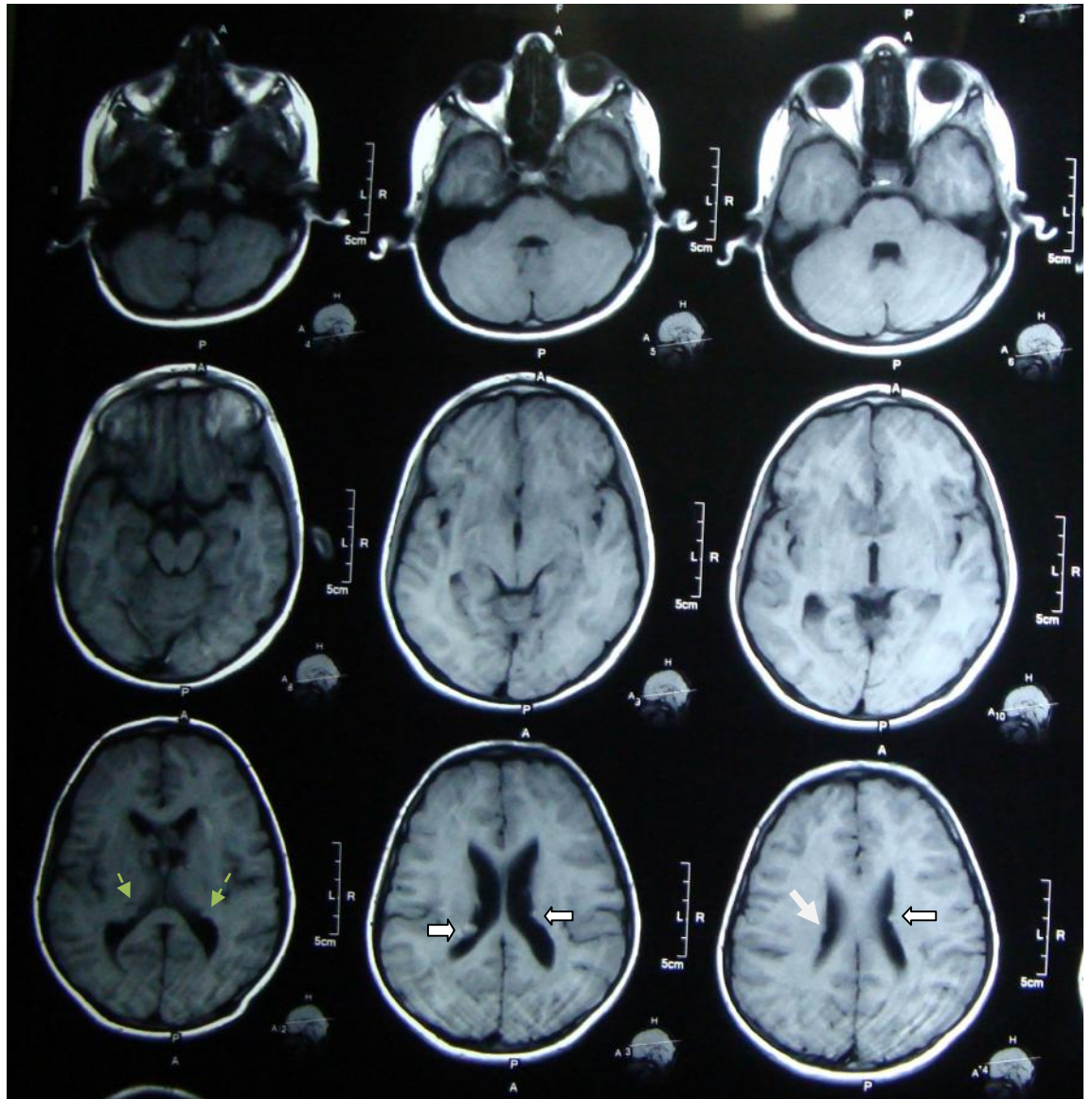
175

176

177

178

Fig. 3. Hypo pigmented macular ash-leaf lesions and shagreen patches over the lumbosacral regions. (Case 1)



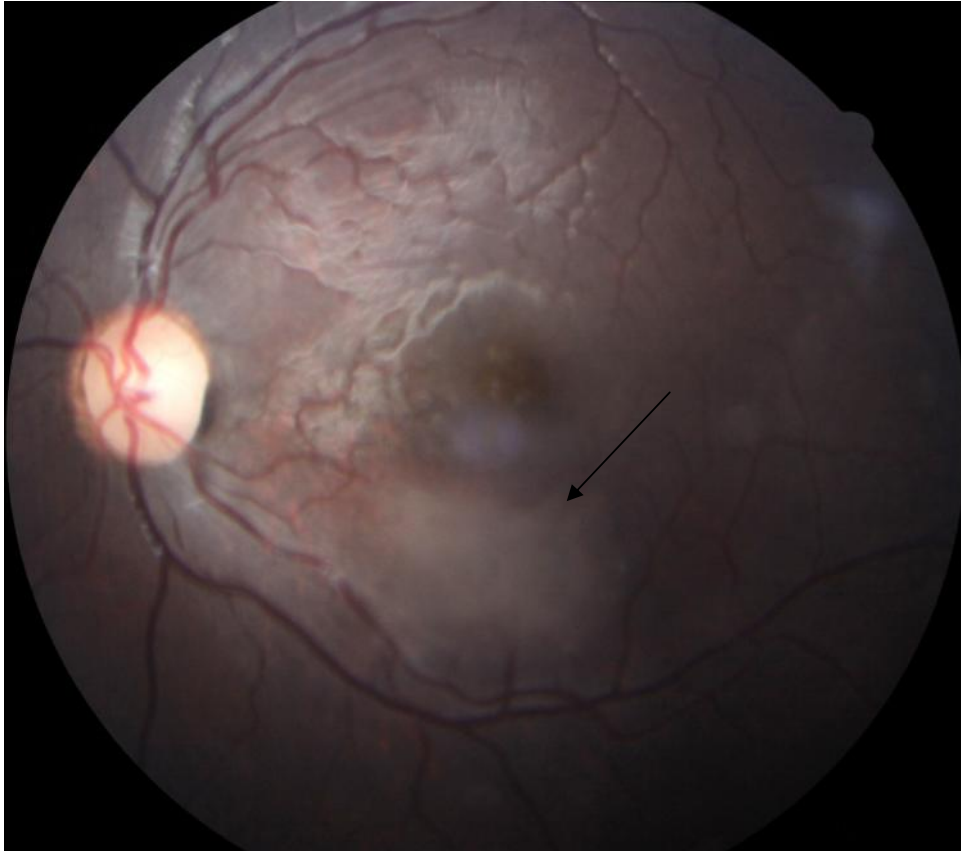
179

180 **Fig. 4. The MRI of the brain showing multiple subependymal nodules, white matter**

181 **lesions and nodules in foramen of monro. (Case 1)**

182

183



184

185 **Fig. 5. Fundus of left eye with a single flat, translucent, smooth lesion just inferior**
186 **and temporal to the disc of 1disc diameter. (Case 2)**

187



188

Fig. 6. Ash leaf spot over the abdomen (Case 2)

189
190
191