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Magnetic resonance imaging determination of gliomatosis cerebri

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Summary. Gliomatosis cerebri is a rare condition characterized by diffuse overgrowth of large portions of the brain and spinal cord by glial cells in varying stages of differentiation. The tumor process is primarily an infiltrative, rather than a destructive one. Hence, pre-operative diagnosis by traditional imaging studies, including computed tomography (CT), has been difficult. Magnetic resonance imaging (MRI), with its unique sensitivity for cerebral pathology, is an ideal modality for demonstrating this lesion. We present three cases of gliomatosis cerebri in which high-field MRI clearly delineates the extent of the pathologic process.

Key words: Gliomatosis cerebri – MRI

Gliomatosis cerebri is an unusual condition characterized by diffuse overgrowth of large parts of the central nervous system by glial cells, with preservation of the underlying neuronal architecture [1]. Clinical diagnosis is difficult since initial symptoms are frequently subtle and nonlocalizing. Both computed tomography (CT) and angiography may yield equivocal results. Occasional case reports have demonstrated diffuse mass effect without distinct delineation of the tumor [2, 3]. Magnetic resonance imaging (MRI) offers unique sensitivity and is clearly able to depict the presence and extent of this lesion. This report will discuss the MRI findings in three patients with this rare tumor.

Patients and methods

Three patients, two male and one female, aged 13, 19, and 49 years respectively, were examined on a General Electric 1.5 tesla (T) Signa scanner using T1 and T2 weighted spin-echo pulsing sequences. An initial T1 weighted sagittal scan was obtained using a repetition time (TR) of 600 ms and an echo delay time (TE) of 20 or 25 ms. This sequence was followed by T2 weighted axial scans employing a TR of 2000 or 2500 ms and TE's from 30 to 80 ms. Sagittal or coronal scans employing similar T2 weighted sequences completed the study. Slice thickness was 5 mm on a matrix of 256 × 128. CT studies on third- and fourth-generation scanners had been done prior to MRI. All patients underwent brain biopsy.

Results

The clinical presentation and CT findings varied; however, the MRI picture revealed similar findings in all cases. The biopsy specimens all demonstrated

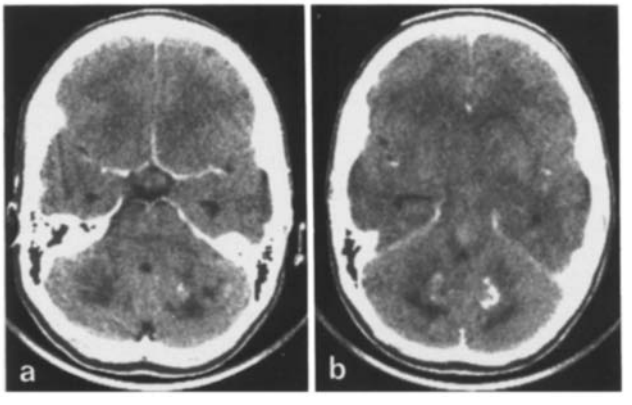

Fig. 1 a and b. *Case 1.* **a** Scan through optic chiasm and mid-pons. **b** Scan through level of basal ganglia and pontomesencephalic junction. Contrast-enhanced CT reveals diffuse mass effect involving midline structures, with enlargement of the pons and optic chiasm, and compression of the ventricles. Enhancement is seen solely in the superior aspect of the pons. The cerebellum demonstrates bilateral low densities associated with calcifications, presumably dystrophic.

