

Case study**Retinal astrocytoma: a supportive finding in Tuberous sclerosis.**

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ABSTRACT

Aim- 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 guided to the supportive 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 worthful to rule out retinal phakomatosis which aids in the establishment of the disease.

33 **Keywords-**Astrocytoma; hamartoma; tuberous sclerosis.

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35 INTRODUCTION

36 Tuberous sclerosis(TS) is a complex disorder characterized by a variety of
37 hamartias and hamartomas, including congenital ash-leaf macules, facial
38 angiofibromas,intracranial paraventricular or subependymal astrocytomas, cardiac
39 rhabdomyoma, renal angiomyolipoma and retinal astrocytic hamartomas.

40 In 1880, Bourneville, described the autopsy findings in a girl with the triad of
41 mental retardation, seizures, and vesiculopapular rash on the face. In 1908, Vogt
42 described the classic triad of epilepsy, mental retardation, and adenoma sebaceum;
43 later Van der Hoeve in 1920 described the retinal tumors of tuberous sclerosis.¹

44 Tuberous sclerosis is autosomal dominant with 65% to 75% of new cases
45 representing spontaneous mutations.² Its prevalence is approximately 1:10,000 to
46 1:15,000.³

47 Though the classical triad of TS is Salaam seizures, facial angiofibroma and
48 developmental delay, approximately one half of all patients affected by TS develop
49 at least one retinal astrocytoma in one eye. And multiple lesions in both eyes occur
50 in 40-50% of cases.⁴ These hamartomas are the lesion in the retinal nerve fiber
51 layer(RNFL) arising from undifferentiated glioneurocytes during the
52 embryological development of the retina commonly in the posterior pole and can
53 be of following morphological types⁵

Type 1. Is the most common type, relatively flat, smooth-surfaced, and translucent lesions.

Type 2. Raised, calcified, mulberry-like tumors, 80% within 2 disc diameters of the optic nerve.

Type 3. The least common, intermediate type shows features of types 1 and 2.

54 Non-retinal findings of TS are less frequent and include angiofibromas of the
55 eyelids, coloboma of the iris, lens and choroid, strabismus, poliosis of eyelashes,
56 papilloedema and sectoral iris depigmentation.⁶

57 Astrocytic retinal hamartomas usually do not affect vision and require no
58 treatment. Vitreous seeding ,vitreous hemorrhage and serous retinal detachment
59 have been reported in association with phakomata, but these are rare. Vitreous
60 haemorrhage as a complication of retinal hamartoma may resolve spontaneously,
61 but pars plana vitrectomy represents a successful therapeutic strategy in cases of
62 persistent and recurrent vitreous haemorrhage.

63 Treatment of the affected individuals is purely symptomatic.Periodic physical
64 examination and imaging of CNS and abdominal-thoracic viscera by CT/MRI are
65 mandatory.

66 The life expectancy of individuals with TS is reduced substantially compared with
67 normal population.⁷ The common causes of early death is renal failure secondary
68 to angiomyolipomas,obstructive hydrocephalus due to Central nervous system

69 astrocytomas and status epilepticus. Herein we report the cases of two children
70 with infantile seizure and skin lesions whose definitive diagnosis of tuberous
71 sclerosis was established only after the identification of concomitant presence of
72 retinal astrocytoma in the fundus.

73 **PRESENTATION OF CASES**

74 **Case-1**

75 A 14 years old boy who was suspected as a case of Tuberous sclerosis was referred
76 to the eye OPD from the dermatology department for ocular evaluation in
77 November 2011 where he had presented with the complaint of eruption over the
78 face and body since past 9 years associated with episodes of seizures on and off.
79 Based on the clinical features and supporting investigation reports he was
80 suspected as a case of Tuberous sclerosis.

81 Though he had an uneventful birth history; the development of milestones were
82 abnormal with delayed speaking and walking. He had poor memory power so his

83 performance in the school was not good for which he had aborted school. The
84 family history was negative.

