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A Case of Cardiac Light Chain Deposition Disease in a Patient with Solitary Plasmacytoma

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Male, 31
Final Diagnosis: Light chain depsotion disease
Symptoms: —
Medication: —
Clinical Procedure: None
Specialty: Hematology

Objective: Rare co-existance of disease or pathology

Background: Light chain deposition disease is a systemic disease characterized by deposition of immunoglobin light chains in various organs. Cardiac involvement of light chain deposition disease, also known as cardiac nonamyloidotic immunoglobin deposition disease (CIDD), is a rare clinical entity, where clinical outcome is very variable and best treatment approaches are not well known.

Case Report: We present the case of a 31-year-old man with a solitary thoracic plasmacytoma and cardiac light chain deposition disease with evidence of congestive heart failure by echocardiography and cardiac markers. The patient underwent surgical resection of the plasmacytoma followed by systemic therapy with 50% VDT-PACE and then VRD with near-normalization of his heart function. A melphalan-based stem cell transplant is planned in this young patient to achieve the best possible long-term remission.

Conclusions: CIDD is a very rare disease, with previous reports showing diverse manifestations with variable outcome. A high level of clinical suspicion should be maintained in such cases and early intervention, as in our patient, can restore cardiac function. There is very little literature on the optimal management of these patients. A combination of surgery and chemotherapy were pursued in our patient with very good results.

MeSH Keywords: Antineoplastic Combined Chemotherapy Protocols • Heart Failure • Immunoglobulin Light Chains • Plasmacytoma

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/895762

Background

Light chain deposition disease (LCDD) is a rare disorder associated with clonal proliferation of plasma cells or B lymphocytes, which synthesize abnormal monoclonal immunoglobulin light chains. Cardiac involvement [also termed cardiac nonamyloidotic immunoglobin deposition disease (CIDD)] is characterized by immunoglobin deposition in the myocardium and is a very rare entity with variable outcome. We report a patient with thoracic plasmacytoma who on further work-up was found to have light chain deposition disease of the heart manifested by decreased ejection fraction and increased NT-proBNP levels.

Case Report

A 31-year-old man was found to have an incidental pleural effusion on a routine chest X-ray obtained as a part of pre-employment screening. Further evaluation with computed tomography of the chest and magnetic resonance imaging of the thoracic spine showed a 10×7×4 cm lesion in the paravertebral and prevertebral soft tissue, extending from T4 to T8 (Figure 1) with prominent erosion and destruction of the vertebral bodies (Figure 2), and with moderate-sized pleural effusion on the right side. CT-guided biopsy of the para spinal mass was consistent with plasma cell neoplasm (Figure 3 depicts sheets of plasma cells that stain for CD138 in Figure 4). No further lesions were detected on PET CT and diffusion-weighted image MRI.

The blood cell counts were as follows: hemoglobin 14.7 gm/dl, white blood count 6980/µL, and platelet count 264 000/µL. Biochemical assay includes a fasting blood sugar of 96 mg/dL, serum sodium 141 mEq/L, potassium 3.9 mEq/L, calcium 9.3 mg/dL, phosphorus 4.1 mg/dL, BUN 21mg/dL, creatinine 0.9 mg/dL total protein 7.5 g/dL, albumin 4.1 g/dL, NT-proBNP 5213 pg/mL, LDH 181IU/L, and beta -2 microglobulin 2.3 mg/L. Immunochemistry findings included IgG 1570 mg/dL with Kappa 3.45 mg/dl, lambda 13.65 mg/dl, and a monoclonal protein of 0.7g/dL. IgA and IgM were in the normal range, with 307 mg/dL and 114 mg/dL, respectively. Urinalysis showed 300 mg/dL of proteinuria and urine electrophoresis showed 960 mg/dl of proteins with 81% albumin and negative monoclonal protein. Serum and urine immunofixation showed IgG lambda paraproteinemia.