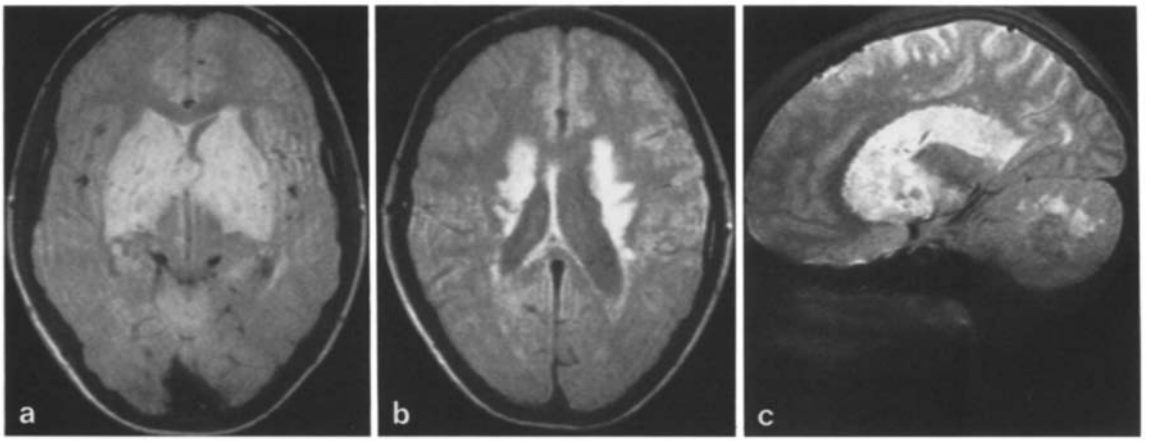

Fig. 2a–c. *Case 1.* **a** and **b** Axial. TR = 2000 ms, TE = 30 ms. **c** Parasagittal. TR = 2000 ms, TE = 60 ms. Axial and parasagittal T2WI show bilateral and symmetric hyperintensity of the basal ganglia, internal and extreme capsules, corona radiata, centrum semiovale, anterior thalami and septum pellucidum, with associated compression of the right frontal horn. Cerebellar involvement is also present

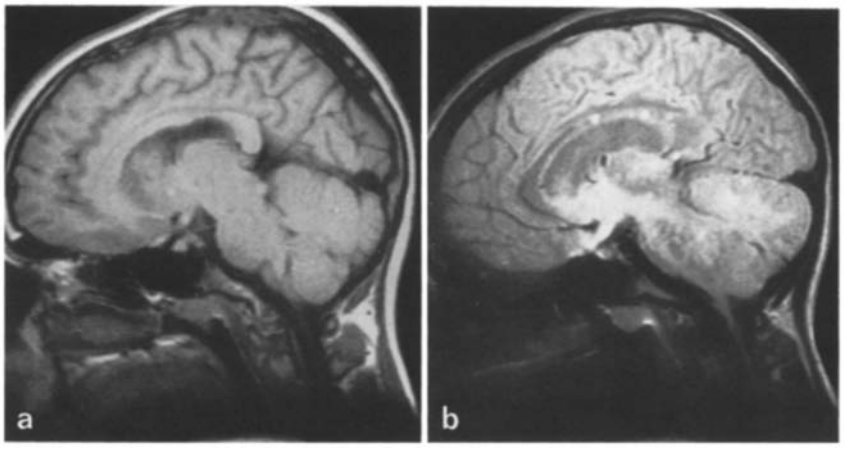

Fig. 3a and b. *Case 1.* Parasagittal view. Comparison of T1WI and T2WI for examination of gliomatosis cerebri. **a** T1WI. TR = 600 ms, TE = 20 ms. **b** T2WI. TR = 2000 ms, TE = 30 ms. Note enlargement of the optic chiasm, hypothalamus, midbrain and pons, which are isointense on T1WI and hyperintense on T2WI. Additional involvement of the cerebellum is demonstrated on T2WI

diffuse overgrowth of astrocytes and rounded immature glial cells. Mitotic figures were rare, and there was no evidence of neovascularity or of areas of necrosis. These findings were felt to be consistent with gliomatosis cerebri.

Case 1. A 13-year-old male had progressively worsening school performance and increasing clumsiness over the previous two years. On physical examination he demonstrated briskly reactive pupils, dysarthria, dysmetria of the upper extremities, mild truncal ataxia and diffuse hyperreflexia. His CT scan showed thickening of the optic chiasm and narrowing of the subarachnoid spaces and ventricles, with particular compression of the right lateral ventricle. Hypodensities and calcifications were present in the dentate regions of the cerebellum bilaterally. Contrast enhancement was apparent solely in the superior aspect of the pons (Fig. 1).

MRI using T1 weighted images (WI) revealed thickening of the optic chiasm and hypothalamus, with enlargement of the midbrain and pons (Figs. 2 and 3). Inhomogeneous hypointense signal intensity was present in the cerebellar hemispheres. On T2WI high intensity was seen in the above regions, with additional bilateral involvement of the basal ganglia and periventricular white matter. The septum pellucidum was obliterated.

Case 2. A 49-year-old woman complained of progressive subjective retardation of thought processes and of frontal headaches over a one year period. She then developed exercise-related bilateral upper extremity weakness. CT examination was reported to show a right anterior thalamic mass.

