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Isolated intracerebral light chain deposition disease: novel imaging and pathologic findings☆

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Abstract

Light chain deposition disease (LCDD) is a rare clinicopathologic entity first described in 1976 and is characterized by a monoclonal gammopathy resulting in nonamyloid immunoglobulin light chain tissue deposition. Only four cases of intracerebral LCDD have been previously reported, all in the setting of a known plasma cell dyscrasia or in the presence of local mature plasma cells. We present the first case of intracranial LCDD in the absence of a known plasma cell dyscrasia or local mature plasma cells.

Keywords

Light chain deposition disease; Amyloidoma; Monoclonal immunoglobulin deposition disease; MRI

1. Introduction

Light chain deposition disease (LCDD) is a rare clinicopathologic entity first described in 1976 in two patients with end-stage renal disease with granular deposition of free light chains that did not stain with Congo red on kidney pathologic evaluation [1]. Even in the absence of detectable urine or serum monoclonal immunoglobulin, a single clone of plasma cells is usually responsible for the overproduction of either kappa or rarely lambda light chains that can be demonstrated via immunofluorescence [2]. LCDD most commonly

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presents in the setting of a plasma cell dyscrasia and is associated with multiple myeloma in two thirds of reported cases but may also be associated with other B-cell neoplasms such as lymphoma and chronic lymphocytic leukemia [3,4].

While renal involvement is the most common manifestation of LCDD, it can also involve the heart, liver, lungs, and in rare instances the central nervous system (CNS) [3,5]. Neurological involvement in the setting of LCDD is thought to be largely attributable to systemic protein deposition, which may affect the nerves in a manner similar to that of amyloidosis and like amyloidosis, clinically manifests as a nonspecific polyneuropathy. In very rare instances, large intracranial deposits of LCDD are seen but owe their extraordinary rarity to the blood–brain barrier, which is thought to protect the CNS from circulating polymerized misfolded proteins with only four reported cases of intracerebral LCDD reported in the literature [5]. The case presented herein is the first report of an intracerebral LCDD in the absence of known lymphoproliferative disease or the presence of local plasma cells and serves to widen our appreciation of the various clinical manifestations of LCDD within the CNS.

2. Case report

2.1. History and examination

A 44-year-old woman came to neurosurgical attention after the incidental discovery of a large right frontal mass lesion. In early 2013, after undergoing two breast biopsies, she was found to have elevated serum prolactin levels and subsequent pituitary gland magnetic resonance (MR) imaging incidentally revealed a large right frontal mass. At the time of presentation, the patient disclosed no history of seizures, headaches, or personality changes. A thorough neurologic examination revealed no focal neurologic deficit, her speech was fluent and she had full motor strength in all four extremities.

Dedicated MR imaging of the whole brain revealed a T1 hypointense, T2/FLAIR hyperintense, nonenhancing mass lesion centered in the right frontal lobe superior and middle frontal gyri measuring 4.7×3.9×3.8 cm (anteroposterior×transverse×craniocaudal) with local mass effect and effacement of overlying sulci and subjacent anterior horn of the right lateral ventricle. The large intracranial mass demonstrated no intrinsic magnetic susceptibility artifact to indicate hemorrhage or calcification, complete absence of postcontrast enhancement, and homogeneous facilitated diffusion. Targeted dynamic gadolinium-enhanced axial perfusion imaging of the mass demonstrated no cerebral blood volume as compared to contralateral white matter (Fig. 1).

2.2. Operative course

After a lumbar puncture was performed with 15 cc of clear cerebrospinal fluid (CSF) obtained for cytology and oligoclonal bands, the patient was placed supine on the operating table. BrainLab registration was performed and a careful trajectory was planned. The patient was then prepped and draped in the usual sterile fashion and a 4-cm coronal scalp incision was made. A small 1-cm burr hole was made and the dura was subsequently opened. A biopsy arm was set up and a superficial area was biopsied with four subsequent deeper

biopsy samples then taken. Gelfoam was placed on the surface and a burr hole cover plate was placed. The galea was then closed with 3-0 vicryl and overlying skin was stapled.

2.3. Histological evaluation

Analysis of CSF fluid obtained prior to the burr hole craniotomy revealed benign CSF without evidence of oligoclonal expansion. The frozen histological section showed extensive lymphocytic invasion. On permanent tissue sections (Fig. 2), tissue samples showed large amounts of amorphous eosinophilic, proteinaceous parenchymal, and vascular deposits associated with mild chronic perivascular inflammation. Immunohistochemical staining with appropriate reactive controls revealed strong and diffuse immunoreactivity for kappa light chains and no immunoreactivity for lambda light chains, transthyretin, and amyloid beta with occasional small perivascular T lymphocytes, small mature B-cells, and rare plasma cells. Congo red staining was negative for apple-green birefringence as was fluorescent staining for thioflavin S.

