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Case Report

Primary solitary retro-clival amyloidoma

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Abstract

Background: Amyloidosis encompasses a group of disorders sharing the common feature of intercellular deposition of amyloid protein by several different pathogenetic mechanisms. Primary solitary amyloidosis, or amyloidoma, is a rare subset of amyloidosis in which amyloid deposition is focal and not secondary to a systemic process or plasma cell dyscrasia.

Case Description: This 84-year-old female presented with history of multiple syncopal episodes, dysphagia, and ataxia. Motor strength was 3+/5 in the right upper extremity. Rheumatoid factor, cyclic citrullinated peptide (CCP), and anti-nuclear antibody (ANA) were normal. Serum and urine immune-electrophoresis detected no abnormal bands. Computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated a non-enhancing soft-tissue mass extending from the retro-clivus to C2 posteriorly, eccentric to the right with severe mass effect on the upper cervical medullary junction. Endoscopic trans-nasal debulking of the retro-clival mass was performed with occiput to C5 posterior instrumentation for spinal stabilization.

Conclusions: Primary solitary amyloidosis, unlike other forms of amyloidosis, has an excellent prognosis with local resection. Diagnosis requires special stains and a degree of suspicion for the disease. This is the first report to document an endoscopic trans-nasal approach for removal of a primary solitary amyloidosis of the retro-clivus. Management of vertebral amyloidoma involves aggressive local resection of the tumor when feasible and spine stabilization as the degree of tumor involvement mandates. Complete evaluation for the diagnosis of systemic amyloidosis is essential for the management and prognostication. Surgeons encountering such lesions must maintain high suspicion for this rare disease and advise pathologists accordingly to establish the correct diagnosis.

Key Words: Amyloidoma, cervical instrumentation, cervical spine, primary solitary amyloidosis

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INTRODUCTION

The term amyloidosis encompasses a group of disorders that have as their common feature the intercellular deposition of the fibrillary protein, amyloid, by several different pathogenic mechanisms.[8] Primary solitary amyloidosis or amyloidoma is a disease characterized by localized deposition of amyloid in which no plasma cell dyscrasia or abnormal serum proteins are detectable.[2] Primary solitary amyloidosis of the cervical spine is a rare entity with only nine previously reported cases.[2,4,5,11,20-23,27] In this report, we describe the first case of primary cervical amyloidoma extending to the clivus that was treated via an endoscopic trans-nasal approach for initial resection. Clinicians should maintain a high degree of suspicion for this disease process when encountering spinal masses and should utilize non-invasive laboratory studies during the perioperative period to assess prognosis.

CASE REPORT

Presentation

An 84-year-old right-handed female with a past medical history of paroxysmal atrial fibrillation, congestive heart failure, and colon resection presented with a several-month history of progressive ataxia and dysphagia. She had been at a rehabilitation center for the past month due to multiple syncopal episodes. At initial presentation the patient was able to ambulate only short distances with a walker. She also described some difficulty with fine motor skills with her hands. Her family states that she had been able to ambulate as recently as several months ago. She denied any additional constitutional symptoms including fever, chills, or nausea. She denied neck pain. She had not undergone any spine procedures previously. Her preoperative modified Rankin score (mRS) was 3.

Examination

On physical examination motor strength was 3+/5 in the right upper extremity. The remainder of the neurologic and general examination was unremarkable. Rheumatoid factor, cyclic citrullinated peptide (CCP), and ANA were normal. The serum and urine immune-electrophoresis detected no abnormal bands.

Imaging

Computed tomography (CT) and magnetic resonance imaging (MRI) were performed and showed a non-enhancing soft-tissue mass extending superior from the retro-clivus to C2 posteriorly, eccentric to the right with severe mass effect on the upper cervical medullary junction [Figures 1 and 2]. Differential diagnoses based on CT and MRI findings may include Central Nervous System (CNS) lymphoma, high grade gliomas, and cerebral metastases,[18,19] and calcifying pseudoneoplasms of the neuraxis (CAPNON).[7]

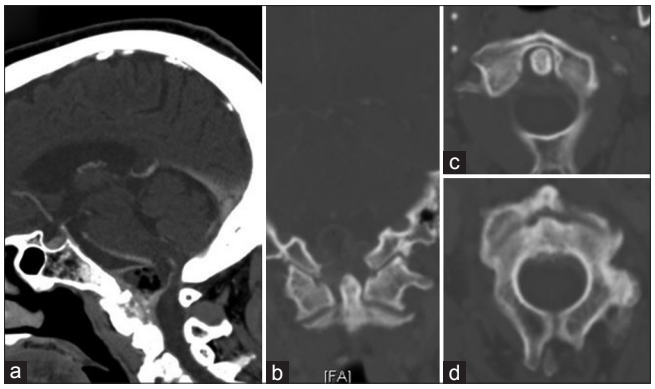

Figure 1: Initial sagittal (a) and coronal (b) computed tomography scan obtained at presentation demonstrate a non-enhancing mass centered along the posterior aspect of the clivus and C2, eccentric to the right, with soft tissue air. Not associated with erosive bony changes of either the dens (c) or the body of C2 (d)

