SUBEPENDYMAL GIANT CELL ASTROCYTOMA WITH TUBEROUS SCLEROSIS—CASE REPORT

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Tuberous sclerosis is a rare disease of autosomal dominant inheritance and may affect any organ, and less than 2% have a subependymal giant cell astrocytoma. In the present report, a 6-year-old girl with clinical features of tuberous sclerosis had an intraventricular tumor. CT scan and MRI of brain showed a tumor in the lateral ventricles extended into the Foramina of Monro and third ventricle causing severe hydrocephalus. She underwent left frontal craniotomy with partial removal of the tumor. The pathology was subependymal giant cell astrocytoma. Patient's neurological condition improved postoperatively and postoperative CT scan showed no hydrocephalus. Clinical and radiological follow-up of patients with tuberous sclerosis who had subependymal nodules in early childhood is important due to its possibility of subsequent transformation into intraventricular tumor.

Key words: Subependymal Giant Cell Astrocytoma, Tuberous Sclerosis

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Tuberous sclerosis, also called tuberous sclerosis complex, was first described by Friedrich Daniel von Recklinghausen in 1862[1]. It is a rare disease and may affect any organ. The intraventricular tumor which has been called a subependymal giant cell astrocytoma occurs in association with tuberous sclerosis and this type of tumor is unique and histologically different from other astrocytoma. In this paper, we report a girl with tuberous sclerosis who had an intraventricular tumor with obstructive hydrocephalus.

CASE REPORT

This 6-year-old girl first experienced generalized tonic-clonic seizure when she was 3 months old and was diagnosed as infantile spasm. Her EEG showed continuous, generalized polymorphic slow waves with hypsarrhythmia. She was born by normal delivery without abnormal gestational or perinatal events and her family history was negative for neurological disease. At the age of 7 months, she was first evaluated by CT scan of brain. There were multiple periventricular calcifications characteristic of tuberous sclerosis (Fig. 1). At the age of 3 years she was found to have an adenoma sebaceum in the face while neurological examination was unremarkable except for mental subnormality.

In 1992, at the age of 6 years, the patient began to have headaches which gradually worsened. She developed weakness of the four limbs and became progressively unconscious with nausea and vomiting one week later. When we examined the patient she was stuporous. She had adenoma sebaceum in the face. Shagreen patches in the neck and hypomelanotic macules on the trunk. A CT scan of brain after administration of contrast medium showed a moderate - enhanced, dumbbell-shaped tumor extending into the left frontal born, obstructing the foramina of Monro bilaterally and causing hydrocephalus (Fig. 2A). MRI of the brain with pre- and post-contrast enhanced images also revealed a dumbbell-shaped intraventricular tumor occupying the bilateral foramina of Monro and third ventricle and causing marked hydrocephalus (Fig. 2B).

On August 4, 1992, the tumor was removed through a left frontal craniotomy with

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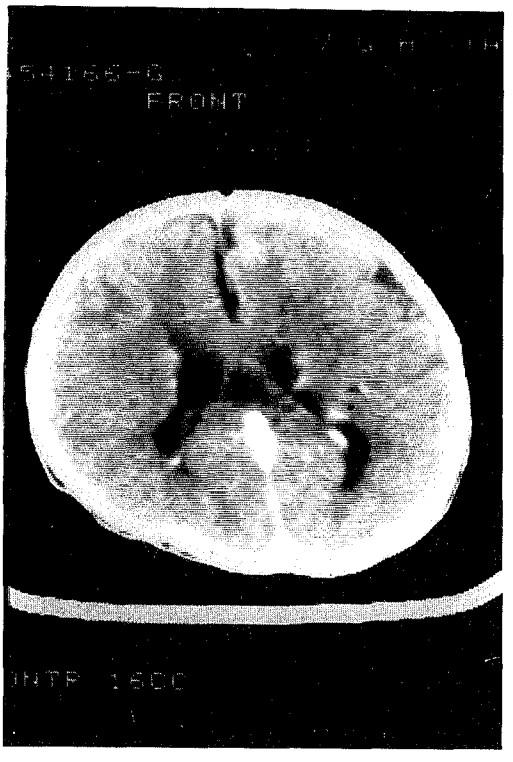

Fig. 1. CT scan of brain at the age of 7 months showing multiple periventricular nodular calcifications.

