CASE REPORT

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Incidental Cardiac Rhabdomyomas: A Significant Finding Necessitating Additional Investigation at the Time of Autopsy

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ABSTRACT: Cardiac rhabdomyomas are rare lesions forming part of the tuberous sclerosis complex that may be responsible for sudden death. As well as remaining clinically occult for variable periods of time, they may, along with other manifestations of tuberous sclerosis, be quite difficult to detect clinically and pathologically. A patient is described in whom multiple cardiac rhabdomyomas were an incidental finding at autopsy following fatal potassium fluoride poisoning. Other gross pathological lesions typical of tuberous sclerosis were present but were quite subtle in appearance. Awareness of the association of cardiac rhabdomyomas with tuberous sclerosis is important so that full examination of organ systems for characteristic lesions can be undertaken during the autopsy, and so that fresh and frozen tissue can be obtained at the time of dissection for further investigation.

KEYWORDS: pathology and biology, cardiac rhabdomyomas, tuberous sclerosis, sudden death

Multiple cardiac rhabdomyomas are a rare finding in children, associated with tuberous sclerosis [*1–4*]. There is also an association of this finding with sudden and unexpected death [*5*]. Because of the inherited nature of a significant number of cases of tuberous sclerosis, establishment of the diagnosis is extremely important for subsequent family studies and counseling [*6*]. A patient with clinically unsuspected multiple cardiac rhabdomyomas is presented to demonstrate the potential for underdiagnosis of the associated skin and cerebral lesions. A strong suspicion at the time of autopsy of tuberous sclerosis in patients with cardiac rhabdomyomas is essential so that the wide range of associated lesions can be specifically checked for and so that fresh and frozen tissue can be provided for optimal laboratory chromosome and deoxyribonucleic acid (DNA) analysis.

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Case Report

A 13-month-old boy was admitted to a hospital cyanosed and in shock following ingestion of a potassium-fluoride-containing soldering flux. He soon became tetanic, with a serum calcium of 1.7 mmol/L (the normal range is 2.25 to 2.65 mmol/L), and suffered a cardiac arrest. His initial successful resuscitation was followed by decline and death approximately 12 h after ingestion of the flux.

At autopsy, the major findings relating to the poisoning were reddening of the stomach mucosa and pulmonary and cerebral edema. The fluoride levels were 2 mg/L (blood), 3 mg/L (liver), 30 mg/L (stomach), and 300 mg/L (rib). (Normal tissue level are 0.4 to 0.8 mg/L; the lethal blood level is >2 mg/L [*7,8*].) An important incidental finding was the presence of multiple small (<1 cm in diameter) cardiac rhabdomyomas scattered throughout both ventricular walls. On closer inspection, slight scaling was noted over both cheeks, representing mild facial angiofibromas. The brain, which appeared superficially normal, did have slightly abnormal-appearing gyri in the anterior aspect of the frontal lobe (Fig. 1). On palpation, these gyri were firmer than the surrounding cortex, and additional quite hard areas were also found in other areas of the hemispheres. These firmer areas were much more difficult to detect after tissue fixation. There were no other associated malformations or lesions of the central nervous system (CNS) or other organ systems.

On microscopy, it was revealed that the cardiac tumors were composed of aggregates of large "spider" cells, having abundant vacuolated cytoplasms with radiating cytoplasmic extensions (Fig. 2). Positive staining with periodic acid/Schiff stain revealed intracytoplasmic glycogen, which did not stain after pretreatment with diastase. Cross striations were apparent with phosphotungstic acid and hematoxylin (PTAH) staining. Features of malignancy such as anaplasia, nuclear hyperchromatism, and abnormal mitotic figures were not present.

Examination of sections from the firm cortical areas showed aggregates of large abnormal neurons and astrocytes, interspersed with smaller, more normal-appearing cells characteristic of the cortical tubers of tuberous sclerosis (Fig. 3). Subpial gliosis and

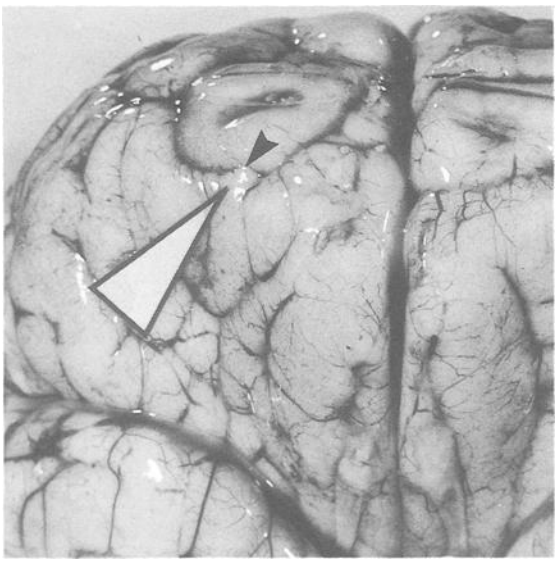

FIG. 1—*Inferior aspect of the frontal lobe showing a mildly abnormal-appearing gyrus on the right* (arrow heads).

