Primary demyelinating disease simulating glioma of the corpus callosum

Report of three cases

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Computerized tomography (CT) has made it easier to distinguish tumoral from nontumoral diseases of the central nervous system. In the presence of mass effect, however, this distinction may be difficult or impossible to make. Primary demyelinating disease may occasionally present as a focal cerebral mass. The authors report three cases of primary demyelinating disease of the brain involving the corpus callosum and periventricular white matter and associated with mass effect, which proved difficult to differentiate from infiltrating “butterfly” gliomas.

Keywords: demyelinating disease, multiple sclerosis, central nervous system, brain tumor, computerized tomography.

The computerized tomography (CT) findings in primary demyelinating processes of the central nervous system (CNS) have been described, including the CT appearance of multiple sclerosis, the most common of the demyelinating diseases. The CT findings in multiple sclerosis include: 1) focal areas of low attenuation in the white matter, 2) areas of normal or low attenuation in the white matter with focal contrast enhancement seen in the active phase of the disease, and 3) localized or diffuse cerebral atrophy. It should be noted that, particularly in the early stages of the disease, normal CT scans are frequently encountered.

Focal cerebral space-occupying lesions in demyelinating disease are unusual, but have been reported in patients with progressive multifocal leukoencephalopathy, adrenoleukodystrophy, and recently in a patient with multiple sclerosis. In the presence of a mass lesion, it may be difficult to differentiate demyelinating disease from a neoplasm. We present three cases of primary demyelinating disease involving the corpus callosum and periventricular white matter associated with mass effect and contrast enhancement which were essentially indistinguishable from infiltrating “butterfly” gliomas.

Case Reports

Case 1

In this 42-year-old white woman, multiple sclerosis had been diagnosed in 1959. Symptomatology had been characterized by bilateral lower extremity parasthesias. After multiple relapses, the patient’s condition had been stable since 1977. In January, 1978, the patient presented with progressive, persistent, right-sided headaches leading to confusion and increasing somnolence. Neurological examination revealed decreased attention and short-term memory, a left temporal field cut, and decrease in position sense. Cerebrospinal fluid (CSF) analysis showed elevated protein (80 mg/100 ml) and glucose (77 mg/100 ml), normal immunoglobulin G value, and 16 white blood cells (15 lymphocytes).

Radionuclide brain scan demonstrated increased...
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uptake in the centroparietal region, and CT (Fig. 1 left) showed a deep bilateral lesion in the white matter, involving the posterior corpus callosum, and characterized by low attenuation with mass effect and contrast enhancement. Cerebral arteriographic studies, including bilateral carotid and vertebral artery examinations, failed to show abnormal vascularity. Mainly because of the CT findings, cerebral surgical exploration was seriously considered.

Following a 10-day course of steroids, analysis of the CSF was normal for protein and glucose. A repeat radionuclide brain scan was normal, and a control CT study showed improvement. Two months later, a repeat CT scan revealed no evidence of mass or enhancement (Fig. 1 right).

Case 2

This 23-year-old white woman developed frontal headaches and photophobia, and became quiet and withdrawn. The neurological examination demonstrated a flat affect with inappropriate response. Frontal signs, including glabellar, snout, and rooting reflexes, were detected. Hoffman and Babinski reflexes were also evident.

Computerized tomography (Fig. 2 left pair) demonstrated a large, asymmetrical, periventricular mass lesion involving the corpus callosum with peripheral contrast enhancement. The differential diagnosis included “butterfly” glioma of the corpus callosum, and a biopsy was performed. The pathological findings from the brain biopsy were equivocal: “possible low-grade glioma; demyelinating disease cannot be excluded.” A repeat CT scan after 6 weeks of steroid therapy showed less mass effect and contrast enhancement (Fig. 2 right pair), despite the fact that the clinical improvement was minimal. A radionuclide scan at this time was positive, with increased uptake bifrontally. Cerebral angiography demonstrated an avascular mass lesion involving the corpus callosum.

Repeat brain biopsy, 10 weeks after initial surgery, confirmed a primary demyelinating process. The neuropathological findings included marked demyelination in the white matter with sparing of the cortical neurons and axons. Intense active gliosis was present in the region of demyelination. Macrophages contained myelin debris, periodic acid-Schiff (PAS)-positive granules, and lipid droplets (Fig. 3). Steroid
Case 2

A 1-μ thick plastic section of cerebral tissue from a brain biopsy. Loss of myelin around the axons is extensive (arrows). Macrophages containing round, lucent lipid droplets predominate in the parenchyma and in the perivascular space. Reactive astrocytes are present (arrowhead). Toluidine blue, × 1000.