2.4. Postoperative course

The patient's immediate postsurgical course was uneventful and without complication. The patient was discharged home 2 days following surgery on levetiracetam as a seizure prophylactic. Following her uneventful discharge, the patient has since been closely followed by hematology. One month postoperative, bone marrow biopsy and fat pad fine needle aspiration disclosed no evidence of plasma cell dyscrasia, lymphoproliferative disorder, or evidence of amyloid deposition. Serum albumin, IgA, IgG, IgM, beta-2-microglobulin, SPEP, serum kappa, and lambda light chains as well as a 24-h urine protein and complete blood counts all returned values within normal limits as did results obtained 2 and 5 months postoperatively. Follow-up MR imaging obtained 3 months and 5 months postoperatively demonstrated expected small postsurgical changes with no interval change in the size or imaging characteristics of the large intracranial mass. The patient continues to do well with no subsequent seizures.

3. Discussion

LCDD and amyloidosis are both disorders marked by the overexpression and deposition of extracellular misfolded protein, which subsequently leads to end-organ damage. LCDD and amyloidosis are both characterized by the monoclonal expansion of bone marrow plasma cells producing either kappa or lambda light chains that subsequently misfold and form insoluble aggregated beta pleated sheets that deposit in affected tissues [6]. Based both on the type and systemic location of these protein deposits (fibrils), LCDD and amyloidosis can present with clinical presentations as widely varying as renal failure/nephrotic syndrome and restrictive cardiomyopathy.

Within the brain, amyloidosis most commonly presents as scattered parenchymal plaques but amyloid underlies the pathogenesis of numerous other neurodegenerative disorders including Alzheimer's disease, encephalopathy of Kuru, and Creutzfeldt–Jakob disease [7–10]. While amyloid deposition, both within the brain and elsewhere, most commonly presents as small focal deposits within target tissues, it can also present as large tumor-like

deposits. Within the brain, these amyloidomas are the least common presentation with fewer than 40 reported cases in the literature [7,11–13].

Kappa and lambda light chains have also been shown to deposit in a manner similar to amyloid with some amyloidogenic properties, but on closer inspection, stain Congo red negative and are histologically distinct from amyloid and amyloidomas [14–16]. These cases are uniquely designated as LCDD and, in comparison to CNS manifestations of amyloid, are exceedingly rare. Both amyloidomas and intracranial LCDD likely owe their rarity to the presence of the blood–brain barrier, which restricts the crossing and deposition of protein macromolecules and aggregates within the brain [5,16]. To date, there have been only four reported cases of intracerebral LCDD in the literature, and in each instance, the mass was documented to be associated with underlying lymphoproliferative disease or closely associated plasma cells [16].

In the case described herein, the absence of congophilia as well as the lack of immunohistochemical staining for beta amyloid with strong positive staining for kappa light chains on permanent sections reveals that our case is a rare instance of intracranial LCDD. Additionally, given the lack of evidence of an underlying systemic lymphoproliferative disease (as demonstrated by the aforementioned clinical laboratory findings) or the presence of local mature plasma cells adjacent to the mass in our biopsy samples, these findings further suggest that our case is a singularly unique entity. All four previous reports of intracranial LCDD were discovered in the setting of a known plasma cell dyscrasia or in the presence of local mature plasma cells whose local synthesis of light chains generated the intracranial mass, both of which are conspicuously absent in the case presented herein.

The imaging features of this unique case of LCDD also mirror the surprising pathologic findings. Unlike the previously reported cases of intracerebral LCDD, MR imaging of our mass reveals no evidence of post-gadolinium contrast enhancement on T1-weighted images and no evidence of significant tissue perfusion on dynamic gadolinium-enhanced perfusion imaging (Fig. 1). Both imaging features stand in stark contrast to the reported imaging findings of prior reports of LCDD, which demonstrated varying degrees of enhancement on postcontrast imaging. The lack of enhancement observed in our case likely reflects the novel underlying pathologic findings. This unique case reflects a growing understanding of the varying radiologic and pathologic features LCDD within the CNS and a growing appreciation of a more heterogeneous disease process than previously thought.