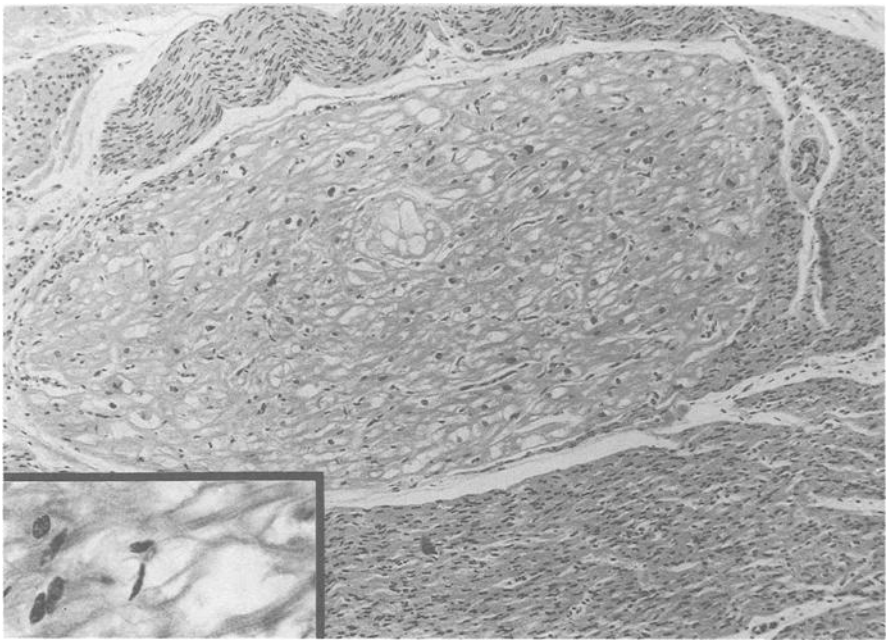

FIG. 2—*Section of myocardium showing a well-circumscribed rhabdomyoma composed of vacuolated "spider" cells. The inset shows cytoplasmic vacuoles and cross striations in tumor cells (hematoxylin and eosin stain; magnification, ×70; inset magnification, ×440).*

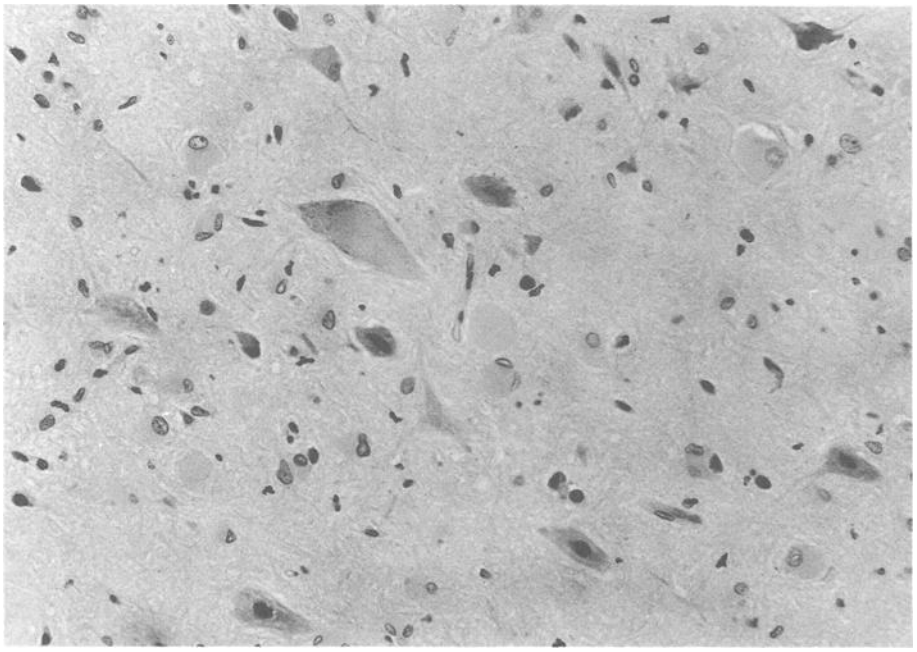

FIG. 3—*Histologic section of the tuber pictured in Fig. 1, showing disorganized astrocytes and large neurons (hematoxylin and eosin stain; magnification, ×175).*

central demyelination were noted. Subependymal nodules were infrequent, and heterotopic tissue was not found in the white matter.

