Central nervous system amyloid presenting as a mass lesion

Report of two cases

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Amyloidomas of the central nervous system are rare. Two cases involving middle-aged patients with neurological symptoms are presented. Massive focal accumulations of amyloid in the cerebral hemispheres were confirmed pathologically.

KEY WORDS • central nervous system amyloid • primary amyloidosis • amyloidoma

Focal lesions secondary to amyloid deposition in the central nervous system (CNS) are rare. Deposits of amyloid in cortical senile plaques or within cerebral vessel walls (congophilic angiopathy) occur more frequently, but these conditions are usually diffuse. In 1979, Harris and Rayport reported a patient with headache and seizures who was found to have a large frontal lobe deposition of amyloid. Spaar, et al., in 1981, reported a walnut-sized amyloid nodule in the occipital lobe of a 46-year-old woman. We wish to report two further cases of cerebral amyloid deposition presenting as mass lesions.

Case Reports

Case 1

This 47-year-old woman's mental functions had gradually deteriorated during the last 3 years of life. She was admitted to the hospital in August, 1968, because of slowly progressive personality changes. During the last year of life, gradual and progressive anemia, dysphasia, dyslexia, and increasing memory loss for recent events was noted. Her health in the past had been excellent except for the removal of a benign thyroid adenoma 8 years prior to admission.

Examination demonstrated mental dysfunction, but no systemic abnormalities were found. Cerebrospinal fluid (CSF) examination revealed 95 mg/dl of protein, no cells, a nonreactive serology, and a flat colloidal gold curve. Routine blood count and urinalysis were normal. A brain radionuclide scan demonstrated a 3 x 7 cm area of abnormal uptake in the left frontal lobe. Carotid angiograms revealed absence of venous filling in the left frontal region. Electroencephalography (EEG) documented transient focal slowing in the frontal area. Since the lesion did not appear to represent a neoplastic growth or vascular problem, the patient was discharged home and died approximately 1 year later. At autopsy only the brain was examined.

On coronal sections of the brain, two areas of firm yellow tissue were found in the cerebral hemispheres. The larger mass was in the left anterior centrum semiovale (Fig. 1), and the smaller involved the right optic radiation. Prominent blood vessels were visible in both lesions. Microscopic examination revealed large deposits of amorphous acellular pink material within the parenchyma of the white matter. Many vessels were surrounded by these deposits (Fig. 2). Perivascular plasma cells and lymphocytes were prominent in some areas. The homogeneous material stained positively with eosin, crystal violet, periodic acid Schiff, thioflavin-T, and Congo red. Polarized light demonstrated the typical birefringence of amyloid. Ultrastructural examination revealed the fibrillar characteristics of amyloid.
Case 1

The patient was a 50-year-old man who presented with a right homonymous hemianopsia in July, 1977. An arteriogram was normal, but the computerized tomography (CT) scans demonstrated an enhancing lesion in the region of the left trigone. In November, 1977, the patient experienced transient episodes of left facial weakness and twitching accompanied by weakness in the left arm. These lasted minutes to hours and occurred sporadically over the next few months. An EEG demonstrated a focal abnormality in the left parieto-occipital area.

Examination in March, 1979, demonstrated the right homonymous hemianopsia, and slight left central facial weakness with mild ptosis. A mild decrease in hearing was noted on the right. The remainder of the neurological examination was normal. Laboratory data revealed a normal total serum protein of 7.1 gm/dl, and albumin of 3.8 gm/dl. No protein electrophoresis was performed. ACT scan revealed the same high-density lesion that had enhanced with contrast injection in 1977, lying within the white matter of the left occipital lobe lateral to the ventricle. Angiograms were normal, and no change was noted since 1977. A craniotomy was performed.

At operation, the ependyma in the left occipital horn was grossly thickened and discolored. A subependymal zone of tissue measuring approximately 8 mm in thickness was grayish-yellow in color and waxy in consistency. Approximately 1 gm of tissue was submitted for pathological examination. The majority was fixed in 10% buffered formalin and the remainder was immersion-fixed in 1.5% glutaraldehyde for routine electron microscopy. Microscopically, the tissue demonstrated large amorphous deposits of pale pink homogeneous material in the subependymal white matter. The majority of the deposits appeared in the parenchyma, although some were adjacent to or involving small vessels (Fig. 3). Congo red staining showed scattered green birefringence in the amorphous deposits. Electron microscopy revealed the deposits to be composed of fibrillar material approximately 7.5 nm in diameter, thus confirming the diagnosis of amyloid. The patient regained his preoperative neurological status and was discharged home. At the present time (April, 1981), the patient is well with no recurrence of symptoms.