85 However he had no ocular complaints. On examination, the vision in both eyes
86 were 20/20. The anterior segment findings were normal. Upon fundus examination
87 under mydriasis, there were yellow-white elevated intraretinal astrocytic
88 hamartomas with mulberry appearance in both the eyes. In the right fundus, the
89 hamartomas were three in number ranging from half disc diameter to more than
90 one disc diameter (Figure-1). And in the left eye, the hamartoma was single in
91 number. The tumor was relatively vascular. The intraocular pressure in both the
92 eyes were 16mmHg. The axial length in right eye was 23.4mm and in left eye was
93 23.76mm. The retinoscopy reading was normal.

94 On systemic evaluation, adenoma sebaceum was present in face sparing the
95 eyelids (Figure-2). Multiple hypopigmented macular ash-leaf lesions over the
96 abdomen and shagreen patches over the lumbosacral regions were present (Figure-
97 3). Renal and cardiac cysts and tumors were ruled out by ultrasound of abdomen

98 and echocardiography respectively. The MRI of the brain revealed multiple
99 subependymal nodules, white matter lesions and lesion in foramen of monro
100 probably subependymal giant cell astrocytoma (Figure-4).

101 On the basis of skin lesions, intracranial manifestations and retinal astrocytic
102 hamartomas, the diagnosis of TS was established. The patient was advised for
103 carbondioxide laser therapy for the facial lesions and neurosurgeons had advised
104 for excision of astrocytic lesion over foramen of monro only if it produced the
105 features of obstructive hydrocephalus. The family members were also advised for
106 systemic workup but no similar problem was revealed in the family.

107 From the ophthalmology point of view, the patient and the parents were counselled
108 about the disease and was advised for regular follow to observe the progression or
109 regression of the retinal astrocytoma.

110 The fundus of the patient was reevaluated after 3 months and the findings were
111 static.

112 **Case -2**

113 A 3 years female was referred to the eye OPD on February 2012 by the
114 pediatrician to rule any ocular involvement in a case of infantile seizure suspected
115 of tuberous sclerosis.

116 The parents gave the history of normal prepartum and intrapartum period but the
117 child had multiple episodes of tonic –clonic seizures since the age of 3
118 months. This was followed by skin lesions over the face and abdomen, the facial
119 lesions resolved over time but the lesions in the abdomen and lumbosacral region
120 persisted. There was delay in development of milestones of the child and till the
121 date the child was unable to speak, respond, stand and walk. The family history was
122 negative.

123 On examination of eyes, the visual acuity could not be recorded but the child could
124 follow and fixate the light. The anterior segment findings were normal. Upon
125 examination of dilated fundus, the right eye was normal but in the left eye there was
126 a single relatively flat, smooth surface almost translucent lesion just inferior and

127 temporal to the disc of 1disc diameter (Figure-5).No facial lesions were present at
128 the time of ocular evaluation.

129 The retinoscopic reading was grossly normal.On systemic evaluation,the
130 intelligence level of the child was subnormal associated with hemiparesis of left
131 upper and lower limbs. There were few ash leaf spots over the abdomen and back
132 of around 5 x 2cm size(Figure-6).The ultrasonography of addomen ruled out the
133 presence of renal angiofibromatosis.The MRI brain showed multiple
134 subependymal nodules and white matter lesions inthe brain and the probable
135 radiological diagnosis was tuberous sclerosis. The child was under clonazepam
136 0.5mg daily regularly.

137 Only after the ocular evaluation the diagnosis of tuberous sclerosis was confirmed.
138 We advised the parents for regular follow up to evaluate the progression or
139 regression of the retinal phakoma.

140 **DISCUSSION**

141 Any child with the history of seizure and skin lesions should be paid attention for
142 the ocular evaluation. The principle ophthalmic manifestations of TS is
143 hamartoma of the retina, which rarely interfere with visual functions. From
144 embryological point of view the retina and the optic nerve are derivatives from the
145 central nervous system. Therefore it seems logical that alteration in the retina and
146 the optic nerve may involve the optic chiasm in the embryonic terminal lamina,
147 and that agreement exist between the severe ocular involvements and the
148 midcranial morphology.