FIG. 4. Case 2. Follow-up scans showing marked improvement. The areas of hypodensity and mass effect have essentially disappeared. Also, the enhancement is no longer evident. Mild enlargement of the ventricles has occurred.

therapy was continued, and the last follow-up CT scans 14 weeks later showed return toward normality (Fig. 4).

Case 3

This 38-year-old man had a progressive CNS disease, manifested by increasing leg weakness and spasticity as well as bladder and bowel incontinence since 1965. Previous CSF studies were negative, and CT had shown only generalized atrophy. The patient presented at this time with generalized seizures which were increasing in frequency. He had also developed a fever. Physical examination revealed a slightly febrile (99.2°F), lethargic, but arousable patient. Cranial nerves were normal. A spastic quadriplegia with decreased muscle mass was present, with ankle clonus and extensor plantar response bilaterally. Analysis of the CSF showed elevated protein with normal IgG. Glucose was normal and no abnormal cellularity was noted.

Computerized tomography revealed a large bilateral lesion in the frontal lobes with involvement of the corpus callosum and an enhancing rim (Fig. 5). The possibility of brain abscess was considered, and treatment of the patient with antibiotics was initiated. Needle biopsy of the brain was reported to show a demyelinating process with no evidence of tumor or abscess. Following discharge, the patient was stable, taking Dilantin (phenytoin) for control of seizures. Four months later, he died from aspiration pneumonia.

Neuropathological findings at autopsy revealed cerebral demyelination in the occipital and frontal lobes with degeneration of some of the spinal cord tracts. Bilateral adrenal atrophy led to consideration of adrenoleukodystrophy or adrenomyeloneuropathy. Additional studies, however, including histochemis-
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Fig. 5. Case 3. Postcontrast computerized tomography scans demonstrate peripheral enhancement of bilateral white matter hypodense lesions in the frontal area. There is deformity of the frontal horns secondary to involvement of the corpus callosum.

try, electron microscopy, and review of adrenal material, did not support these diagnoses. Search for CNS viral inclusions was negative. The final diagnostic impression was that of multiple sclerosis.

Discussion

With the introduction of CT, it has become easier, in many instances, to distinguish tumoral from non-tumoral disease of the CNS. With the newer generation scanners we are able to clearly differentiate white from gray matter. Certain patterns of contrast enhancement are quite characteristic for specific pathological processes.

Primary demyelinating disease of the CNS generally does not produce focal or diffuse mass lesion. This feature has been used to distinguish demyelinating processes from brain tumors, as well as from inflammatory disease. If, however, areas of demyelination and associated inflammatory cellular response are marked and confluent, this may result in a focal space-occupying lesion often associated with contrast enhancement due to loss of integrity of the blood-brain barrier. These findings may be hard to differentiate from those encountered in tumor and pure inflammatory lesions.

Progressive multifocal leukoencephalopathy may present as a cerebral expanding lesion. Also, in adrenoleukodystrophy, inflammatory zones may be found in association with large areas of gliosis and astrocytosis, and may result in a mass effect.

Recently, mass effect and peripheral contrast enhancement have been demonstrated on CT in a patient with multiple sclerosis. In this case, in contrast to our patients, the corpus callosum was not involved. Our three cases appear to represent slightly different manifestations of primary demyelinating disease. Both progressive multifocal leukoencephalopathy and adrenoleukodystrophy were excluded by neuropathological studies in Cases 2 and 3 and by the history in Case 1.

The most instructive feature of our cases is the importance of considering primary demyelinating disease in the differential diagnosis of cerebral mass lesions involving and infiltrating the corpus callosum. When associated with mass effect and contrast enhancement on CT, a diagnosis of brain tumor or abscess may be considered, and inappropriate treatment instituted. Even brain biopsy, which was performed in two of our cases and seriously contemplated in a third (Case 1), may give equivocal results. In cases such as these, conservative management with steroid therapy and serial control CT scans may be the best means of substantiating a diagnosis of demyelinating disease.

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