Death was attributed to potassium fluoride poisoning in a patient with incidental and previously undiagnosed tuberous sclerosis. Specifically, there had been no history of developmental delay or evidence of retardation or epilepsy. Enquiries elicited no evidence of tuberous sclerosis in other family members.

Discussion

Cardiac rhabdomyomas are rare lesions of the heart that are generally confined to infancy and childhood [*1*,*4*,*9*]. Histologically, they are composed of characteristic "spider" cells, which are enlarged myocytes packed with glycogen. Their association with tuberous sclerosis is well known and was first reported by von Recklinghausen in 1862 [*4*]. Subsequently, tuberous sclerosis has been reported in 24 of 28 cases of multiple cardiac rhabdomyomas (86%), and, conversely, rhabdomyomas were detected in 6 out of 7 children with established diagnoses of tuberous sclerosis (86%) [*4*]. It has even been suggested that the discovery of cardiac rhabdomyomas in isolation, particularly when multiple, represents a *forme fruste* of this protean disorder [*6*].

Fibroblast cultures from patients with tuberous sclerosis have recently been shown to manifest consistent karyotypic variations [*10*]. The gene locus has also been shown to be linked to the ABO blood group and the ABL oncogene loci at q34 on the long arm of Chromosome 9 [*11*]. There is genetic heterogeneity with another locus for tuberous sclerosis on Chromosome 11 [*12*]. As both of the above techniques may assist in future family studies by providing supportive laboratory evidence, recognition of this disorder at the time of gross dissection is important so that tissue specimens can be taken and appropriately processed. For example, fibroblast culture studies require fresh tissue to be removed in as sterile a manner as possible and placed in tissue culture medium. In addition, standard Southern blotting methods for restriction fragment length polymorphisms (RFLPs) utilize fresh material, although the development of successful techniques for DNA extraction from formalin-fixed, paraffin-embedded tissue and for DNA amplification by means of polymerase chain reaction (PCR) may make possible increased use of archival material in the future [*13*,*14*].

The patient described demonstrates certain important features, as well as potential pitfalls, that may be encountered in such cases. Significantly, he was not known to have cardiac lesions prior to autopsy examination, and the finding of cardiac rhabdomyomas was incidental to the established cause of death, which was ingestion of a potassium-fluoride-containing soldering flux. Although there had been no antemortem indication of mental retardation or epilepsy, further detailed gross examination revealed the presence of scattered facial angiofibromas and slightly flattened gyri on the anterior aspects of both frontal lobes. The subtle nature of the latter finding, which on microscopy proved to be cortical tubers, can be appreciated when viewing Fig. 1. The value of gently palpating the brain for firm areas is also emphasized.

While typical cases of tuberous sclerosis, with the presenting triad of mental retardation, epilepsy, and facial angiofibromas, are relatively easy to diagnose, the expression of this inherited disorder is variable [*3*,*15*]. The diagnosis in infancy and early childhood may be even less obvious, as other characteristic features, such as renal angiomyolipomas, subungual fibromas, and subependymal tumors, may either not have developed or not yet had time to manifest themselves clinically. For this reason, the first suggestion of the disorder may occur at the autopsy table, where characteristic lesions may be quite subtle in appearance and therefore missed [*4*]. The importance of establishing the diagnosis of tuberous sclerosis in a patient in whom cardiac rhabdomyomas have been discovered lies in the inherited nature of 20 to 50% of cases [*6*,*9*]. Particular attention should, therefore,

be paid to the brain, kidneys, skin, lungs, bones, and eyes in looking for characteristic lesions that may support this significant diagnosis.

In conclusion, this case has been reported to emphasize the subtle nature of a number of the lesions of tuberous sclerosis, a condition that may be associated with sudden and unexpected death. Accuracy of diagnosis at the time of autopsy is particularly important so that (1) the nature and extent of the lesions can be documented and (2) tissue can be submitted for further investigation.

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