149 Though type 2 and type 1 retinal astrocytic lesions were present in our two cases
150 respectively, all three types of retinal hamartomas may be found in young children.
151 There is no correlation between age and the predominant type of lesion.⁵

152 Most retinal lesions remain stable and change little with time. Spontaneous
153 symptomatic progression of these lesions is reported in 11 cases in the world
154 literature.⁸ In rare instances, the retinal astrocytic hamartoma can show progressive
155 growth and cause severe local complications. Moderate progression of retinal

156 hamartoma from a flat to a more elevated lesion without symptomatic changes may
157 occur. Marked enlargement of retinal astrocytic tumors eventually causing total
158 retinal detachment and neovascular glaucoma that required enucleation of the
159 affected blind painful eye have also been reported in the literature.⁹

160 **CONCLUSION**

161 Emphasis should be given by the clinicians and parents in a child of seizure with
162 skin lesions. The presence of retinal phakomas in form of astrocytic hamartomas
163 can aid in the diagnosis of the disease. Examination of family members to look for
164 a familial pattern is also appropriate for which genetic testing is of great value but
165 it was not possible to perform genetic studies in our patients due to unavailability
166 in Nepal.

167 Hence TS is a multidisciplinary medical problem and ophthalmologist may play an
168 important role in establishing such disease where there is the diagnostic dilemma.
169 Though retinal hamartoma is a relatively stationary lesion with little potential for

170 aggressive behavior but long term observation is warranted to assess the
171 progression thereby preventing untoward visual loss and amblyopia in a child.

172 **Completing Interest:** None

173 **Authors' Contribution:**

174 RKS and BS were involved in evaluation and management of the patients. RKS,
175 NP and JKS were involved in literature review, conception, design and preparation
176 of manuscript draft. JKS critically reviewed and provided important intellectual
177 contents.

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206 **LEGENDS**

207 **FIGURE 1-** Fundus of right eye showing multiple astrocytic lesions of

208 various sizes in the retina. (Case 1)



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



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FIGURE 3- Hypopigmented macular ash-leaf lesions and shagreen patches over the lumbosacral regions. (Case 1)



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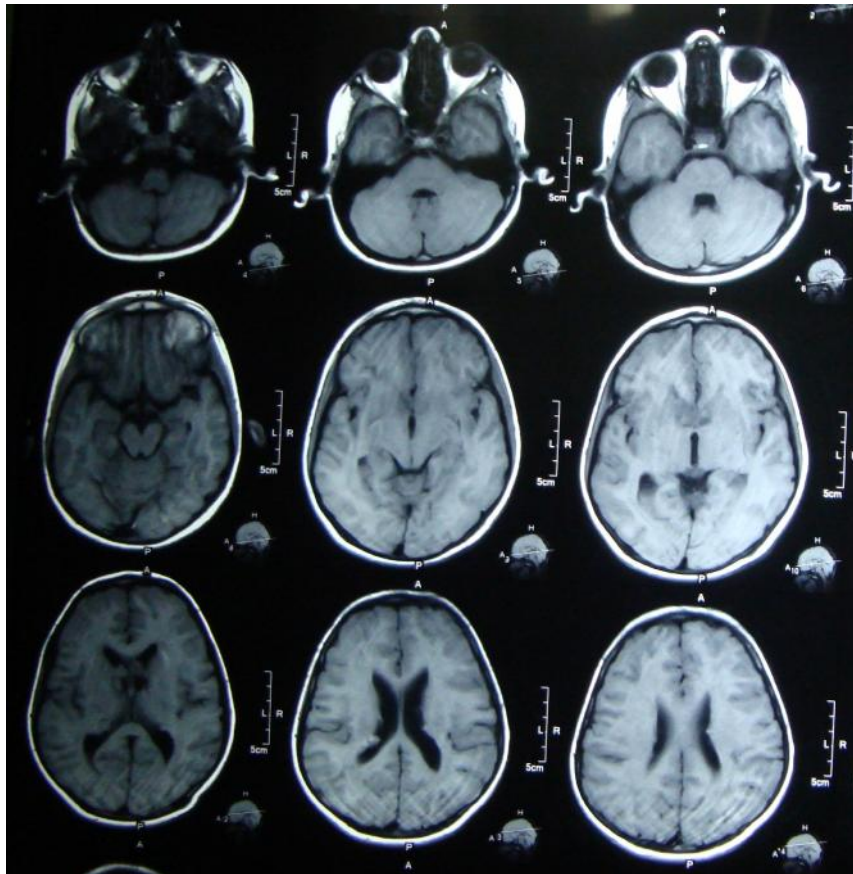
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FIGURE 4- The MRI of the brain showing multiple subependymal nodules, white matter lesions and lesion in foramen of monro probably subependymal giant cell astrocytoma. (Case 1)

