Primary Amyloidoma of the Brain Parenchyma

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Amyloidoma can occur within the brain parenchyma. Periventricular amyloidomas developed in a man aged 69 years as gadolinium-enhancing lesions on magnetic resonance imaging. The lesions were composed of amyloid AL with congophilia resistant to potassium permanganate. There was no evidence of systemic amyloidosis or an underlying inflammatory or neoplastic disorder.

Amyloid is an insoluble fibrillar protein not stored in normal tissue. Under pathologic circumstances, it is deposited in the extracellular and intracellular spaces to produce amyloidosis. Proteins or polypeptides form characteristic fine fibrils. Both systemic and tissue-specific deposits have been reported in humans. The factors that determine nodular vs diffuse amyloid accumulation remain uncertain. Amyloid nodules as localized space-occupying lesions are called amyloidomas. They appear in the settings of plasma cell dyscrasia, renal cell carcinoma, and medullary carcinoma of the thyroid and rarely without generalized amyloidosis or hematologic abnormalities. The major subunit protein in all primary amyloidomas is derived from immunoglobulin light chains (AL-\(\lambda\) subtype).

Primary amyloidomas have been described within soft tissue of various organs, as well as salivary glands and the vertebral axis. Within the central nervous system, neuraxial or extra-axial masses arise.

Report of a Case

A man aged 69 years noted an occasional tendency of leaning toward the right side without experiencing falls during a 1-year period. His memory had been poor for approximately 20 years. His mother (aged 94 years) had senile dementia. At the initial evaluation, results of the examination were unremarkable save for difficulties in short-term memory. The T1-weighted magnetic resonance image (MRI) with gadolinium enhancement showed 5 lesions in the tegmentum of the upper right pons, periaqueductal gray matter, and right and left subinsular region (extreme capsule) and adjacent to the midbody of the left lateral ventricle (subependymal; Figure 1). The lesions were hyperintense on T1-weighted MRI and showed gadolinium enhancement. Findings on computed tomographic scans of the abdomen, pelvis, chest, and bone were normal. Two brain biopsies were performed. Results of the first were nondiagnostic. After the first biopsy, the patient’s imbalance worsened; he was fatigued and his speech became slurred. Results of the neurological examination were remarkable for mild dysarthria. Strength and sensation, including proprioception, were normal. No dysmetria or dysdiadochokinesis was detected. His gait was wide-based, and he had slight difficulty initiating locomotion. Results of serum protein electrophoresis were normal. The cerebrospinal fluid was acellular, with levels of glucose, protein, IgG, and albumin within reference ranges, and no banding on agarose gel electrophoresis. No bacterial or fungal growth, cryptococcal antigen, or positive VDRL test results were found. Total-body positron emission tomography using fludeoxyglucose F 18 showed unremarkable findings.
During the course of 3 months, the pontine lesion grew. The second biopsy was performed 4 months after the first. The second biopsy specimen was investigated using standard protocols (hematoxylin-eosin and Congo red staining), polarized light examination, and immunohistochemistry (prealbumin and λ and κ light chains). For immunoglobulin heavy chain (IgH) gene rearrangement analysis, DNA was isolated from paraffin-embedded tissue using the Qiagen DNA Mini Kit (Qiagen, Valencia, Calif) according to the manufacturer’s protocol. Consensus primers for the complementarity-determining region III of the IgH gene were used for polymerase chain reaction. The polymerase chain reaction products were separated on a 12% polyacrylamide gel.

Numerous deposits of acellular amorphous material that bound Congo red stains and showed apple green birefringence under polarized light were found within the neurophil (Figure 2). The material was immunoreactive for the λ light chain (Figure 3), with negative findings for prealbumin. Results of the IgH gene rearrangement analysis did not show any evidence of a clonal cell population of the B-lymphocyte lineage.

Investigation failed to reveal systemic amyloid. Results of urine analysis for Bence Jones protein and biopsy of abdominal fat were negative. Computed tomography of the chest and abdomen, radionuclide scan of bone, echocardiography, and nerve conduction studies had normal findings. The electrocardiogram showed no conduction anomaly.

**COMMENT**

We herein report the case of a patient with primary amyloidomas of the brain parenchyma and a clinical syndrome characterized by cognitive decline, cerebellar dysfunction, and focal motor signs. Imaging studies showed 5 lesions in the subcortical white matter of the cerebral hemispheres as well as the brainstem. The lesions were hyperintense on T1-weighted images and showed gadolinium enhancement. These imaging characteristics are consistent with what is reported in the literature.1 However, the masses did not explain the neurological findings. We assumed that amyloid deposition was more widespread and of microscopic density, and thus not identified on MRI studies.

