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SUBEPENDYMAL GIANT CELL ASTROCYTOMAS IN TUBEROUS SCLEROSIS*

*M. Memet Özek MD***, *Eren Özek MD****, *M. Necmettin Pamir MD*****
*A. Fahir Özer MD******, *Canan Erzen MD*******

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Two cases of tuberous sclerosis with subependymal giant cell astrocytoma are presented. This rare autosomal dominant disorder was also detected in family members of the patients who had never had any symptoms of cerebral involvement. Both patients underwent surgery because of signs of increased intracranial pressure.
Key words: tuberous sclerosis, subependymal giant cell astrocytoma.

Tuberous sclerosis (TS) is a neurocutaneous disorder inherited as an autosomal dominant trait which affects various organ systems with different clinical manifestations. The estimated incidence figure is 1 in 30,000[1].

It is well known that subependymal tumors in the periventricular region, termed subependymal giant cell astrocytomas, may occur in TS. These tumors have a definite appearance, with predominantly elongated astrocytes and giant cells[2]. Although they are histopathologically benign lesions, they can appear after the acute onset of hydrocephalus and increased intracranial pressure. Therefore, early detection of a subependymal giant cell astrocytoma (SGCA) is of clinical importance in a TS patient and computed tomography (CT) screening of first degree relatives of these patients is advised.

Case Reports

Case 1

A 12-year-old boy, who was right-handed and had normal mental development, first experienced generalized seizures at the age of eight. A diagnosis of TS was

* From the Departments of Neurosurgery and Pediatrics, Marmara University Faculty of Medicine, İstanbul.
** Assistant Professor of Neurosurgery, Marmara University Faculty of Medicine.
*** Assistant Professor of Pediatrics, Marmara University Faculty of Medicine.
**** Professor of Neurosurgery, Marmara University Faculty of Medicine.
***** Associate Professor of Neurosurgery, Marmara University Faculty of Medicine.
****** Professor of Radiology, Marmara University Faculty of Medicine.

then established. The patient, the product of a normal delivery, had a normal gestational and perinatal history. His parents were not related, but his 35-year-old father, who was mentally retarded, had intractable seizures. The neurological examination was unremarkable except for ash-leaf spots, adenoma sebaceum and bilateral papilledema. A CT scan revealed an intraventricular mass, with mild enhancement, arising from septum pellucidum which obstructed both foramen of Monro. Both lateral ventricles were dilated and severe periventricular edema was present (Fig. 1a).

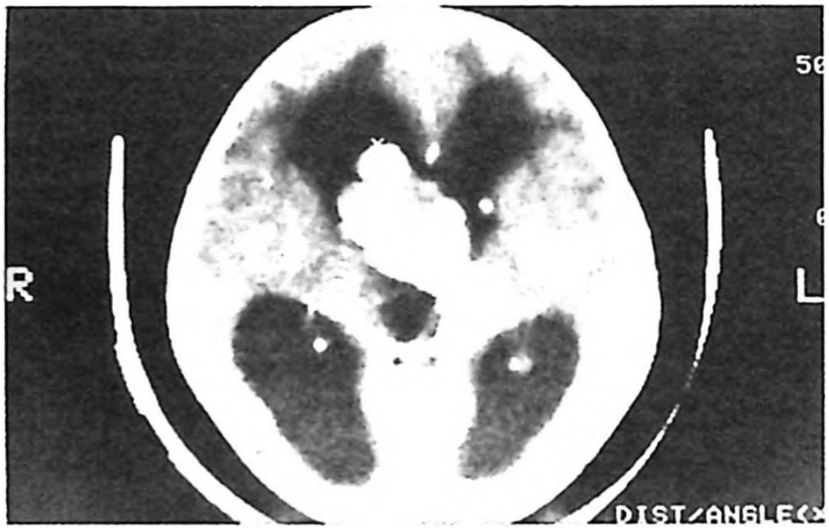


Fig. 1a: Intraventricular mass obstructing both foramen of Monro resulting in hydrocephalus.

