TUBEROUS SCLEROSIS

S G S Krishnan, P Devakar Yesudian, M Jayaraman, V R Janaki, J M Boopal Raj

Although tuberous sclerosis has been described with a diagnostic triad, it is not present consistently in all cases. Variety of skin manifestations were reported in tuberous sclerosis. This studay was undertaken to assess the frequency of various skin changes in tuberous sclerosis. Ten consecutive cases of tuberous sclerosis were studied. Angiofibroma was the commonest cutaneous manifestation. Atypical fibroxanthoma, dermatofibroma and neurofibroma were also noticed as interesting associations.

Key Words : Epiloia, Adenoma sebaceum

Introduction

Tuberous sclerosis is a complex genetic disorder first recognised as a specific disease early in the 19th century. Even though Rayer was the first to describe the condition, it was Bournville who classified it as a distinct entity. Later Sherlock coined the word 'epiloia' to indicate the diagnostic triad of epilepsy, low intelligence and adenoma sebaceum.[1]

Although a diagnostic triad has been described, it is not consistently present in all cases. The pleotropic variation of a single genetic aberration gives rise to a variety of manifestations. Many cutaneous features have been elaborated in the description of the disease including classical adenoma sebaceum, shagreen patches, white leafy macules and periungual plaques. Other cutaneous manifestations include fibromatous plaques, pedunculated fibromas and poliosis.[2]

Materials and Methods

Ten cases of tuberous sclerosis who presented themselves to the Dermatology OPD over a period of one and a half years were screened for the presence of angiofibromas, shagreen patches, ash white macules and Koenen's tumours. All cases were biopsied to confirm the diagnosis of angiofibroma. Patients were also examined for other cutaneous manifestations and when present were biopsied and subjected to histopathological examination. Diagnosis of tuberous sclerosis was made on the presence of adenoma sebaceum, epilepsy and low intelligence. Out of the 10 patients, 9 were males and one was a female. The findings are listed in Table I.

From the Department of Dermatology, Madras Medical College and Government General Hospital, Madras, India.

Address correspondence to : Dr M Jayaraman 222 R K Mutt Road, Mylapore, Madras-600004.

Results

In our series all cases had angiofibromata. Among them 3 developed the lesions after the age of 15 years. Five patients had white leafy macules. When present they occurred from birth. Eight patients had shagreen plaques distributed over the trunk. Koenen's tumours were present in 3 cases. In all these patients, the tumours appeared at puberty. Associated epidermal naevi were present in 3 of the patients.

One elderly patient had a firm globular swelling on the anterior aspect of the neck of 6 months duration which was excised. On histopathological examination it was found that the tumour was composed of large fibroblastic and histocytic cells, some of which were atypical multinucleate giant cells, lymphocytes and ectatic vascular spaces. Cells were arranged in a haphazard fashion and few

Table I. Clinical findings of the patients

Case no.	1	2	3	4	5	6	7	8	9	10	%
Adenoma sebaceum	+	+	+	+	+	+	+	+	+	+	100
Shagreen plaque	+	+	+	+	-	+	+	+	-	+	80
White leafy macule	+	+	+	-	-	+	+	-	-	+	50
Koenen's tumours	-	+	-	-	-	+	+	-	-	-	30
Associated features	Epidermal naevi	None	None	None	Epidermal naevi	Amyloid Atypical fibroxanthoma	Epidermal naevi	Tumor of maxilla and gums Mucosal polyp right maxilla		Neurofibroma	
Special characteristics				Late onset angiofibroma (15-16 years)	Only angiofibroma	Associated with a rare tumour	Late onset angiofibroma	Late onset angiofibroma	Only angiofibroma	Left facial hemiatrophy	

mitotic figures were present giving the picture of atypical fibroxanthoma. Patient also had a few papular lesions in the infraclavicular area which on biopsy showed evidence of cutaneous amyloidosis.

One adolescent male patient had a rapidly growing tumour of the gums which extended to the maxilla and eroded the maxillary bone. On biopsy it proved to be a histiocytoma. Another 9-year-old boy had left sided facial hemiatrophy and a plexiform neurofibroma over the occiput.

Discussion

Angiofibromata were the commonest cutaneous manifestation seen in 100% of our cases. They commonly appear in early childhood from 2-8 years of age and are seen in 80-90% of the cases.[3] Three of our patients developed these lesions only after 15 years of age.

Ashy leafy macules seen in 85% of patients usually manifest from birth and thus are the earliest cutaneous manifestation.[4] In our series, 50% of cases showed these macules from birth. Shagreen plaques first described by Hallopeau were reported to be present in 20-50% of cases of tuberous sclerosis.[5] But 80% of our patients had this feature. Koenen's tumours seen in 3 patients appeared at puberly.[3]

The associations with neurofibroma[6] and epidermal naevi also show the not too infrequent overlap of tuberous sclerosis with other neurocutaneous syndromes and have been reported.

The occurrence of atypical fibroxanthoma has not been reported in tuberous sclerosis earlier. This is a potentially malignant tumour of low grade malignancy usually seen over exposed areas and areas of radiodermatitis. It may occur as nodules or plaques and has a red fleshy granulomatous appearance.[7] Histologically they are related to

malignant fibrous hisiocytoma.

Dermatofibroma occurring in the alveolar margins has been reported.[8] However the reapidly expanding erosive nature of the lesion gives it a character of low grade fibrosarcoma as in our case. Therefore early intervention is recommended in these lesions with rapid growth however benign they appear histopathologically.

None of our patients had poliosis, cafe-au-lait spots, multiple skin tags over the neck and shoulders, multiple acquired naevi or confetti skin lesions.

This case series shows that due to pleotropism of any genetic disorder, there can be a whole spectrum of changes in the skin. It reveals that not all components of a syndrome need to be present in any given patient.

Finally and most importantly it emphasizes the need for careful observation and follow up in every one of these cases due to the increased incidence of various cutaneous tumours. Shelly called it a playground of tumours and there wouldn't be more apt a description of this fascinating disorder.

References

1. Morgan JE, Wolfort F. The early history of tuberous sclerosis. Arch Dermatol 1979; 115: 1317-9.
2. Harper J. Genetics and genodermatoses. In: Champion RH, Burton JL, Ebling FJG, eds. Texbook of dermatology. Oxford : Blackwell, 1992: 327-8.
3. Monaghan HP, Krafchik BR, MacGregor DL, et al. Tuberous sclerosis complex in children. Am J Dis Child 1981; 135: 912-7. As quoted in Dermatology clinics. Alpher JC, ed. Genodermatoses. Philadelphia : WB Saunders, 1987; Vol 5: 205.
4. Fitzpatrick TB, Szabo G, Hori Y, et al. White leaf shaped macules. Earliest visible sign of tuberous sclerosis. Arch Dermatol 1968; 98: 1-6.
5. Cassidy SB. Tuberous sclerosis in children: Diagnosis and course. Comp Ther 1984; 10: 43-51. As quoted in Dermatology clinics. Alpher JC, ed. Genodermatoses. Philadelphia: WB Saunders, 1987; Vol 5: 205.
6. Charles M, Phillips, Rye B. Neurofibromatosis type I and tuberous sclerosis. A case of a double phakomatosis. J Am Acad Dermatol 1994; 31: 799-800.
7. Mackie RM. Soft tissue tumors. In: Champion RM, Burton JL, Ebling FJG, eds. Textbook of dermatology. Oxford : Blackwell, 1992: 2080-81.
8. Papanayotou P, Vezitzi E. Tuberous sclerosis with gingival lesions. Oral Surg 1975; 39: 578.