On CT, amyloidomas generally are hyperattenuating and enhance following contrast administration.[18,19] Similarly, most primary CNS lymphomas are hyperattenuating and show enhancement on CT.[13] High grade gliomas, on the other hand, characteristically appear to have irregular thick margins that are highly cellular and hyperattenuating with irregular hypodense necrotic centers. Marked mass effect, edema, hemorrhage, and heterogeneous enhancement of the margins may also be observed.[3] Unlike amyloidomas, cerebral metastases range from isodense to hypodense to hyperdense on pre-contrast imaging. Enhancement is also variable with contrast and may appear nodular or ring-enhancing.[9] CAPNONs on CT appear as a well-defined leptomeningeal or parenchymal mass that is heavily calcified.[1]

On MRI, amyloidoma signal characteristics are variable. T1 and T2 images range from hypointense to hyperintense. There is vivid contrast enhancement on T1-contrast images, and peripheral radial enhancement may be observed. Additionally, on T2 susceptibility weighted images (SWI), microhemorrhages may be observed.[18,19] T1 images for CNS lymphomas are usually hypointense to grey matter.[15] High-grade tumors show homogenous enhancement with contrast, whereas low-grade tumors may have absent enhancement.[14] Like amyloidomas, T2 characteristics of CNS lymphomas are variable.[15] High-grade gliomas on T1 appear hypointense within the white matter with a necrotic heterogenous signal in the center. With contrast, the lesion has peripheral enhancement with nodular components surrounding the necrosis. T2/FLAIR imaging appears hyperintense with vasogenic edema and, occasionally, flow voids.[3] Unlike amyloidomas, SWI characteristics for high-grade gliomas include a low-intensity irregular rim from blood product usually located inside the peripheral enhancing component.[26] Brain metastases typically are

isointense or hypointense on T1 imaging. There may be intrinsic intensity if the lesion is hemorrhagic. Enhancement patterns with contrast are usually intense but variable, ranging from uniform to punctate to ring-enhancing. Unlike amyloidomas, T2 imaging of metastases are usually are hyperintense, although hemorrhage may alter the signal.[9] CAPNONs are isointense to hypointense on T1 and have varying enhancement with contrast. There is low signal on T2/FLAIR.[1] The non-vascular pannus and calcium pyrophosphate deposition [Figure 2] may appear similar to findings that are characteristic of CAPNON lesions.

Surgery

The decision was made to proceed with operative intervention for decompression of her cervical spinal cord and to obtain tissue for diagnostic pathologic examination. As the amyloid tumor arose posterior to C2 and extended caudally to the retro-clivus, we decided on an endoscopic trans-nasal approach with combined posterior stabilization. A transoral approach was considered, but ultimately, was not chosen because of the retroclival nature of the lesion. Although a transoral approach can provide a wider surgical field, the trans-nasal approach allowed better visualization of the clivus as well as structures posterior to C1 better.[24] The patient underwent endoscopic trans-nasal resection of the retro-clival mass with the assistance of an ENT colleague. A pre-operative lumbar drain was inserted to decrease the risk of cerebrospinal leak post-operatively. During the course of surgery, the vertical portion of the cruciate ligament was identified and appeared to be markedly thickened and thus, incised and resected in order to gain exposure to the lesion. An autologous fat graft was utilized at the termination of the procedure. Due to the violation of the atlanto-axial ligaments, the team decided it was prudent to follow the anterior surgery with a second stage posterior instrumentation procedure. Arthrodesis was completed from occiput down to C5 due to the patient's age and poor bone quality.

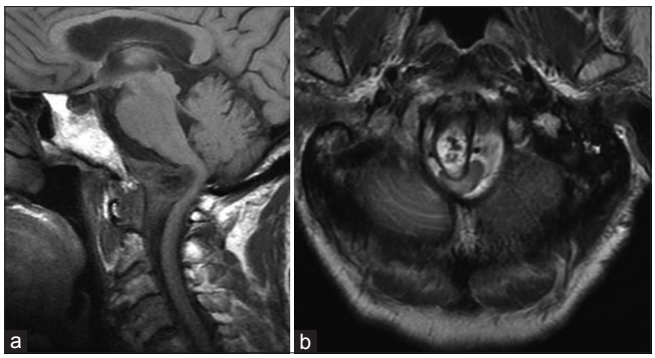

Figure 2: Sagittal T1-weighted (a) and axial T2-weighted (b) magnetic resonance imaging demonstrate a soft-tissue mass posterior to C2. The soft-tissue mass exerts severe mass effect on the upper cervicalmedullary junction with associated abnormal cord signal