The tumor, with the exception of a small part infiltrating the mesencephalon, was removed using the transcortical, transventricular approach. Histopathological examination revealed giant astrocytes as the predominant cell type and pyramid-shaped cells with short, stubby processes. There were no mitotic figures

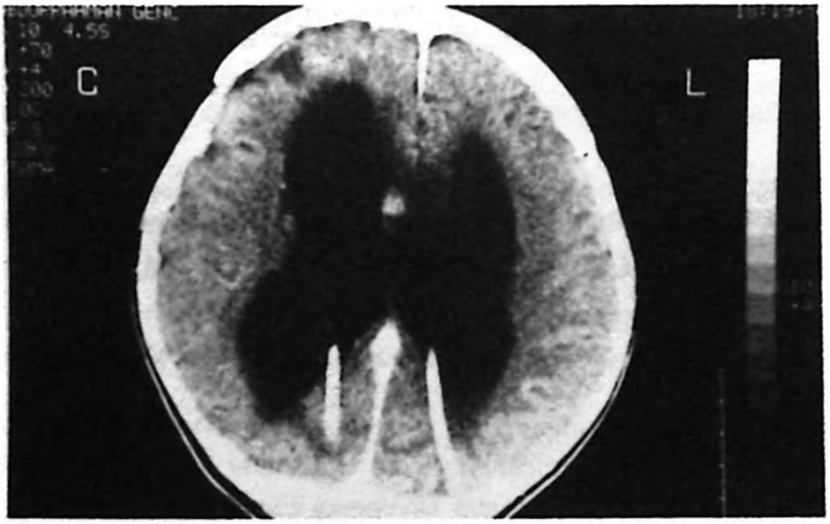


Fig. 1b: Postoperative CT scan demonstrating a residual intraventricular mass and the inserted shunt system into both lateral ventricles.

or anaplastic changes. The tumor was diagnosed as a subependymal giant cell astrocytoma. The postoperative course was uneventful, and the patient's seizures were completely controlled with medical therapy. Because of the subtotal excision of the tumor and the presence of hydrocephalus, a biventriculoperitoneal shunt was inserted two months after the first operation. A CT revealed a small residual tumor which had decreased in ventricular size (Fig. 1b). The 35-year-old father of this patient was also examined by CT scanning which showed multiple areas of periventricular calcification (Fig. 2). The patient's 3-year-old sibling also had areas of periventricular calcification, though he had never experienced any symptoms of cerebral involvement associated with TS (Figs. 3,4).

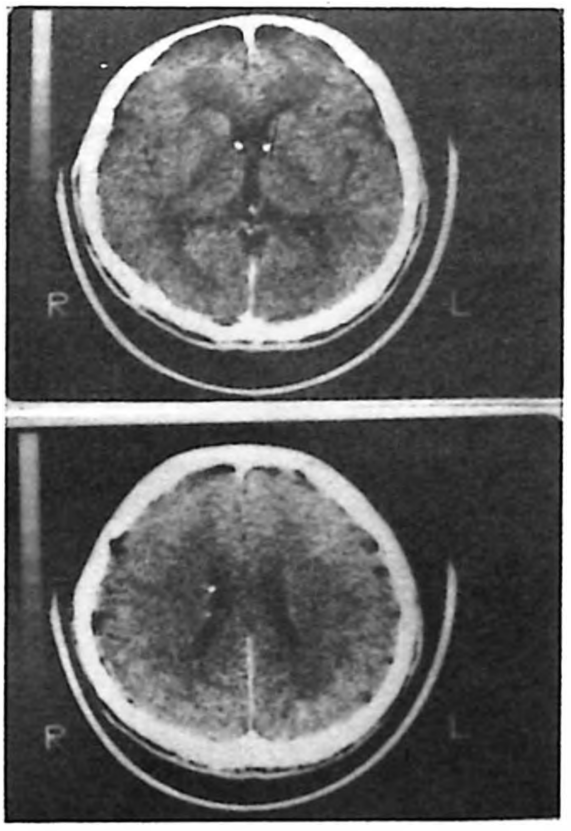


Fig. 2: Multiple areas of periventricular calcification in the 35-year-old father.