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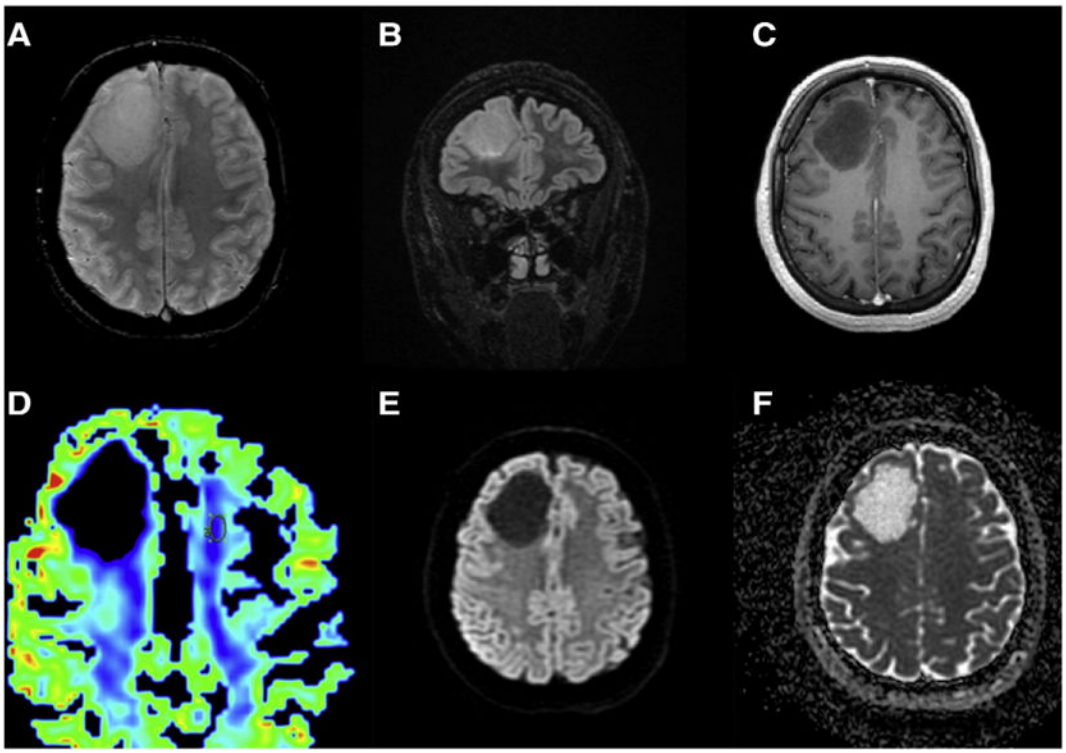

Fig. 1.

Conventional MR, diffusion-weighted, and MR perfusion imaging: (A) Axial T1-weighted post-gadolinium, (B) coronal T2/FLAIR, (C) axial susceptibility weighted, and (D) dynamic enhanced axial perfusion imaging shows an expansile T2/FLAIR hyperintense nonenhancing mass in the right superior and middle frontal gyri without evidence of superimposed hemorrhagic blood products. Perfusion imaging (D) reveals no significant cerebral blood volume (CBV) as demonstrated by black color within the lesion, matching the black color of sulci. In comparison, white matter is colored shades of blue and cortex is colored red, yellow, and green reflecting higher relative CBV. Diffusion-weighted image (E) and ADC map (F) of the mass demonstrate no evidence of restricted diffusion.

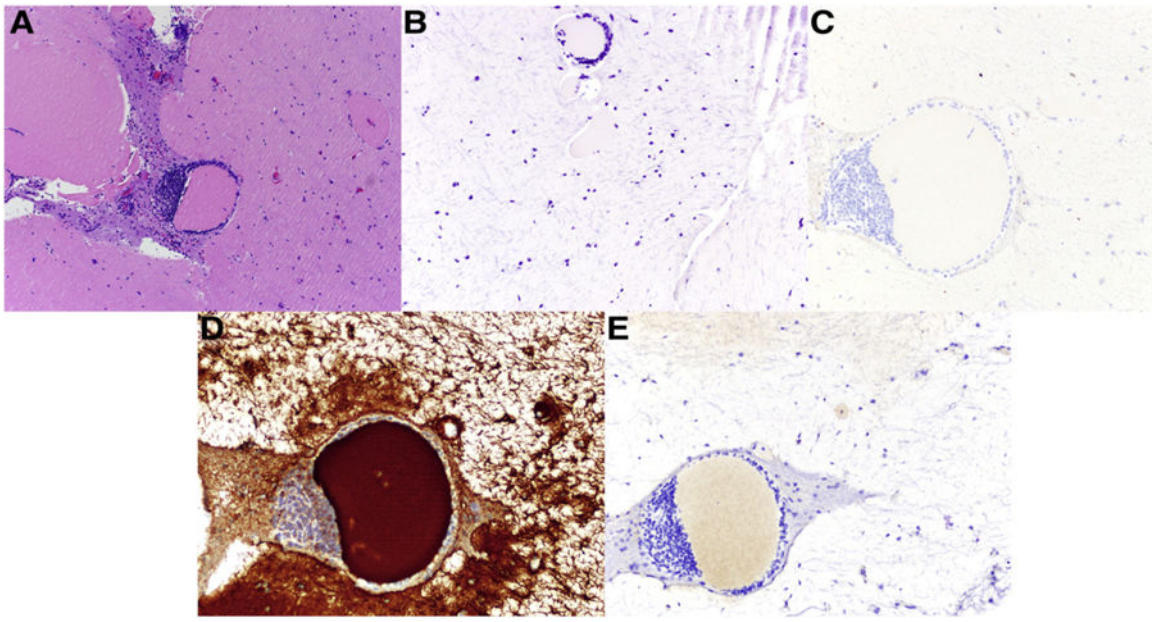

Fig. 2.

(A) Hematoxylin and eosin, (B) Congo red, (C) amyloid beta immunohistochemistry, and (D) kappa and (E) lambda immunohistochemistry. Deposition of amorphous eosinophilic proteinaceous material, some of which was in a vascular distribution, was associated with chronic lymphocytic inflammation (A). Histochemical staining for amyloid with Congo red was negative (B). The deposits showed strong positive staining with the antibody for kappa light chain (D), but immunoreactivity for beta amyloid and for lambda light chain were absent (C and E).