Discussion

Amyloid is composed of protein fibrils measuring 7.5 to 10 nm in width, and focal or diffuse depositions have been documented in most tissues. Glenner has suggested the term “β-fibrilosis” to encompass all forms of amyloidosis. This would be consistent with the fibrillar pleated-sheet structure of the deposits which produces the characteristic birefringence after Congo red staining.
Cerebral amyloidoma

Distinct clinical entities are recognized. “Primary” amyloidosis involves diffuse deposition of amyloid from an immunocyte-derived monoclonal protein. The depositions are usually confined to mesenchymal organs, and no other underlying disease is found. The plasma cell myeloma-associated deposition of amyloid is similar, but the plasma cells in this condition are neoplastic. A “secondary” form of amyloidosis has long been recognized accompanying chronic inflammatory or infectious processes. The amyloid in “reactive systemic amyloidosis,” as termed by Glenner, has been shown in some cases to be composed of A protein in contrast to the immunoglobulin light chains found in “primary” amyloidosis. These deposits tend to be in parenchymal organs. Large deposits of amyloid confined to one organ have been described. These so-called “tumor forming” masses have been found in bone, breast, eyelids, Gasserian ganglia, larynx, lungs, orbit, pituitary, skin, stomach, and urinary tract. The majority of these patients had no other systemic findings of amyloid and no immunoglobulin abnormalities.

Amyloid of the CNS may be an isolated finding or associated with systemic amyloidosis. Central amyloid is found in senile plaques and in congophilic angiopathy. This encrustation of CNS vessels by amyloid leads in some cases to massive cerebral hemorrhage and rarely to foci of demyelination. In 1938, Scholz described perivascular deposition of amyloid (drusige entartung) within brain parenchyma.

A reactive type of amyloid deposit occurs in the brain. Radiation necrosis and vascular malformations have been associated with amyloid deposits. In 1969, Mandibur and Gore demonstrated typical birefringence in two cases of radiation necrosis with amyloid. More recently, Bruni, et al., reported a vascular malformation with amyloid in the surrounding neuropil. Only a small amount of amyloid was present in the walls of the abnormal vessels.

Focal masses of amyloid (amyloidomas) in brain parenchyma rarely have been documented. In 1935, Saltykov described several hazel nut-sized masses in the cerebral cortex of a psychiatric patient. They were waxy in appearance and demonstrated metachromasia with methyl violet staining, thus pointing to their amyloid character. Harris and Rayport presented a case in 1979 of a 28-year-old woman with headaches and focal seizures. A 3.5 × 4.0-cm frontal lesion was found and, at biopsy, large parenchymal deposits of amyloid were demonstrated by special stains and electron microscopy. Anti-kappa and anti-lambda immunofluorescent studies were both positive. A CSF protein electrophoresis showed a moderate increase in kappa light chains and immunoglobulin G (IgG), with a minimal increase in lambda light chains and IgM. Spaar, et al., documented a walnut-sized cerebral mass of amyloid with scattered plasma cells and lymphocytes. The outer border of the mass demonstrated IgM deposits by immunofluorescence. Many vessels contained amyloid, although no vascular malformation was evident. None of these cases had any evidence of systemic disease or blood dyscrasias. Surgical excision in the most recent cases has been beneficial. Our two cases appear morphologically and clinically similar, and the postoperative course in Case 2 was excellent. Amyloidomas in parenchymal organs have a very good prognosis after surgical excision. Although some have recurred after many years, re-excision is the treatment of choice.

The pathogenesis of amyloidomas is unknown. Extramedullary plasmacytomas do not usually produce large amounts of amyloid. Only five out of 272 cases presented by Wiltshaw had demonstrable amyloid on biopsy. Amyloidomas are found at multiple sites, and the majority contain scattered plasma cells, lymphocytes, histiocytes, and occasional foreign-body giant cells. Page, et al., demonstrated immunoglobulins in pulmonary amyloidosis. These may represent “burnt out” plasmacytomas, as suggested by Glenner, and certainly the case presented by Glass, et al., would strengthen this hypothesis. Their patient developed a conjunctival mass which, on biopsy, demonstrated mature and immature plasma cells. Nine years later, this mass was rebiopsied and contained masses of amyloid with only a few scattered plasma...
cells. The histology in the second biopsy was similar to other reports of amyloidomas.

Cerebral amyloidomas are morphologically similar to those in the systemic circulation and appear to enlarge slowly. Although rare, these masses should be considered benign and may be treated surgically if so indicated. The prognosis appears excellent.

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References


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