Diffuse cerebrospinal gliomatosis

Case report

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A case of diffuse cerebrospinal gliomatosis is presented, with widespread involvement of the brain, cranial nerves, and spinal cord. This case showed a far more extensive distribution of tumor cells than previously reported cases of gliomatosis cerebri. The clinical picture and oncogenesis of gliomatosis cerebri is briefly discussed.

KEY WORDS • gliomatosis • gliomatosis cerebri • astrocytoma • spinal cord extension • cerebrospinal gliomatosis

The term “gliomatosis cerebri” was first used by Nevin in 1938. Although many reported cases have appeared under various names, 64 of these cases reviewed by us were considered to belong to this category. We are reporting the present case as the tumor cells showed an extraordinarily extensive infiltration involving the cerebrum, cerebellum, brain stem, cranial nerves, and spinal cord down to the lower thoracic level.

Case Report

A 47-year-old Japanese woman was admitted to Kitasato University Hospital on May 31, 1974, because of blurred vision and a mild degree of mental deterioration. She had been well until February, 1974, when she first developed a persistent dull headache followed by blurring of vision. She visited another hospital and was found to have bilateral papilledema. She was referred to our hospital for definitive diagnosis and treatment. Her family history was noncontributory.

Examination. The patient was a well nourished middle-aged woman. She had no café au lait spots or cutaneous nodules. Neurologically, she was slightly inattentive and showed little expression. The optic fundi showed marked bilateral papilledema and retinal hemorrhages. Deep tendon reflexes were slightly increased on the right side but there was no demonstrable motor weakness, sensory disturbance, or cerebellar or meningeal signs. Following admission, metrizamide ventriculography was performed. This revealed generalized narrowing of both lateral ventricles without showing any space-occupying lesions (Fig. 1). Bilateral carotid angiography was considered to be within the normal range. All the venous sinuses were patent. On lumbar puncture, the cerebrospinal fluid (CSF) examination revealed an initial pressure of 240 mm H₂O and, after removal of 9 ml of CSF, the final...
pressure was 130 mm H₂O. The total protein was 19 mg/dl, the glucose 81 mg/dl, the cell count was 2/cu mm, and the cytological study was reported to be negative.

Course. The patient’s state of consciousness gradually deteriorated, and steroid hormone and mannitol therapy were instituted, but the effect of these treatments was transient. A ventriculoperitoneal shunting procedure was performed. This resulted in a temporary improvement of consciousness followed by deterioration, during which time she had episodes of epileptic seizures, forced laughing, and later she became comatose with generalized rigidity. She died on July 21, 1975.

Postmortem Examination. General autopsy findings were bronchopneumonia, benign adenoma of the adrenal cortex, and myoma of the uterus. The brain weighed 1285 gm, and appeared to be moderately swollen with flattened gyri; uncal and tonsillar herniations were noted bilaterally. The pons and medulla oblongata were considerably enlarged. The cut surface of the brain showed granular semitranslucent areas with grayish discoloration. The brain had a moderately firmer consistency in the paraventricular region and in the basal ganglia. The septum pellucidum and corpus callosum were thickened remarkably but no localized mass lesion was found. The ventricular system was markedly narrowed. In the white matter of the right frontal lobe, an area of old softening and hemorrhage was observed (Fig. 2).

Microscopically the lesion was far more extensive and diffuse than was suspected from gross examination. As illustrated in Fig. 3, tumor cell infiltration was observed widely in the cerebral hemispheres, basal ganglia, brain stem, and around the dentate nucleus of the cerebellum. The optic chiasm, and oculomotor and trochlear nerves were also infiltrated by the tumor cells. In the spinal cord, continuous tumor extension was observed down to the T-9 level. A small focus of glial accumulation was found in the posterior column of the lumbar spinal cord without showing a definite neoplastic nature (Fig. 4). The tumor cells took various forms, having oval or fusiform nuclei of moderate

Fig. 1. Metrizamide ventriculogram demonstrating a ventricular system that is almost normal except for a slight narrowing. Left: Frontal view. Right: Lateral view.

Fig. 2. Coronal section of the brain. Tumor mass cannot be observed. Note moderate thickening of the septum pellucidum and corpus callosum.

Fie. 2. Coronal section of the brain. Tumor mass cannot be observed. Note moderate thickening of the septum pellucidum and corpus callosum.
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pleomorphism with bipolar or multipolar processes in which neuroglial fibrils were observed in some fields (Fig. 5 left). Giant cells and mitoses were seen frequently; however, no necrotic foci were found in these areas. In the corpus callosum, tumor cells had a fibrous appearance in a stream-like pattern.

The tumor cells had infiltrated the brain tissue with minimal destruction of pre-existing cerebral architecture. Aggregations of tumor cells were prominently observed around ganglion cells and blood vessels (Fig. 5 right). Subpial glial formation was widely seen in the brain, but subarachnoid spread was only found over the cerebellar cortex.

The pathological diagnosis was gliomatosis cerebri fitting into the category of diffuse cerebrospinal gliomatosis that was proposed by Moore in 1954.¹¹

**Discussion**

The present patient died of intracranial hypertension without exhibiting definitive localizing signs and symptoms. Extensive neuroradiological examinations also failed to demonstrate any localized mass lesions. As many authors have reported, clinical diagnosis of gliomatosis cerebri in its early stage is very difficult. Signs and symptoms of gliomatosis cerebri reviewed by Couch and Weiss in 1974⁴ coincide with those observed in the present case. In almost all cases, neuroradiological studies have no diagnostic value, except for narrowing of the ventricular system observed by Bebin and Tytus,¹ Couch and Weiss,² Finkemeyer and Tzonos,⁶ Nevin,¹² Sarhaddi, et al.,¹⁵ and us in the present case. In its early stage, it is necessary to differentiate “encephalitis” and benign intracranial hypertension of various causes. Lack of focal signs and negative radiological studies except for narrowing of the ventricles, however, rather point to the presence of gliomatosis cerebri.

Pathologically, in the present case malignant astrocytic cells showed exceptionally widespread infiltration in the central nervous system with the preservation of pre-existing anatomical structure. These histological features are considered similar to those reported by Nevin¹² and others. Infiltration of tumor cells into the optic chiasm, and oculomotor and trochlear nerves is often seen in cases of gliomatosis cerebri,²,⁵,¹⁰,¹¹,¹², eighteen but tumor extension into the spinal cord has


**FIG. 4.** Isolated focal glial accumulation in the posterior column of the lumbar spinal cord. H & E, × 48.
FIG. 5. Photomicrographs of the tumor cells. Left: Fine neuroglial fibrils are observed. PTAH, × 300. Right: Perineuronal aggregation of tumor cells. Tumor cells infiltrate diffusely in the brain with minimal destruction of pre-existing structure. H & E, × 150.

been reported in only three cases. Moreover, infiltration as far down as the lower thoracic spinal cord has never been reported in the world literature.

There has been a quite interesting discussion concerning the oncogenesis of gliomatosis cerebri. The possibilities considered were whether the condition is caused by widespread glial cells with a dysgenetic abnormality of blastomatous malformation transforming to neoplastic cells, or whether it is an astrocytoma with extraordinarily widespread extension. The latter was called "astrocytoma diffusum" by Elvidge, et al.

In the present case, it is difficult to conceive of this tumor spreading so rapidly and diffusely from a unicentric focus. The presence of discrete glial concentrations in the lumbar spinal cord found in the present case and also reported by Sarhaddi, et al., may support the process of widespread neoplastic transformation as a cause of diffuse cerebrospinal gliomatosis.

References

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