T1WI revealed generalized and fairly symmetric thickening of all midline structures, which converted to increased signal intensity on T2WI (Fig. 4). The optic chiasm, hypothalamus, basal ganglia and thalami, midbrain and pons were diffusely involved and were hyperintense on T2WI. Bilateral extension occurred into the periventricular white matter and cen-

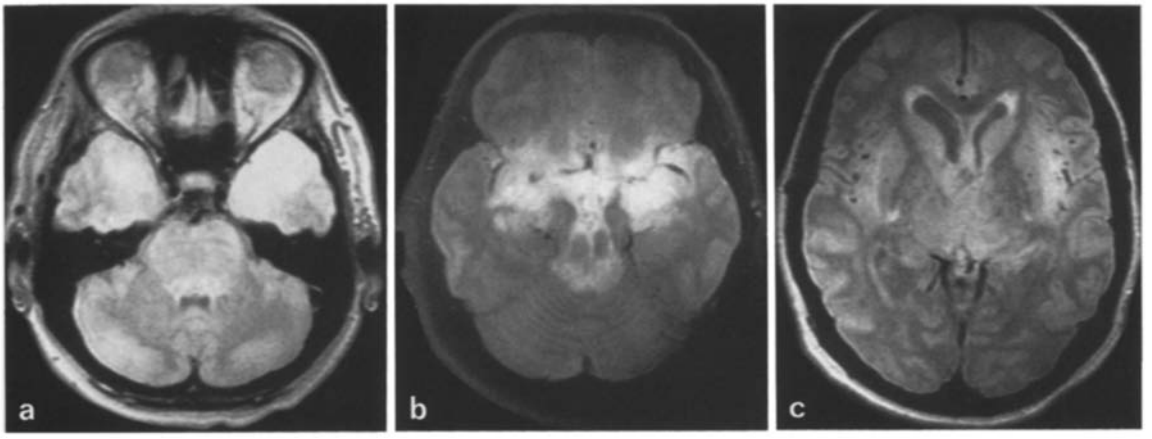

Fig. 4a–c. *Case 2.* **a** TR = 2500 ms, TE = 35 ms. **b** TR = 2500 ms, TE = 70 ms. **c** TR = 2500 ms, TE = 35 ms. Axial T2WI reveal diffuse hyperintensity of the midbrain and pons, enlargement of pons, bilateral involvement of the basal ganglia, thalami and extreme capsules, and sparing of the internal capsules. The left insular cortex and the medial and anterior aspects of the temporal lobes are also involved

trum semiovale. The medial temporal regions, including both white matter and cortex, were also affected. The septum pellucidum was thickened and the third ventricle and aqueduct were compressed, resulting in obstructive hydrocephalus.

Case 3. A 19-year-old male with partial complex seizures presented with a non-enhancing hypodense mass on CT in the region of the optic chiasm and hypothalamus extending into the right temporal lobe. A partial resection of his right temporal mass was performed, followed by radiation therapy and local chemotherapy. Over the next 15 months he developed progressive bilateral loss of visual acuity, ataxia and diminished dexterity of the right hand. Repeat CT examination demonstrated widening of the optic chiasm and hypothalamic structures with obliteration of the suprasellar cistern. The wings of the ambient cistern were splayed. Low density was present diffusely in the cerebral white matter, right caudate nucleus and uncus, and perivermian regions. No discrete areas of abnormal contrast enhancement were visualized.

The MRI examination demonstrated thickening and abnormal signal in several contiguous areas with the suprasellar region, including optic chiasm and hypothalamic structures, being most profoundly involved. The subfrontal and medial temporal white matter, septum pellucidum and peri-third ventricular tissue were affected, as were the right internal capsule, adjacent basal ganglia and periventricular white matter, right more than left. Extension occurred into the midbrain in the region of the aqueduct, the pons, and the cerebellar vermis and white matter. As in the previous cases, the findings were well delineated as a large area of high intensity on T2WI.

Discussion

Gliomatosis cerebri is an uncommon entity. Controversey surrounding its etiology led to a number of appellations being applied to it in the early literature. The condition has been variously reported as "diffuse glioma of the brain," "gliomatous hypertrophy," "blastomatous type of diffuse sclerosis," "diffuse systematic overgrowth of the glial apparatus of the brain", "central diffuse Schwannosis", and "astrocytoma diffusum" [4]. "Gliomatosis cerebri," coined by Nevin in 1938 [5], and "diffuse cerebral glioblastosis," as reported by Scheinker and Evans in 1943 [6], have become the preferred terms, the former being favored in the English literature [1].

