Pathol. Oncol. Res. (2010) 16:249–252
DOI 10.1007/s12253-009-9218-1

Extraosseus Plasmacytoma of the Pharynx with Localized Light Chain Deposition. Case Report

Nina Zidar · Samo Zver · Vesna Jurčić

Received: 4 August 2009 / Accepted: 20 October 2009 / Published online: 5 December 2009

Abstract Light chain deposition disease (LCDD) is a rare disorder associated with a clonal proliferation of plasma cells, which synthesize abnormal monoclonal immunoglobulin light chains. It is characterized by systemic deposition of light chains in various organs, with the kidneys being most commonly affected. There have been few reports of isolated LCDD, i.e. in the brain, lungs and cervical lymph nodes. We here report on another patient with an isolated form of LCDD, which was limited to the pharyngeal mucosa and was associated with an extraosseus plasmacytoma of the pharynx, expanding the spectrum that has been recognized for LCDD. The patient was treated by local radiotherapy, with an excellent response. A less aggressive clinical course can probably be expected than in the usual form of LCDD, but a long-term follow-up is necessary to establish the clinical significance of this variant of LCDD.

Keywords Light chain deposition disease · Isolated · Pharynx · Extraosseus plasmacytoma

Presented at 22nd European Congress of Pathology, Florence, Italy, 2009.

N. Zidar (✉) · V. Jurčić
Institute of Pathology, Faculty of Medicine,
University of Ljubljana,
Korytkova 2,
1000 Ljubljana, Slovenia
e-mail: nina.zidar@mf.uni-lj.si

S. Zver
Department of Haematology,
University Medical Centre Ljubljana,
Zaloška 7,
1525 Ljubljana, Slovenia

Introduction

Light chain deposition disease (LCDD) is a rare disorder associated with a clonal proliferation of plasma cells or B lymphocytes, which synthesize abnormal monoclonal immunoglobulin light chains. It is characterized by systemic deposition of light chains along the basement membranes in various organs, with the kidneys being most commonly affected [1–4]. There have been only few reports of isolated LCDD, i.e. in the brain [5], lungs and cervical lymph nodes [6, 7]. It is controversial whether or not a true localized LCDD really exists or it rather represents an initial expression of a silent systemic LCDD [7]. We here report on another patient with an isolated form of LCDD which was associated with an extraosseus plasmacytoma of the pharynx.

Case Presentation

Clinical History A 50-year-old man presented with a painless swelling on the dorsal wall of the pharynx, covered by pale mucosa. He felt it disturbing, similar to pharyngeal symptoms of a nonspecific viral infection. Regional lymph nodes were not enlarged. The remaining clinical findings and routine laboratory examinations, including serum urea, creatinine, calcium, serum free light chains levels, urin and serum immunofixation, and urin analysis were all within normal limits. An excisional biopsy of the pharyngeal lesion was performed, which revealed changes consistent with the diagnosis of LCDD associated with plasmacytoma of the pharynx.

Following the biopsy result, complete skeletal X-ray survey, bone marrow histology including karyotyping and CT scan of the head and neck region were performed but

showed no abnormalities. He was treated by local radiotherapy of the pharyngeal lesion and later no further systemic treatment was added. After completion of radiation therapy, oropharyngeal examination revealed excellent response with complete regression of the dorsal pharyngeal infiltrate.

Three months after pharyngeal irradiation was completed, a whole body PET CT scan was performed, which showed no excessive accumulation of FDG (flourideoxyglucose) in the pharyngeal region or in any other anatomical site of the body. The finding was consistent with the diagnosis of a localized form of LCDD, being in complete remission after local radiotherapy. During regular disease follow-up, PET CT scan was repeated a year later, the finding was again completely within normal range, with no excessive FDG accumulation. Serum free light chain levels and immunofixation analysis were also within normal limits.

Pathological Findings Tissue samples were fixed in 10% buffered formalin, embedded in paraffin and cut at 4 microns for H&E slides. Additional sections were cut for Congo red staining, immunohistochemistry and direct immunofluorescence. After pretreatment with a heat-induced epitope retrieval method, immunohistochemistry was performed using a sensitive peroxidase-streptavidin method with monoclonal antibodies against P-component and light chains (Dako, Denmark). For direct immunofluorescence, tissue sections were incubated with antisera to human kappa and lambda light chains (Dako, Denmark).

The excised pharyngeal mucosa measured 1.5×1.2 cm. It was covered by an intact squamous epithelium. In subepithelial stroma, there were amorphous eosinophilic deposits in the blood vessel walls, along the basement membrane of the glands and in the lamina propria, focally surrounded by foreign body multinucleated giant cells (Fig. 1a). These deposits did not stain with Congo red, and did not react with anti-protein P by immunohistochemistry, but stained intensively for kappa light chains by immunofluorescence (Fig. 1b) and immunohistochemistry, suggesting the diagnosis of LCDD.

