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Tuberous Sclerosis and Cardiac Arrhythmia in Three Zulu Patients

J. E. COSNETT,* M.D., B.SC., M.R.C.P.; B. H. GIBB,† M.B., M.R.C.P.ED., M.R.C.P.GLASG.

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Summary: Cardiac arrhythmias, in the form of multiple atrial or ventricular extrasystoles together with various types of conduction defect, occurred in three Zulu patients with tuberous sclerosis. Probably this association occurs more often than has been suspected.

Introduction

A case of tuberous sclerosis reported by Taylor (1968) emphasized the rarity of association between this disease and cardiac arrhythmias. A computer-based literature retrieval search involving "385,000 articles in 2,500 journals in 28 languages" had yielded no report of the association in the previous three years. During a period of four months at Edendale Hospital we have seen three Zulu patients with features of tuberous sclerosis and associated with cardiac arrhythmia which was otherwise unexplained.

Case 1

A 21-year-old woman, 34-weeks pregnant, was referred from the antenatal clinic because she was found to have an irregular pulse. Apart from complaints of mild dyspnoea on exertion and of palpitations, there were no symptoms.

She had the typical facial appearance of adenoma sebaceum (Fig. 1). Apart from multiple extrasystoles the heart and cardio-

FIG. 1.—Case 1.

FIG. 3.—Case 2.

FIG. 2.—Electrocardiograms: A and B, Case 1; C, Case 2; D, Case 3.

vascular system appeared normal. A crescentic streak of opaque nerve fibres in the right ocular fundus was present, whereas the left fundus was normal. She was of average intelligence, and no apparent abnormality was present in the nervous system. X-ray pictures of the chest and skull were also normal. The E.C.G. showed multiple multifocal ventricular extrasystoles (Fig. 2A), which persisted in several subsequent recordings (Fig. 2B).

On further questioning, the patient told of epileptic fits, which had occurred between the ages of 4 and 8 years and had ceased spontaneously. The facial lesions had appeared at about 12 years of age, and had since become darker and more obvious. She had one previous pregnancy. This baby had appeared normal at birth, but after the first month had begun having fits, which became more frequent until they were occurring two or three times a day. At the age of 6 months the baby had died at home following a succession of fits. Neither of the patient's parents nor any of her

* Principal Physician, Edendale Hospital, Pietermaritzburg, Natal, South Africa.

† Visiting Physician, Edendale Hospital.

five brothers and four sisters had similar facial lesions nor ever suffered from epilepsy.

After her second baby was born it appeared normal at first, but then also developed epileptic fits during the second month of life. On examination at 3 months no abnormalities were found.

Case 2

This 25-year-old woman had no symptoms. Her condition was noticed when she brought her child (Case 3) to hospital for treatment of burns. Her face showed the typical appearance of adenoma sebaceum (Fig. 3). There was an occasional irregularity in the pulse, and a soft pansystolic apical murmur. In all other respects, however, the cardiovascular system appeared normal. Similarly, no abnormalities were found in the fundi or the central nervous system. Her intelligence was apparently normal.

X-ray examination of the skull showed multiple rounded densities of various sizes. Tomography confirmed that these densities were areas of intracerebral calcification, situated supratentorially. Furthermore, E.C.G. recordings on admission to hospital, showed an intermittent partial heart block of the Wenckebach type (Fig. 2 C). Subsequent repeated E.C.G. recordings showed that the original conduction defect had disappeared, and the only abnormality was occasional ventricular extrasystoles. Exercise and carotid sinus pressure did not influence the rhythm.

The patient denied having had fits at any time, and stated that the facial lesions, which had been present since infancy, had become more obvious with time. A maternal aunt had also had similar facial lesions but not epilepsy. Two paternal uncles, however, had suffered from fits. The elder of the patient's children, aged 7 (Case 3), was mentally defective and epileptic, whereas the younger aged 2 years was said to be normal. An opportunity to examine this child did not arise.

Case 3

This patient was the 7-year-old daughter of the second patient. She had been brought to hospital for treatment of ulceration and contracture of the left hand which had resulted from burns sustained during a fit some months previously.

She was a mental defective, and had suffered from epilepsy since the age of 7 months. Her fits were becoming increasingly frequent, occurring two or three times a day at the time of her admission to

hospital. At rest she had some athetoid movements of her head and limbs. No other signs of neurological disease, however, were present. The ocular fundi were also normal. Shortly after admission to hospital she had numerous generalized epileptic fits, but these were readily controlled by phenobarbitone.

Though she did not have typical adenoma sebaceum, there were a few papules, each smaller than a pin's head, on the nose and cheeks. These might have been the earliest stage in the development of adenoma sebaceum. The heart rhythm was irregular, and there was a soft ejection systolic murmur at the left sternal border.

On x-ray examination there were signs of some general cardiac enlargement (Fig. 4), the cardiothoracic ratio being 0.67, while in films of the skull there were multiple rounded opacities in the cortex and subcortical zones over the convexities of both hemispheres. No calcification, however, was present in the periventricular areas, temporal lobes, or posterior fossa.

E.C.G. recordings (Fig. 2 D) showed frequent atrial ectopic beats, which in some tracings followed two normal beats, thus producing trigeminy. The atrial extrasystoles occurred early in diastole—with the result that some were blocked—while others were conducted with ventricular aberration. T-wave inversion was present in leads V1 to V3. This arrhythmia persisted throughout the period the child was under observation in hospital.

Discussion

The cardiac arrhythmias associated with tuberous sclerosis presumably indicate the presence of "rhabdomyomata" of the heart. Since the neoplastic nature of these lesions is in doubt, a better descriptive term is that used by Gould (1960)—namely, "congenital nodular glycogenic infiltration of the myocardium."

Two of our patients (Cases 1 and 2) illustrate the observation that the syndrome need not be complete, and that *formes frustes* are common. Neither patient was mentally defective, yet both had adenoma sebaceum. Case 1 had been free of epilepsy since childhood—illustrating that long remissions in the epilepsy may occur. Though Case 2 had extensive cerebral calcification she never had epilepsy, whereas her daughter (Case 3) showed a more complete form of the condition. The occurrence of three African cases is of interest in the light of Brain's (1955) statement that "the disorder is almost confined to the white races."

These findings, together with those of Taylor (1968), would indicate that the cardiac arrhythmias associated with tuberous sclerosis consist of ectopic beats—either atrial or ventricular—and conduction defects at either atrioventricular or intraventricular level.

Though Taylor emphasized the rarity of reports associating cardiac arrhythmias with tuberous sclerosis, our three cases suggest that this link might occur more often than has been suspected. The reason for the failure to detect or report the association in the past might be that cases of tuberous sclerosis are usually observed and investigated in mental hospitals, where electrocardiography is not done routinely. Probably closer cardiac investigation of patients with tuberous sclerosis would yield more examples of this association.

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FIG. 4.—Radiograph showing cardiac enlargement.