Routine cardiac work-up prior to chemotherapy was performed; electrocardiography (ECG) showed regular sinus rhythm and left atrial enlargement with no specific T wave changes in the inferior lead. The echocardiography revealed ejection fraction of 35% with moderate diffuse hypokinesis with left ventricular concentric hypertrophy with decreased diastolic compliance consistent with restrictive cardiomyopathy. There was

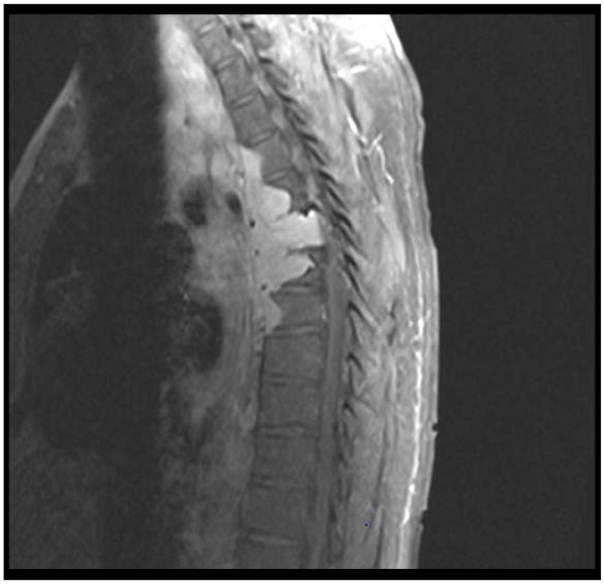

Figure 1. Magnetic resonance imaging of the thoracic spine showed a 10×7×4 cm lesion in the paravertebral and prevertebral soft tissue extending from T4 to T8.

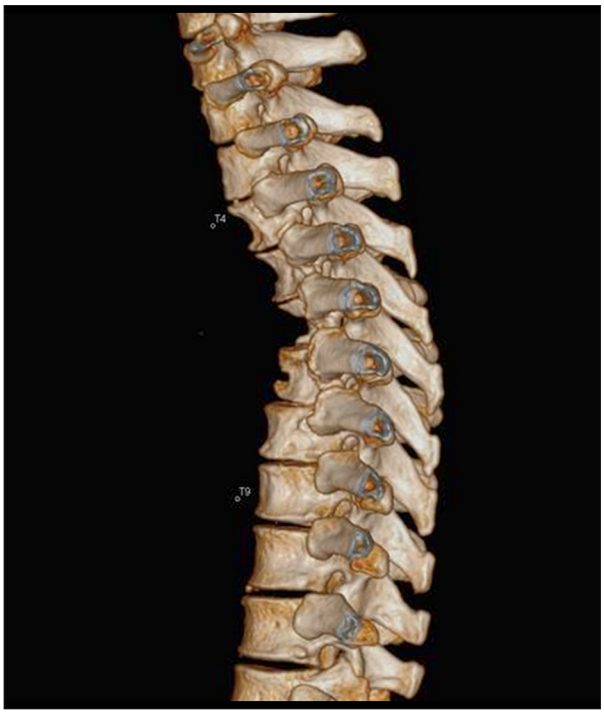

Figure 2. CT Reconstruction images showing erosion and destruction of the vertebral bodies.

minimal pericardial effusion without any evidence of constriction. Cardiac MRI showed systolic dysfunction and grade III diastolic dysfunction. Left ventricular concentric hypertrophy was noted with marked enlargement of the left atrium, mild thickening of the right ventricle, and increased inter-atrial septal thickness. A patchy non-territorial nulling abnormality of the

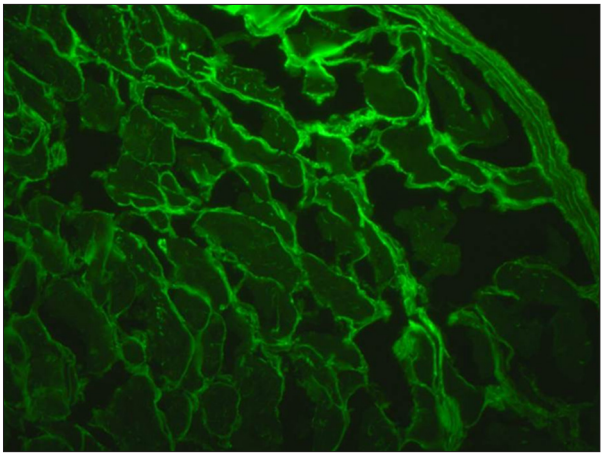

Figure 3. Immunofluorescence staining of the myocardium showing diffuse linear lambda light chain around each muscle fiber.