In addition, subepithelial stroma was infiltrated by plasma cells. In situ hybridisation and immunohistochemistry revealed positive reaction for kappa light chains in the vast majority of cells (Fig. 2a) and almost negative reaction for lambda light chains (Fig. 2b) suggesting the diagnosis of extraosseus plasmacytoma. Electron microscopy was performed on tissue obtained from paraffin blocks revealing abundant granular deposits along the basement membranes, in the blood vessel walls and in the interstitium (Fig. 3).

On the basis of these features, a diagnosis of an isolated form of LCDD associated with extraosseus plasmacytoma of the pharynx was made.

Discussion

Excessive production of abnormal monoclonal immunoglobulin light chains is associated with a clonal proliferation of plasma cells or B lymphocytes, biologically either benign or malignant. Monoclonal light chains can deposit in tissues in two forms: as AL amyloidosis (AL=amyloidosis light chain) or light chain deposition disease (LCDD). Under light microscope, deposits in both diseases look similar. However, AL amyloid is characterized by a β-pleated sheet configu-

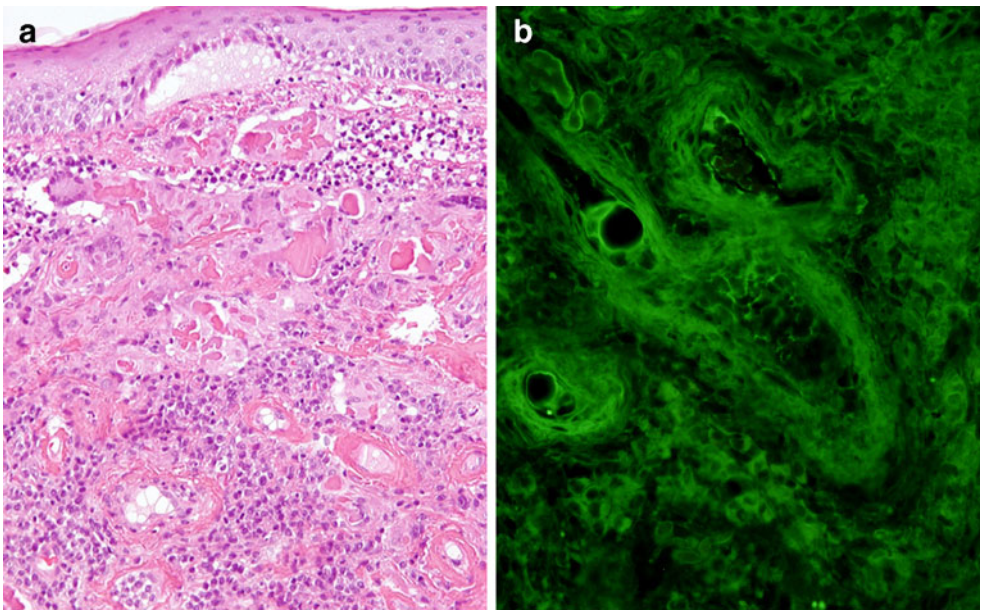

Fig. 1 **a** Pharyngeal mucosa with amorphous eosinophilic deposits in the blood vessel walls, along the basement membrane of the glands and in the lamina propria, surrounded by foreign body multinucleated giant cells. Hematoxylin and eosin, orig. magnification × 20. **b** Deposits stain intensively for kappa light chains by direct immunofluorescence. Orig. magnification × 40