Histopathology

Multiple specimens of the lesion were taken and underwent pathologic examination. Microscopic examination revealed amorphous, eosinophilic deposits. Special stains revealed focally strong congophilia with Congo red stain for amyloid, consistent with cerebral amyloidoma.[6] Examination under polarized light revealed focal apple green birefringence to polarized light [Figure 3]. The kappa and lambda light chain immune stain found no evidence of light chain deposition. Therefore, the pathology of the lesion is amyloid associated (AA), rather than amyloid light chain associated (AL). Stains for bacteria, fungi, acid-fast bacilli, and uric acid stains were negative.

Postoperative course

The patient underwent monitoring in the neurosurgical intensive care unit and gradual tapering of her lumbar drain. Extensive systemic evaluation did not reveal any inflammatory processes, systemic amyloidosis, or plasma cell dyscrasia. Serum rheumatoid factor, CCPs, and ANA were negative. Urine and serum protein electrophoresis and immune-electrophoresis did not reveal a monoclonal gammopathy. The patient was discharged to subacute rehabilitation 2 weeks postoperatively with improved neuro-motor exam. MRI imaging revealed debulking of the retro-clival mass with improvement of cervical medullary kinking. CT imaging demonstrated a stable spine construct [Figure 4]. The patient's postoperative 2-year follow-up MRI showed complete resolution of the retroclival mass. There was no evidence of spinal cord compression [Figure 5]. Her mRS remained 3 and she currently continues to be able to ambulate with moderate assistance.

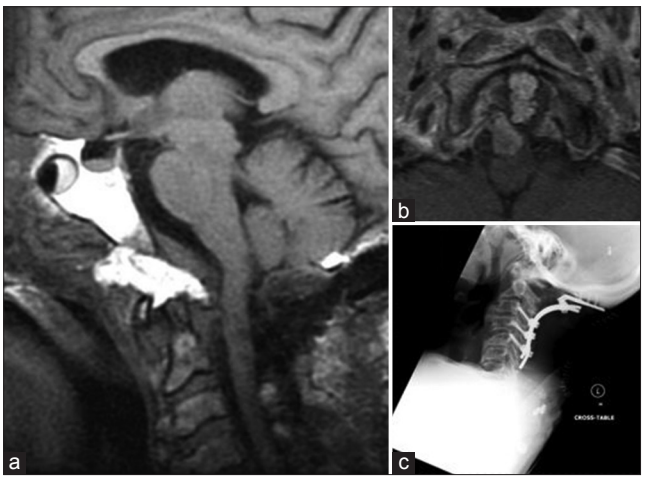

Figure 3: Postoperative T1-weighted sagittal (a) and axial (b) magnetic resonance imaging demonstrate interval postoperative changes including partial debulking of the mass and evidence of the fat graft. There was improvement of the cord kinking at the cervical medullary junction, but persistent moderate canal stenosis. Lateral x-ray films demonstrate a stable construct (c)

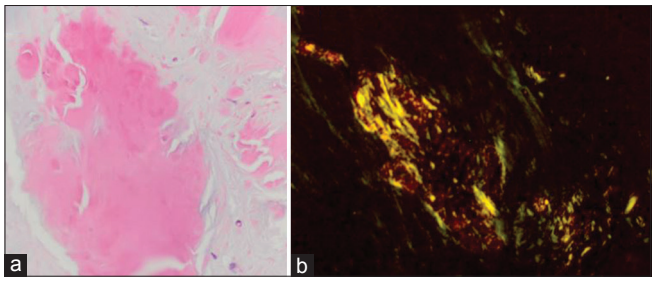

Figure 4: Hematoxylin and eosin (H and E) stain reveals amorphous, eosinophilic deposits (a). Congo red stain under polarized light shows obvious apple green birefringence (b)

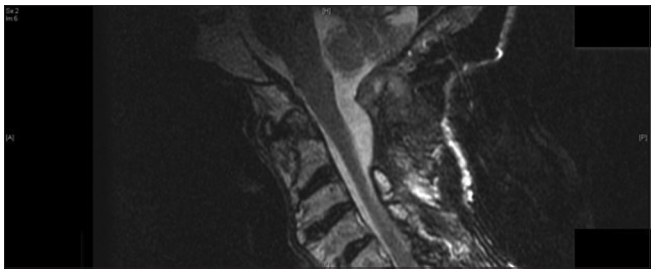

Figure 5: A 2-year postoperative MRI demonstrating complete resolution of retroclival lesion as well as no spinal cord compression