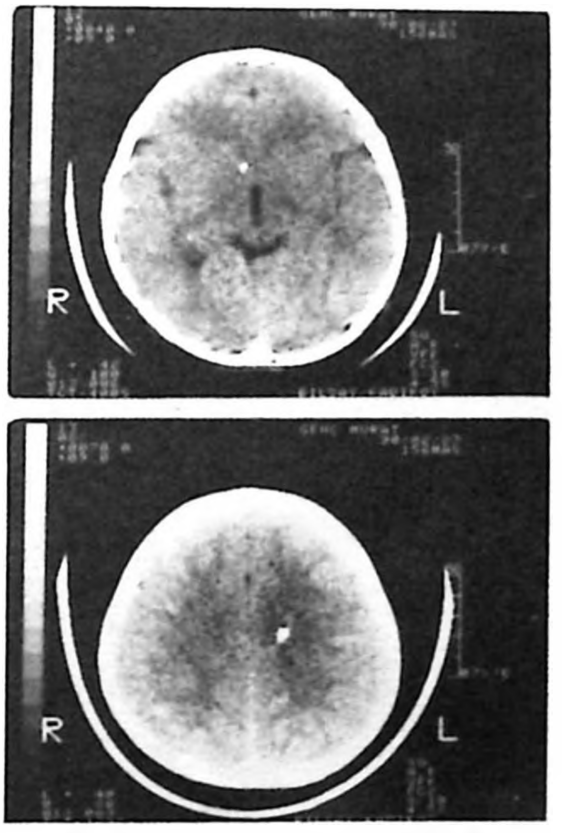


Fig. 3: Two areas of periventricular calcification in the 3-year-old brother.

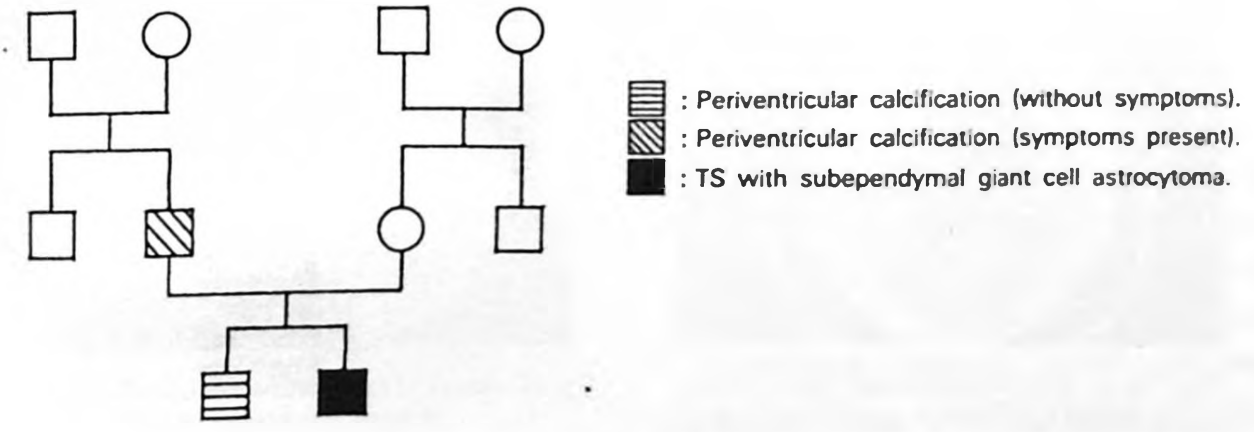
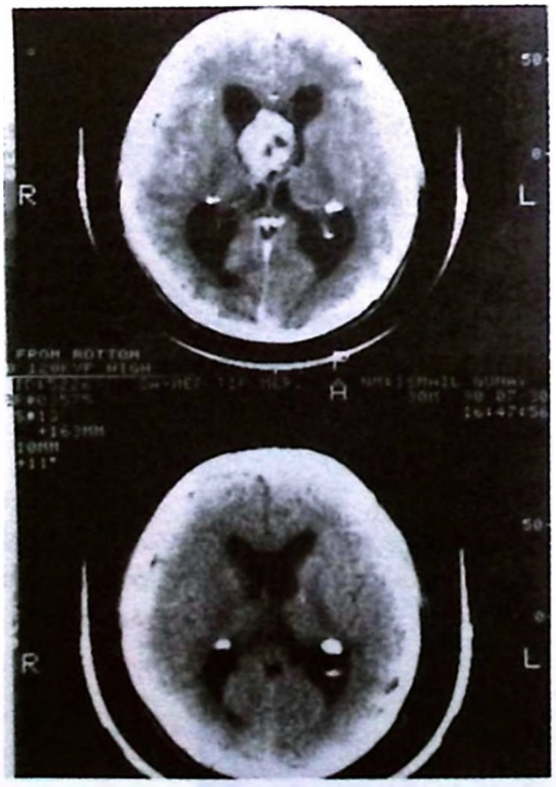


