Cardiac involvement (Wolff–Parkinson–White syndrome) in tuberous sclerosis

Olajide Ijaola, L.C. Festus-Abibo, Olu Lawani and Sonny F. Kuku

Cardiology Department, King’s College Hospital, London SE5 9RS, UK and The EKO Hospital, Lagos, Nigeria

Summary: A surface electrocardiogram showing type B Wolff–Parkinson–White syndrome pattern was part of the cardiac findings in a female of 24 with florid features of tuberous sclerosis. She had cardiomegaly but no intracardiac tumour was demonstrated. Wolff–Parkinson–White syndrome, though rare, has previously been described in association with tuberous sclerosis in children but not before in adults.

Introduction

Tuberous sclerosis is a congenital autosomal dominant inherited disease with incomplete penetrance and variable expressivity. About 60% of cases occur by new mutation. Most patients appear normal at birth but later develop variable clinical features of the disease such as facial adenoma sebaceum, other skin tumours, subungual fibromas, and various affectations of the brain, eyes, lungs, heart, liver, kidneys, adrenals, pancreas and bones. Rhabdomyoma is the cardinal cardiac lesion found. This may produce symptoms by valvular or intracardiac obstructions or congestive cardiac failure because of infiltration by non-contractile tumour tissues. Various types of dysrrhythmias have previously been reported including atrial and ventricular tachycardia, junctional ectopic beats and various degrees of atrioventricular or His bundle branch blocks. Wolff–Parkinson–White syndrome is rare but has been described in children with tuberous sclerosis. We present a case of tuberous sclerosis in a 24 year old female in whom the electrocardiogram showed the pattern of type B Wolff–Parkinson–White syndrome.

Case report

The patient, aged 24, presented with dragging abdominal mass, palpitations and typical cutaneous features of tuberous sclerosis. There was no history of frank haematuria. Her illness dated back to infancy when facial tumours and skin nodules were first noticed. She subsequently developed subungual fibromas which tended to recur after repeated ablations. Two months before presenta-

Correspondence: O. Ijaola, M.B., F.M.C.P. Accepted: 28 July 1993

Figure 1 Facial nodular rashes (adenoma sebaceum) of tuberous sclerosis in a 24 year old patient.
tion she experienced progressive weakness, exertional shortness of breath and palpitations. There was no cough or pedal oedema. About the time of presentation, she became profoundly paranoid, believing that she was bewitched by her father and sister, who is also psychotic. She subsequently became psychotic herself, requiring institutionalized care and treatment with chlorpromazine and benzhexol. There was no history of any other prior drug ingestion.

Her mother died at age 30 years. Her twin sister died in infancy. An older sister and a brother are alive. The sister has schizophrenic psychosis but no other evidence of tuberous sclerosis. The brother is normal. All five siblings (three girls and two boys) by a stepmother are normal.

Clinical and ultrasound examinations of all members of the family, including her psychotic sister, did not reveal any lesion of tuberous sclerosis except the father who has few facial nodules but surprisingly gross scrotal skin tumours. Hypomelanotic spots were, however, not elicited either in him or any other member of the family. None of them gave a history of palpitations and their electrocardiograms were normal, including that of the psychotic sister.

On examination our patient had florid skin lesions of tuberous sclerosis including widespread hypomelanotic macules, adenoma sebaceum, and nodular skin and nail tumours (Figures 1 and 2). She was not in heart failure. She was in sinus rhythm but had frequent ventricular ectopic beats. The arterial blood pressure was normal. There was moderate cardiomegaly but no sustained left ventricular heave. The heart sounds were normal. Her lungs were clear to auscultation. Bilateral renal cystic masses were readily palpable. The liver and spleen were not palpably enlarged. She was of average intelligence but lacked insight into her disturbed mind. No focal neurologic sign was elicited.