Evaluation of Congo red staining of biopsy material under polarizing microscopy visualized the typical pattern of apple green birefringence. As in most of the literature cases, the biochemical subtype of our patient’s amyloid was AL λ. This type is seen in primary amyloidoma, primary amyloidosis without preceding or coexisting disease, and multiple myeloma.

Our case represents the 12th report of a primary amyloidoma in the brain parenchyma (Table). Another 10 examples of primary intracranial extra-axial amyloidomas have been described elsewhere.11-20 Cases outside the cranial cavity have been reported more frequently from the vertebral spinal axis, lung, breast, soft tissues of the legs, mediastinum, nasopharynx, larynx, urinary bladder, and gastrointestinal tract.21-27

Pathogenesis of primary amyloidoma is unclear. Pambuccian et al24 described a 78-year-old man with a scapular amyloidoma, in whom disease progressed within several months to symptomatic generalized amyloidosis with IgM-λ monoclonality (light chain disease). Laeng et al28 found IgH gene rearrangement in 2 of 7 cases of nervous system amyloidomas suggestive of an underlying B-cell neoplasia. We did not find evidence of a clonal B-cell population in the biopsy material of our patient.

The brain parenchyma can be affected by other types of amyloid. In Alzheimer disease, β-amyloid protein is deposited within senile plaques and as congophilic angiopathy. Familial amyloidosis usually affects the peripheral nervous system (AF subtype, prealbumin).
Results of immunohistochemical staining for β-amyloid protein and prealbumin were negative in our case. Evidence of local or systemic light chain disease was absent. Our patient underwent repetitive analysis of peripheral blood for monoclonal populations and of bone marrow for clonal expansion.

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REFERENCES


Table. Reports of Primary Amyloidoma of the Brain Parenchyma

<table>
<thead>
<tr>
<th>Source</th>
<th>Presentation</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saltykov,1 1935</td>
<td>Psychiatric</td>
<td>White matter, cortex</td>
</tr>
<tr>
<td>Harris and Rayport,2 1979</td>
<td>Focal seizure</td>
<td>Frontal white matter</td>
</tr>
<tr>
<td>Spaar et al,3 1981</td>
<td>Woman aged 46 y with a 4-y history of progressive visual loss, associated headaches, and depression</td>
<td>Left occipital lobe</td>
</tr>
<tr>
<td>Townsend et al,4 1982</td>
<td>Case 1, cognitive decline; case 2, visual field defect</td>
<td>Case 1, frontal white matter; case 2, occipital white matter</td>
</tr>
<tr>
<td>Hori et al,5 1988</td>
<td>Autopsy finding in an asymptomatic man aged 60 y</td>
<td>White matter of right occipital lobe, basal ganglia</td>
</tr>
<tr>
<td>Cohen et al,6 1992; Vidal et al,6 1992</td>
<td>Man aged 32 y with 4-y history of secondary generalized seizures, decline of cognitive ability, personality change, and papilledema</td>
<td>White matter, left frontal lobe, left cerebellum, pons</td>
</tr>
<tr>
<td>Erikson et al,7 1993</td>
<td>Autopsy report of a man aged 76 y with sudden onset of seizures 15 y before death, recurrence of tumor 7 y after surgery, and lethal hemorrhage 8 y after recurrence</td>
<td>Right parietal ventricle</td>
</tr>
<tr>
<td>Lee et al,1 1995</td>
<td>Woman aged 61 y with 12-mo history of mental deterioration and tonic-clonic seizures</td>
<td>Left parietal lobe</td>
</tr>
<tr>
<td>Smadja et al,9 2000</td>
<td>Woman aged 46 y with 7-y history of epilepsy</td>
<td>White matter of right frontal and temporal lobes</td>
</tr>
<tr>
<td>Blatter et al,11 2001</td>
<td>Woman aged 26 y with paresis of right hand and dysarthria</td>
<td>White matter lesions in the left parieto-occipital region, and left coronal radiata, and several small lesions in the right hemisphere</td>
</tr>
<tr>
<td>Tabatabai et al (present case)</td>
<td>Man aged 69 y with 12-mo history of drifts to the right side and long-standing history of cognitive decline</td>
<td>Tegmentum of the upper right pons, periaqueuctal gray matter, and right and left subinsular region (extreme capsule) and adjacent to the midbody of the left lateral ventricle (subependymal)</td>
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