Fig. 4: Pedigree of first case.

Case 2

A 30-year-old right-handed male was admitted to our clinic for evaluation of a two-month history of severe headache. A physical examination revealed ash-leaf spots on the skin, while a neurological examination demonstrated bilateral papilledema and visual-field defects. A CT scan showed areas of multiple periventricular calcification and a mass located in the region of the right foramen of Monro (Fig. 5a).

The patient underwent surgery in which the interhemispheric transcallosal approach was used. After reaching the right lateral ventricle, the tumor was totally extirpated and the CSF pathways were reopened. Histopathological examination revealed astrocytes, with extensive homogenous, eosinophilic cytoplasm. The nuclei were eccentrically located, vesiculated and occupied by large nucleoli. There were irregular vascular spaces and calcification. The postoperative course was uneventful. A CT scan taken four months after showed no evidence of the primary tumor. The areas of periventricular calcification remained the same in size (Fig. 5b). The CT scan of the patient's father, who has experienced generalized seizures, disclosed periventricular areas of calcification. An examination of the patient's one-year-old son, who was symptom-free, also revealed multiple areas of periventricular calcification (Fig. 6).



Figs. 5a,b: An intraventricular mass arising from the right side of the septum pellucidum. Appearance after total removal of tumor.

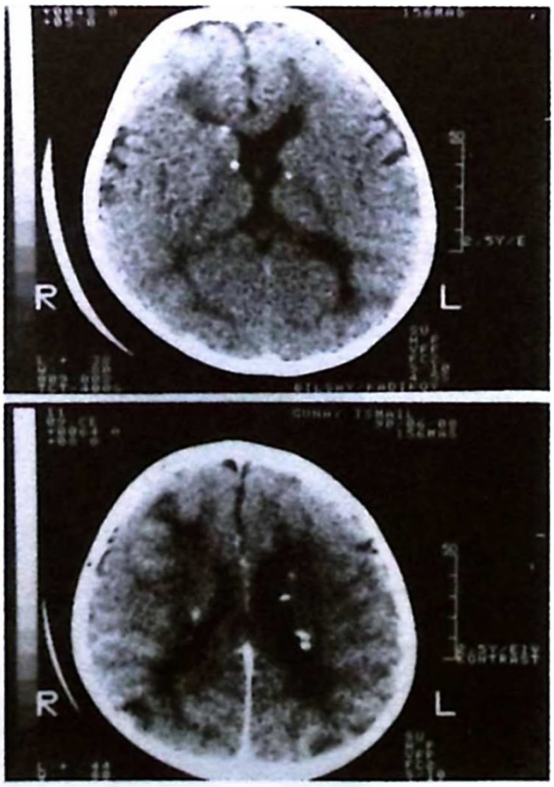


Fig. 6: Areas of periventricular calcification in the child of the second case.