Electrocardiography (Figure 3) showed sinus rhythm but frequent ventricular ectopics. The electrocardiogram was consistently that of type B Wolff–Parkinson–White syndrome with PR interval of 80 milliseconds, widened QRS duration of 12 milliseconds, delta waves which were positive in lead 1 and predominantly negative QRS in V1. No episode of tachycardia or atrial fibrillation was, however, elicited. Her echocardiogram showed enlarged left ventricular end diastolic dimensions of 6.6 cm. No intracardiac mass was seen and the valves were normal. Skull X-rays and electroencephalogram were normal. Histology of the subungual fibroma was consistent with tuberous sclerosis.

Abdominal ultrasound revealed grossly enlarged kidneys bilaterally with cystic degenerations. There were other discrete hyperechoic tissues within

**Figure 2** Subungual fibromas in the same patient.
both kidneys consistent with angiomyolipoma. Her
haematocrit was 27% and the erythrocyte sedimenta-
tion rate was 114 mm/hour. Her haemoglobin
genotype was AA. Urinalysis showed significant
pyuria of 20 cells per high-power field and
albuminuria (1 + ). The liver enzymes were mildly
elevated with both alanine and aspartate aminot-
transferases of 96 units, respectively. Serum
creatinine and electrolytes were normal.

**Discussion**

This patient illustrates a florid case of tuberous
sclerosis with facial, skin, nail, cardiac, kidney and
splenic lesions. She was also psychotic but not
epileptic, two of the common manifestations of
tuberous sclerosis. Tubercous sclerosis has highly
variable expressivity and psychosis without
epilepsy is a recognized sole manifestation. Out
of ten patients in whom the diagnosis of tuberous
sclerosis was eventually made, Rakoff elicted a
history of schizophrenic psychosis in two, one of
whom had no epilepsy. The renal ultrasound in this
patient was consistent with a mixture of both
angiomyolipoma and cystic degeneration. The
cause of her anaemia was not definite but was
presumed to be due, at least in part, to haemor-
rhage which is common but often intermittent in
patients with angiomyolipoma. Her elevated
erthrocyte sedimentation rate could also be
related to the anaemia per se as no other cause was
found.

Partial expression of tuberous sclerosis may also
manifest solely with cardiac rhabdomyoma. Rab-
domyoma occurs in about 30–40% of patients
with tuberous sclerosis in childhood. The tumour
is rare in adults suggesting that it may regress
spontaneously. When associated with tuberous
sclerosis, they are usually intramural, unlike those
found in isolation. The absence of detectable
cardiac mass by echocardiography in this patient,
therefore, does not entirely exclude a previous
occurrence of rhabdomyomata which may be in
various stages of regression, considering her age.
Indeed, the finding of cardiomegaly might suggest
definite cardiac involvement since she was not in
heart failure. The electrocardiographic features of
type B Wolff–Parkinson–White syndrome would
tend to suggest the presence of a right accessory
atrio-ventricular bypass tract.

Wolff–Parkinson–White syndrome has been
described in association with tuberous sclerosis
with or without cardiac rhabdomyoma. Jayakar et al. described two infants who presented
with supraventricular tachycardia and features of
Wolff–Parkinson–White syndrome and who later
developed tuberous sclerosis, one with cardiac
rhabdomyoma. They were among seven patients
with tuberous sclerosis seen over a 9-year period by
these authors who concluded that the probability
of tuberous sclerosis and Wolff–Parkinson–White
syndrome occurring together by chance would be
very low indeed. The frequency of tuberous
sclerosis in their population was 1:20,000 and that
of supraventricular tachycardia was 1:25,000,
while only 23–25% of their children with supraventricular tachycardia had Wolff–Parkinson–White syndrome.

The precise mechanism responsible for the occurrence of Wolff–Parkinson–White syndrome in tuberous sclerosis is not completely certain. Two mechanisms are plausible. Some cells in the cardiac rhabdomyoma in tuberous sclerosis resemble normal Purkinje cells structurally. These Purkinje-like cells have therefore been thought to be capable of functioning as an anomalous conducting tract for pre-excitation syndrome. However, this may not explain the cases in which the tumour does not occur or has regressed. On the other hand it is possible that pre-excitation syndrome may also result from the splitting up of the conduction tract by infiltrating tuberous sclerosis tissues, creating accessory pathways in some patients. It may be of interest to do electrophysiological studies in a cohort of patients with tuberous sclerosis.

References