myocardium was also noted. Cardiac biopsy of the septum showed diffuse linear lambda light chain staining by immunofluorescence around each muscle fiber, with no amyloid deposition by Congo red and thioflavin-t stains confirming the diagnosis of light chain deposition disease lambda type (Figure 3). Bone marrow examination showed no morphological or immunophenotypic evidence of plasma cell neoplasm or amyloid deposition. Lymph node biopsy did not show any evidence of amyloidosis or light chain deposition disease. The fat pad biopsy was negative for amyloid. Cytology from the pleural effusion was negative for malignancy.

The patient had to undergo T1–T11 posterior fusion with resection of the plasmacytoma at T6 level for concerns of spinal instability. Histopathological examination demonstrated sheets of atypical plasma cells infiltrating the soft tissue and the bone consistent with plasma cell neoplasm (Figures 4, 5 showing CD138 stain). Follow-up cardiac evaluation with repeat echocardiogram after surgical removal of his plasmacytoma showed restoration of his EF to 55% with improvement of diastolic function from Grade III to Grade II. NT-proBNP levels decreased from 5213 pg/dL to 1300 pg/dL. Further evaluation showed a reduction of monoclonal protein from 0.7 g/dl to 0.4 g/dl and in Lambda light chain from 13.65 mg/dL to 4.38 mg/dL. Given the size of the plasmacytoma and persistent residual disease after surgery, we decided to start aggressive systemic therapy in this young patient to achieve best long-term disease control. The patient was subsequently treated with 50% VTD-PACE (Velcade 1 mg/m^2, thalidomide 200 mg D1–4, dexamethasone 40 mg po D1–4, cisplatin 5 mg/m^2 D1–4, adriamycin 5 mg/m^2 D1–4, cyclophosphamide 200 mg/m^2 D1–4, and etoposide 20 mg/m^2 D1–4), followed by stem cell collection. He was subsequently started on VRD (Velcade 1 mg/m^2 weekly, Revlimid 25 mg D1–D14 out of 21 days, and Dexamethasone 20 mg weekly). Four months after

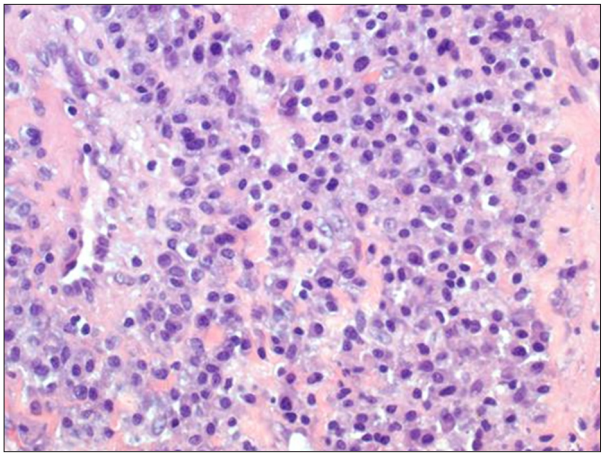

Figure 4. Sheets of atypical plasma cells.