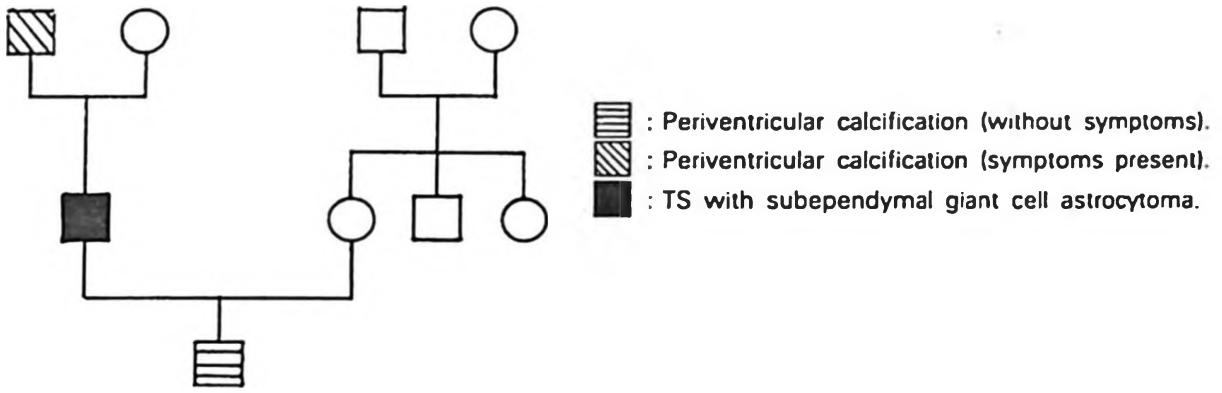


Fig. 7: Pedigree of second case.

Discussion

TS, which was first reported by Von Recklinghausen in 1862, commonly presents with features of Vogt's triad such as seizures, mental retardation and facial adenoma sebaceum[1]. Later it was discovered that the inherited gene in TS is located on chromosome 9. Two different loci for TS genes have been described, but no phenotypic distinction has been recognized in subjects studied[3,4]. Seizures are the most common symptom and may appear anytime after birth. Infantile spasms are particularly common in affected infants[1]. More than 25 percent of patients with infantile spasms will later develop signs of TS[5]. In our report, Case 1 and the father of Case 2 had generalized seizures, but not in the form of infantile spasms.

Mental function varies greatly among TS patients. Although mental retardation is a characteristic feature of the disease, about 33 percent of patients diagnosed by other clinical signs have normal intelligence[4]. Our patients had a normal intelligence quotient.

Some reported cases are close relatives of TS patients who have never experienced symptoms of cerebral involvement, although they have at least one of the pathognomonic hamartomas[3]. This finding is consistent with the relatives of our cases. Therefore, in order to ascertain whether an individual has TS, it is necessary to screen first-degree relatives, as we did. Until recently, a majority of TS cases were diagnosed by skin lesions.

Nowadays, more emphasis is placed on findings, elicited by organ imaging[2,4]. The presence of subependymal nodules in the lateral ventricles, cortical tubers and areas of calcification in the periventricular region, indicate cranial involvement[6]. Computed tomography has become an indispensable method for identifying intracranial pathology in TS, but magnetic resonance imaging, which has only recently been used to study TS patients, demonstrates subependymal nodules with greater clarity than does CT scanning[3,7,8].

Although the incidence of intracranial calcification increases with age, SGCA's are relatively rare. In a 60-patient series, diagnosed as having TS clinically and by CT scans, Maki et al[7] found only one patient with neoplastic changes. Since this entity has been interpreted as being between a neoplasm and a heterotopia, there is some disagreement regarding therapy[9,10]. SGCA's do not appear to be highly sensitive to radiation therapy, and have not been reported as highly invasive tumors in any of the published series[3]. Walker et al[11] considered that the only indication for surgery were signs and symptoms caused by the mass, such as increased intracranial pressure or hydrocephalus. We are also of the opinion that if these conditions are present, then surgical intervention is indicated.

It is well known, that SGCA's grow into the ventricular cavity, and often reach enormous sizes contributing to the high operative morbidity and mortality[3]. Since the total removal of a SGCA indicates a total cure, the importance of early detection of these tumors by screening techniques should be emphasized.

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