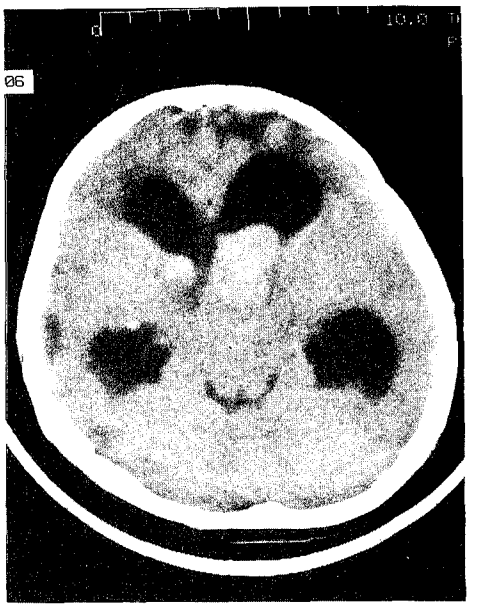

Fig. 2A. CT scan of brain at the age of 6 years showing a moderate-enhanced tumor in the left frontal horn with extension into bil. foramina of Monro.

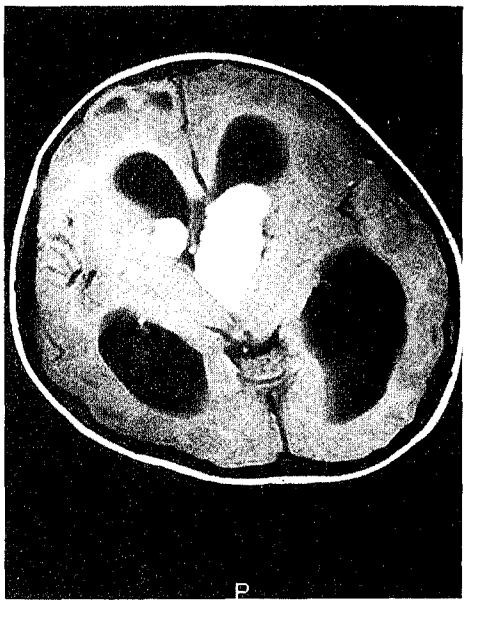

Fig. 2B. MRI of brain also showing the same findings. 1.0 Tesla, VISTA 2055 HP, TR/TE=600/20 msec. Intravenous contrast enhancement with Gd-DTPA.

the transcortical, intraventricular approach. The tumor was sharply defined and highly vascular with a broad attachment to the inferolateral wall of the lateral ventricle. Histologically, it was consistent with a typical subependymal giant cell astrocytoma and no malignancy was found (Fig. 3A). The postoperative course was uneventful and her consciousness improved. No postoperative radiotherapy or chemotherapy was given. Her seizures were completely controlled with medical therapy.

DISCUSSION

Tuberous sclerosis is clinically characterized by seizures, mental retardation and adenoma sebaceum[2]. It may affect any organ and is mostly recognized by lesions in the skin, brain, retina, kidneys, heart, or lungs. A diagnosis of tuberous sclerosis can be made on individuals who harbor at least one of the following lesions: facial adenoma sebaceum, ungual fi-

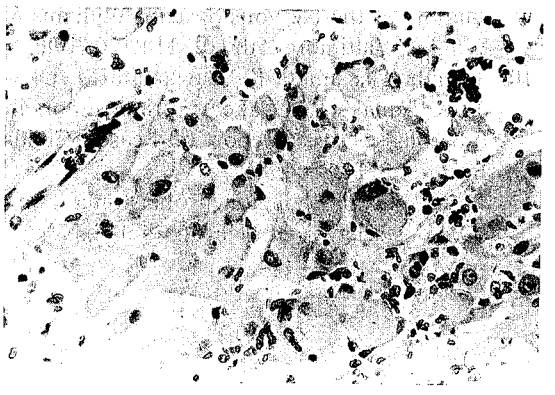

Fig. 3. Pathology showing giant cell with abundant eosinophilic cytoplasm.

broma, retinal hamartoma, cortical tuber, subependymal nodules and renal angiomyolipoma[3]. The subependymal giant cell astrocytoma, a key feature of tuberous sclerosis generally originates from the subependymal glial nodule. The benign tumor may cause obstruction of the CSF circulation at the foramina of Monro and of the third or fourth ventricles and results in intracranial hypertension. The intracranial hypertension should be treated with shunting or removal of tumor to prevent mortality. But when the tumor is small and lack of symptoms and signs, surgical treatment is still not well standardized, since the controversy as to whether the basic nature of the lesion is dysplastic or neoplastic[4-6]. Our patient had the presenting symptoms of infantile spasm and mental subnormality, facial adenoma sebaceum and subependymal nodular calcifications which are pathognomonic signs of tuberous sclerosis. So the diagnosis of tuberous sclerosis was made early in her life. The presence of subependymal nodular calcifications in the lateral ventricles is a classical and consistent expression and allow early diagnosis by CT scan or later by plain skull x-ray film. The CT scan or MRI have become indispensable for identification of intracranial pathology in tuberous sclerosis[7].