Previously reported cases have come from autopsy series. Gross examination demonstrates generalized enlargement of the entire brain or large portions of it. The brain is heavy and in the affected regions the gyri are swollen and flattened [4, 7]. Gray and white matter may be involved, the gray matter having increased consistency and granularity [8] and the white matter revealing areas of thickening and myelin destruction [1, 4, 7, 9]. Demarcation between gray and white matter in affected regions is lost. Any part of the central nervous system may be involved. The process has been described in the cerebral hemispheres, basal ganglia and thalami, optic chiasm, midbrain and cerebral peduncles, brainstem, cerebellum and spinal cord [1, 7, 8]. Local involvement of the leptomeninges has also been found [4, 7].

Microscopically there is extensive infiltration of both gray and white matter by neoplastic glial cells which tend to arrange themselves in a perineuronal, perivascular and subpial distribution [2, 7, 8]. The underlying anatomical architecture is preserved, except in areas of extremely dense cellular overgrowth.

Likewise, the degree of demyelination correlates with the extent of neoplastic involvement. There is no definite tendency toward local tumor mass formation [1, 7]. The neoplastic cells are generally of the astrocytic series and are found in all stages of differentiation [1, 7]. Areas of marked cellular pleomorphism, chromosomal variations and mitotic figures are occasionally found [1, 4].

Clinical signs and symptoms are usually non-specific and non-focal, and are disproportionately mild compared to the extent of parenchymal involvement, reflecting the diffuse yet generally non-destructive nature of the process. The course is most often marked by progressive mental deterioration, personality changes, variable motor deficits, and seizures. Signs of increased intracranial pressure are not infrequent late in the course of illness. Although all age groups are susceptible, the highest incidence occurs in the third and fourth decades. The disease is progressive and duration can last from weeks to years [1, 9]. A favorable response to radiation therapy has been reported, although long-term control of the disease is unlikely [7, 9].

Early reports favored the theory that the process results from a widespread blastomatous transformation related to a congenital malformation of glial tissue. The extensive demyelination suggested to some a blastomatous form of cerebral sclerosis. Later reports have argued that this represents a primary neoplastic dedifferentiation of glial tissue that has arisen simultaneously over a wide field [9]. It is currently believed that this tumor has no distinctive pathologic properties apart from the general group of gliomas, and simply represents a diffuse confluent glioma [10].

The MRI examinations in our patients demonstrated certain constant and, perhaps, stereotypical findings. In each case there was diffuse and more or less symmetric thickening of midline structures. The involved regions were of mixed, but generally low intensity on T1WI, and were of uniformly high intensity on T2WI (Fig. 3). The optic chiasm and hypothalamus were invariably involved, as were the basal ganglia and thalami, although to different extents. Extension into the midbrain and pons was typical, and in two cases the cerebellum was also affected. The cerebral white matter was involved to varying degrees (Fig. 2). Hyperintensity in white matter tracts was felt to represent tumor spread alone or in conjunction with secondary destruction of myelin fibers. Although there was overgrowth and obliteration of the septum pellucidum in all patients, in only one case was there additional compression of the third ventricle and cerebral aqueduct sufficient to cause obstructive hydrocephalus.

The diffuse infiltrative nature of this process renders a preoperative diagnosis by classical neuroradiologic studies impossible. With CT it is possible to recognize mass effect throughout large areas of the brain; however, relative lack of contrast enhancement limits full delineation and characterization of the tumor process. In the few reported cases imaged by this modality, most of the scans were either entirely negative or were suggestive of focal mass affect. The rare occurrence of contrast enhancement was found to correlate with regions of tumor necrosis or hemorrhage [2, 3]. In contradistinction, as our cases illustrate, the changes produced by this entity on MRI can be profound. In all cases MRI reveals a diffuse contiguous central high intensity mass on T2WI. The findings presumably reflect the prolonged T2 effect of the neoplastic tissue, and perhaps, of the associated myelin destruction. The neoplastic involvement of the white matter produces MRI changes (high intensity on T2WI) similar to those of confluent multiple sclerosis. MRI enables accurate depiction of the extent of parenchymal involvement. Gliomatosis cerebri, because of its lack of contrast enhancement and non-specific clinical findings, was a diagnostic dilemma in the pre-MRI era. MRI allows unambiguous delineation and diagnosis of this lesion.

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