Clinical diagnosis of gliomatosis cerebri: report of three cases

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Abstract Distinction of gliomatosis cerebri (GC), a rare entity characterized by a widespread infiltration of the brain by tumor, from diffuse glioma is a difficult clinical problem. Most previously reported cases of GC have been autopsy cases because of the lack of objective and quantitative clinical diagnostic criteria. In order to better define this entity, we report the neuroradiological and pathological findings of three cases of GC. Three patients (one man and two women, aged 46–71 years) presented with symptoms of mild increased intracranial pressure, cognitive impairment, or seizure. Magnetic resonance imaging (MRI) was done with T1-weighted images after gadolinium injection, and with T2-weighted images and fluid attenuated inversion recovery (FLAIR) in all cases. Histological confirmation of glial proliferation was obtained in all cases by craniotomy. The topography of the tumoral infiltration was characteristic, involving mainly the white matter, basal ganglia, thalamus, and commissural fibers. More than two cerebral lobes were affected. Contrast enhancement was absent, and mass effects were minimal compared with the extent of tumoral infiltration, but one patient presented with a small frontal enhanced mass during the clinical course. The pathological analyses demonstrated infiltration of the brains by variably differentiated neoplastic glial cells with destruction of the myelin sheath, but the involved axis cylinder and neuronal cells were preserved. Diagnosis of GC should be faithful to the pathological diagnosis criteria of Scheinker and Evans, and therefore the precise assessment of MRI findings according to these criteria is required for clinical, antemortem diagnosis of GC.

Key words Gliomatosis cerebri · MRI · Clinical diagnosis

Introduction

Gliomatosis cerebri (GC), a rare form of neuroepithelial tumor in which vast areas of the brain are infiltrated by glial cells, was first described and named by Nevin in 1938. The pathological diagnostic criteria were defined in 1943 by Scheinker and Evans, including diffuse enlargement of affected regions with preservation of the general configuration, infiltration of normal brain tissue by proliferating glia, and partial damage to the brain tissue characterized by destruction of the myelin sheath with only slight involvement of the axis cylinder and nerve cells. The World Health Organization (WHO), in its classification of brain tumors, describes GC as a diffuse glial tumor extensively infiltrating the brain, involving more than two lobes (frequently bilaterally), and often extending to infratentorial structures. Therefore, the diagnosis of GC should be limited to patients who present with diffusely infiltrative glioma without an obvious focal tumor mass. However, it is difficult to distinguish GC from diffuse glioma in the clinical diagnosis, and therefore most previously reported cases of GC have been autopsy cases. However, the resistance to therapy and poor prognosis of GC, equal to that of glioblastoma, make it necessary for neurooncologists to give adequate information to patients and their families, including clinical features and treatment outcome.

Recent advances in diagnostic methods, based on magnetic resonance imaging (MRI), have increased the amount of information available for diagnosis of GC. The clinical diagnosis of GC should be based on a combination of radiological and pathological evidence. The authors recently encountered three cases of GC in which we were able to make the clinical diagnosis. The aim of this report is to present the radiological and pathological findings of these three cases, and to better define the clinical diagnostic criteria in order to allow reliable antemortem diagnosis of GC.
Case reports

Case 1

A 54-year-old man was admitted with a 2-month history of head heaviness and depressive mood. Neurological examination on admission revealed a masklike countenance, memory impairment, disturbance of calculation, mild right hemihypesthesia, and left cerebellar hemispheric symptoms. Routine laboratory examinations, including serological studies, yielded normal results. The cerebrospinal fluid showed a mild increase of initial pressure, but it was clear with a normal cell count, protein, and glucose and with negative oligoclonal bands and myelin basic protein. Initial computed tomographic (CT) findings before and after contrast enhancement showed slight effacement of the sulci of the right temporal lobe, with unremarkable mass effect, and slight low density in the white matter of the right temporal lobe and the right external capsule. (Fig. 1A, B) On $T_2$-weighted magnetic resonance imaging (MRI), broad and nodular high intensity in the region noted above extended to the contralateral frontal lobe, hypothalamus, corona radiata, brain stem and cerebellar vermis. The lesion was poorly demarcated and not enhanced by gadolinium-diethylenetriaminopentaacetic acid (Gd-DTPA) (Fig. 1C–F). A cerebral angiogram showed slight swelling of the right temporal lobe without tumor stain. The lesion was noted as a slightly high uptake of thallium-201 scintigraphy. Differential diagnosis from low-grade glioma, viral or parasitic encephalitis, and demyelinating encephalopathies was difficult, and right anterior temporal lobectomy was performed under craniotomy. Macroscopically, the resected brain tissue revealed reactive gliosis in the white matter by Holtzer stain (Fig. 2A), but Klüver-Barrera stain revealed no obvious destruction of myelin. Microscopically, there were atypical oligodendrocyte-like cells infiltrating edematous white matter with reactive astrogliosis. The tumor cells predominantly had round to oval hyperchromatic nuclei and perinuclear haloes with distinct cell borders, and pre-

Fig. 1. Enhanced computed tomography (CT) on admission (A, B) showed slight effacement of sulci and low density in the white matter of the right temporal lobe with no contrast enhancement. $T_2$-weighted magnetic resonance imaging (MRI) (C, D) showed broad and nodular high intensity in the region noted in the right temporal lobe, bilateral basal ganglia, hypothalamus, brain stem, and cerebellar vermis. The lesions were poorly demarcated and not enhanced by gadolinium-diethylenetriaminopentaacetic acid (Gd-DTPA) (E, F)