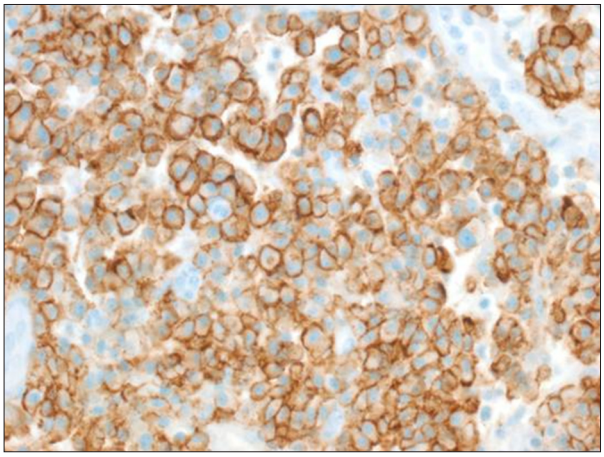

Figure 5. CD138 staining of the plasmacytoma.

initiation of systemic treatment, the patient's EF remains stable at 55% and his NT-proBNP has improved significantly to 207 pg/mL. Monoclonal paraproteinemia has resolved and immunofixation in serum and urine is negative. Proteinuria has decreased significantly from 960 mg/dL to 180 mg/dL, with all of the protein being due to albuminuria. For best long-term results, the plan is to proceed to a Melphalan-based stem cell transplantation followed by maintenance. The presentation is consistent with IgG lambda solitary thoracic plasmacytoma and nonamyloidotic light chains deposition disease of the heart, which is now almost completely reversed after surgical removal of his primary plasmacytoma and systemic therapy.

Discussion

LCDD is a disorder described in association with abnormal clonal proliferation of plasma cells or B lymphocytes, which synthesize abnormal monoclonal immunoglobulin light chains. This disease is rare and most often associated with kappa light chain excess. In heart biopsies, main differential diagnosis is amyloid

disease and is usually distinguished pathologically by the lack of amorphous substance deposition and the absence of Congo red or Thioflavin-T staining in LCDD. The kidneys are almost always affected, while other clinical manifestations of LCDD include retinal detachment, cholestatic liver disease, congestive heart failure, arrhythmias, neuropathy, or sicca syndrome [1–7]. LCDD of the kidneys usually presents with nephrotic range proteinuria. Outcome is variable, with early studies showing rapid progression to end-stage renal disease within 5 years in more than 60% of patients [8,9]. However, the introduction of novel agents and identifying renal LCCD in its early stages have improved clinical outcome in recent years, suggesting reversibility of this condition in some patients [10]. Given the degree of proteinuria and albuminuria in our patient at diagnosis and improvement with therapy, it is most likely the patient also suffered from renal LCDD that responded to treatment.

Cardiac involvement is very rare and occurs about 20% of LCDD [11]. Outcome of CIDD and its response to treatment are not well known, with some reports suggesting reversibility [12] and others showing aggressive disease with no response to treatment [13]. Clinical manifestations range from clinically asymptomatic disease to overt heart failure and dysrhythmias. Immunofluorescence and electron microscopy are diagnostic [14,15].

Our patient presented with cardiomyopathy due to CIDD in the setting of newly diagnosed solitary thoracic plasmacytoma with no clonal plasma cells in a bone marrow sample. This constellation presents a very uncommon clinical entity. Treatment and outcome are not well known. Surgical removal of the plasmacytoma led to resolution of the patient's cardiomyopathy, indicating that CIDD can be reversible (analogous to renal LCDD) if treatment is started early and structural damage has not occurred. In contrast to CIDD, cardiac light chain amyloid disease and its treatment have been subject to extensive recent studies. While chemotherapy and/or novel agents can significantly improve outcomes in early cardiac amyloidosis, those patients with highly elevated NT proBNP and significant changes on echocardiography, as in our patient, have dismal outcome [16–18]. The reason for this difference in outcome and treatment response is not clear, but with amyloid fibril being insoluble and light chain being soluble in blood, it has been postulated that light chains can be readily excreted by the kidneys and organ function can be preserved or improved if no major damage has been done. Early diagnosis and prompt treatment of the underlying plasma cell dyscrasia may result in a favorable diagnosis in CIDD and probably LCDD in general.

Conclusions

A high degree of clinical suspicion can lead to a prompt diagnosis of this clinical condition. Early intervention, as in our patient, can reverse cardiac function. There is very little data on the optimal management of these patients. A combination of surgery and chemotherapy were pursued in our patient, with good results.

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