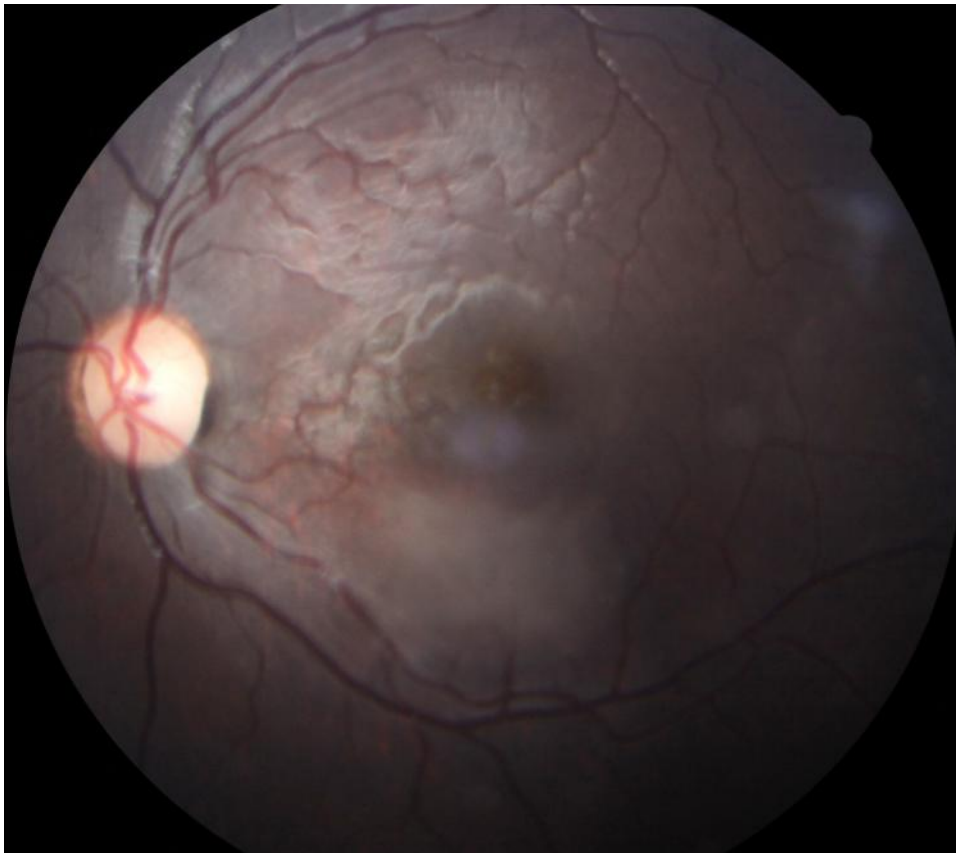


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223 **FIGURE 5-** Fundus of left eye with a single flat,translucent,smooth lesion just

224 inferior and temporal to the disc of 1disc diameter.(Case 2)



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227 **FIGURE 6-** Ash leaf spots over the abdomen (Case 2)



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