DISCUSSION

Amyloidosis is a disease complex resulting from the extracellular deposition of amyloid, an insoluble proteinaceous material with a beta-pleated sheet configuration.[12] Amyloid deposits cause their pathologic destruction by progressive intercellular accumulation and pressure atrophy of adjacent cells. The exact etiology and pathogenesis of amyloidosis is unclear but appears to be multi-factorial in many cases. Accurate diagnosis requires tissue for special staining with Congo red stain and examination under a polarized light.[4] These histopathologic stains are necessary to differentiate amyloid from other hyaline deposits, such as collagen.

Amyloidosis may occur spontaneously (primary amyloidosis) or in response to chronic disease processes (reactive/secondary amyloidosis). The WHO-IUIS nomenclature subcommittee classified amyloid and amyloidosis into 15 types based on the amino acid sequence of the specific amyloid protein involved in each disease type.[5] The two most clinically relevant forms of amyloidosis include the AL type associated with multiple myeloma and primary amyloidosis and the AA type found in secondary/reactive amyloidosis due to chronic infectious and inflammatory conditions.[11]

Most cerebral amyloidomas are AL type resulting from immunoglomulin-derived kappa and lambda light chains, which are likely made from plasma cells.[6,17] Although they have the potential for progression, full resection can prevent recurrence.[6] Clonality of the heavy chain (IgH)[17] and B-cell clonality[10] have also been observed.[17] AA type amyloidomas are usually associated with chronic infection, and but it is not common in the United States, it is often seen in developing countries.[25] It is important to differentiate AA types from the others as this systemic form, if left untreated, has a poor prognosis with a mean survival of less than 1 year.[6] Immunofluorescence microscopy is used to demonstrate light chain restriction to confirm an AL type diagnosis. Immunohistochemistry may be used to detect amyloid A in AA type tissues. In cases for which routine immunofluorescence and immunohistochemical stains that are specific for AL and AA type amyloidomas are not definitive, the Congo red staining is an acceptable alternative with additional subtyping by laser microdissection and mass spectrometry-based proteomic analysis.[16,25]

However, by definition, AL type is associated with plasma cell dyscrasia and is detectable in almost all patients with AL type.[28] Therefore, as specific subtyping with immunohistochemical stain and immunofluoresence was not conducted, the distinct lack of plasma cell infiltrate in this patient's tissue indicated that the lesion is the AA type. Future cases may benefit by staining for AL and AA subtypes routinely.

Prognosis for patients with amyloidosis is dependent on the specific form of amyloidosis. In secondary amyloidosis, treatment of the underlying disease can slow or reverse the progression of amyloid disease with 5- and l0-year survival after diagnosis not uncommon. Patients with immunocytic-derived amyloidosis have the worst prognosis with less than 1-year survival.[8] Primary solitary amyloidosis carries the best prognosis with apparent long-term survival and no increased risk of developing other forms of amyloidosis following diagnosis and treatment.[12] However, the natural history of this variant of amyloidosis cannot be clearly defined due to the limited number of case reports and lack of published long-term follow-up studies.

Skeletal amyloid deposits often have an associated soft-tissue mass that may contain variable amounts of calcification.[20] The majority of spinal column amyloid deposits are associated with secondary causes such as multiple myeloma or systemic amyloidosis.[21]

Primary amyloidosis is characterized by the lack of detectable plasma cell dyscrasia or abnormal serum proteins.[22] Diagnosis requires specific staining of tissue for amyloid and therefore, requires a degree of suspicion for the disease. Imaging studies including CT and MRI can be suggestive but not diagnostic of amyloidoma. Previous reports have described various radiologic findings of spinal amyloid lesions, such as vertebral body fractures and collapse, osteopenia, and lytic lesions. The MR signal characteristics of amyloidomas are similar to those of primary amyloid

lesions in the nasopharynx and sternum[22,23] and include low-to-intermediate signal on T1-weighted images, intermediate-to-high signal on T2-weighted images, and variable enhancement on contrast-enhanced T1-weighted images. In our study, the spinal amyloid deposits appeared as low-to-intermediate signal on T1 and low signal on T2-weighted MR images.

Potential management options reported in the literature include non-invasive approaches utilizing chemotherapy, surgical approaches aimed toward as complete a resection as possible of the tumor with stabilization of the spine.[11,23] The limited number of case reports describing amyloidomas of the cervical column indicates that local resection results in an excellent prognosis similar to that found in patients with primary solitary amyloidosis involving other regions of the body.[5]

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Conflicts of interest
There are no conflicts of interest.

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