Although the incidence of intracranial calcifications increases with age, subependymal giant cell astrocytoma are relatively rare. Maki *et al.*[8] found only one case with neoplastic change among the 60 patients who were diagnosed as having tuberous sclerosis clinically and were evaluated by CT scan. The most commonly found tumor in patients with tuberous sclerosis is subependymal giant cell astrocytoma[9], the others include cerebral hemangiomas[10], spongioblastoma[11], neurinoma[12], and ependymoma[13]. From the study of Mayo Clinic, it was concluded that the subependymal giant cell astrocytoma was unique to tuberous sclerosis[14]. It is thought that subependymal giant cell astrocytomas arise from the subependymal nodules[15,16] located in the walls of the lateral ventricles of patients with tuberous sclerosis. The natural history of the subependymal giant cell astrocytoma is uncertain, and there is no satisfactory explanation of what causes such nodules to grow, obstruct the foramina of Monro and produce raised intracranial pressure, as shown in this patient whose CT scan of brain at the age of 7 months revealed subependymal nodular calcifications. However, it was not until the age of 6 years, when an intraventricular tumor caused obstructive hydrocephalus.

There are no essential differences in morphological characteristics between subependymal nodules and subependymal giant cell astrocytomas[17]. By clinical convention, when a subependymal nodule grows sufficiently to cause symptoms, the lesion is designated a tumor. Similarly by radiological convention, if the lesion is contrast-enhancing on CT scan, it is considered to be a tumor[18].

Histologically, they consist of giant cells with abundant eosinophilic cytoplasm that resembles gemistocytic astrocytes. Positive staining with GFAP is seen in most cases and supports the concept that subependymal giant cell astrocytomas are astrocytic. Some tumors have been reported to show immunoreactivity for neuron specific enolase and for neurofilament protein[19], the findings suggest that these tumors may have a neuronal component. Subependymal giant cell astrocytomas rarely, if ever, become malignant and bleed spontaneously. They have a more favorable prognosis than other giant cell-containing astrocytoma of all grades[14].

There are some disagreements regarding the therapy of subependymal giant cell astrocytoma associated with tuberous sclerosis[4,5]. These tumors have not been reported as highly invasive tumors in any of the published series. Eisenberg[20] considered the only indication for operation to be signs and symptoms caused by the mass, usually raised intracranial pressure or hydrocephalus. Unfortunately this tumor is invariably large and often exceedingly vascular by

the time the tumor comes to medical attention. The operative morbidity and mortality are high and the tumor cannot be totally removed in many instances, as in the presenting case. Boesel[21] *et al.* and Kazuyoshi[16] recommended that early surgery should be carried out whenever the tumor was found. Winter[22] gave a suggestion that periodic CT scan at least every 2 to 3 years for patients with tuberous sclerosis to monitor the possible development of glioma.

Based on our experience and review of the literature we concluded that if CT scan or MRI in patients with tuberous sclerosis showed subependymal nodules, periodic CT scans should be performed. Early diagnosis may increase the chance of total tumor removal and achieve a prolonged survival.

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室管膜下巨大星狀細胞瘤合併結節硬化症一病例報告

李文源　王有智　周德陽

結節硬化症是體染色顯性遺傳相當罕見的疾病，它可能侵犯全身任何的器官，如皮膚、腦、心臟、肺臟以及肝臟等。它們之中有少於百分之二的病人會有一種叫室管膜下巨大星狀細胞瘤的腦室內腫瘤，這種瘤的組織形態、預後及治療方式與其他所有等級的星狀細胞瘤都有所不同。一般人認爲這種巨大星狀細胞瘤是由結節硬化症病人腦室周圍的室管膜下結節所衍生出來的，而在五歲至十八歲時產生顱內壓增高症狀，如不治療將會造成病人的死亡。早期診斷、早期治療這種腫瘤，病人會有比較好的預後。

我們此次報告的病例是一個六歲大的女孩子，她在二個月大時開始有全身痙攣的現象，當時被診斷爲嬰兒點頭痙攣。在七個月大時，她接受了腦部電腦斷層攝影的檢查，發現有腦室周圍結節性的鈣化，而被小兒科醫師診斷爲結節硬化症。三歲大時她臉上出現皮脂腺瘤，她一直在小兒科門診接受抗癲癇的治療，很不幸地在六歲大時，她開始有頭痛、嘔吐的現象，接著又四肢逐漸無力、神智不清而住院檢查治療。住院時病人呈現木僵的狀態，電腦斷層攝影及磁振造影顯示出側腦室有一啞鈴狀的腦室內腫瘤延伸到室間孔及第三腦室而引起相當厲害的水腦。她接受了左側前額顱頭切開術，利用經皮質經腦室的方法把腦瘤去除掉，這腫瘤病理組織學檢查的結果是室管膜下巨大星狀細胞瘤，手術後病人的神經狀況恢復得相當好。她沒有接受術後的放射治療或化學治療，她現在一直在門診追蹤治療，癲癇已能得到很好的控制，我們在這一篇報告裏討論這腫瘤的診斷、臨床表徵、治療方式及預後。

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