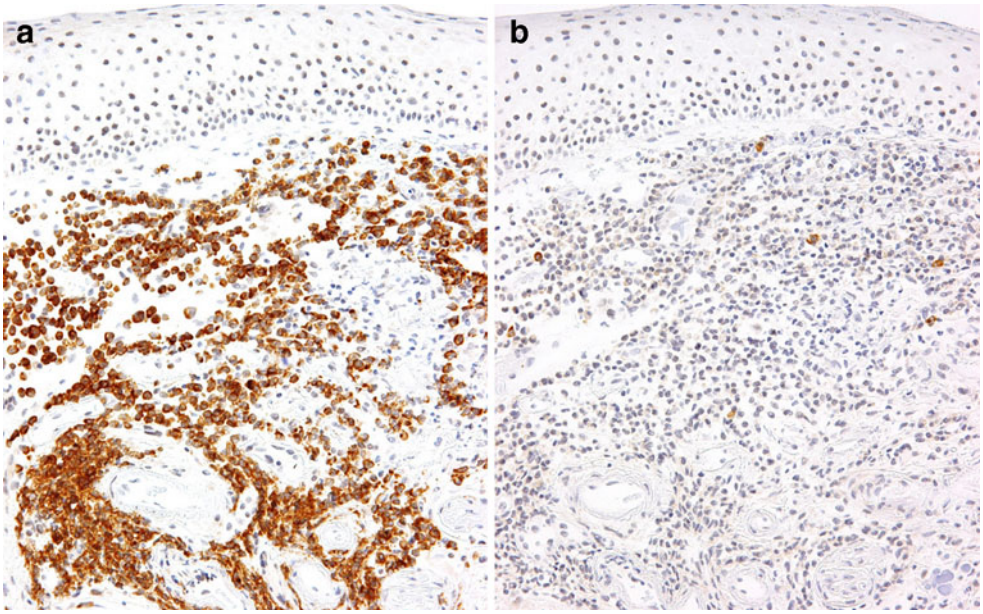

Fig. 2 Immunohistochemistry shows positive reaction for kappa light chains in plasma cells infiltrating subepithelial stroma (**a**), reaction for lambda light chains is almost completely negative (**b**). Orig. magnification × 20

ration with a fibrillar appearance by EM, and distinctive tinctorial property: it stains with Congo red displaying green birefringence under polarization. AL amyloid is composed predominantly of portions of the variable regions of a monoclonal light chain, with λ outnumbering κ chains by ratio 2–3:1. AL amyloid also contains P-component which is common to all amyloids. In contrast, in LCDD the deposits do not have a β-pleated sheet configuration, exhibit a granular structure by EM, and do not stain with Congo red. The deposits in LCDD are composed of portions of the variable regions of the light chain, but with κ chains outnumbering λ, and do not contain P-component [4, 8].

AL amyloidosis is a well recognized disease, whereas LCDD is a rare disease, with limited experience concerning its presentation, treatment and outcome. It was described in 1976 by Randall et al. [9] and is believed to present almost invariably with systemic deposition of light chains along the basement membranes, with the kidneys being almost always affected [1–4]. LCDD has been reported to be associated with monoclonal gammopathy of undetermined significance in 17%, and with multiple myeloma in 58% of cases [1]. The most common clinical presentation is the result of kidney involvement which is due to progressive accumulation of light chains from plasma filtration and includes proteinuria, nephrotic syndrome and/or renal failure [1–4]. Symptomatic extrarenal deposition is rare and has been described in the heart [10, 11], liver [2], lungs, joints [12], central and peripheral nervous system [5]. The lung involvement may rarely dominate the clinical course of LCDD and lead to severe respiratory insufficiency requiring lung transplantation [13–15]. Few cases of isolated LCDD have been described, i.e. in the brain [5], lungs, in the cervical lymph nodes [6, 7], and in the pharynx (present case). It is not certain whether or not localized LCDD really exists or it rather represents an initial expression of a silent systemic LCDD [7].

The median survival in systemic LCDD is approximately 4 years. Prognostic factors include age, presence of plasma cell myeloma and extrarenal light chain deposition [4]. LCDD is an uncommon disease, for which no standard treatment has been established. Some recent studies suggest, that similar treatment modalities as in multiple myeloma (chemotherapy and autologous stem

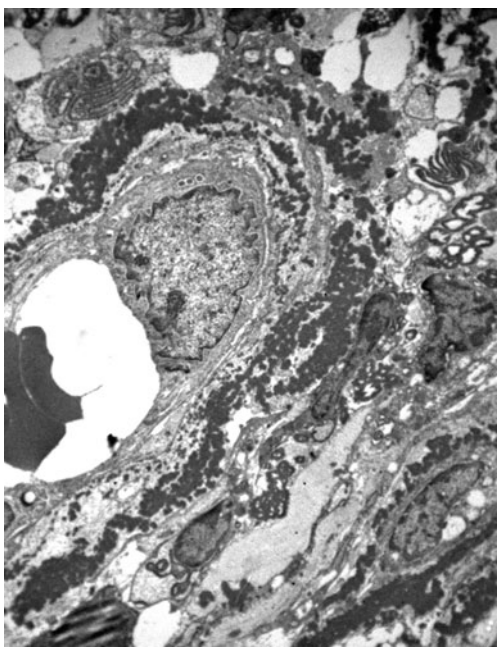

Fig. 3 Electron microscopy reveals abundant granular deposits in the blood vessel walls and in the interstitium

cell transplantation) may be effective, inducing hematologic response as well as regression of light chain deposits, and improvement of function of the involved organ(s) [16, 17].

In the patient reported here, LCDD was limited to the pharyngeal mucosa and was associated with an extraosseus plasmacytoma, further expanding the spectrum that has been recognized for LCDD. Based on the performed laboratory and radiological tests, especially normal serum free light chains levels and PET CT repeated twice, we may conclude that no systemic signs of the disease were present in our patient at any time point of the disease.

Pharynx is one of the commonest locations for extraosseus plasmacytoma [18] and can be accompanied by AL amyloidosis, but the association of LCDD and plasmacytoma of the pharynx is unique, particularly because LCDD is believed to be prone to systemic deposition. However, this and some other cases [5–7] indicate, that localized deposition of proteins which are normally deposited systemically can also occur in LCDD and not only in AL amyloidosis [8], being characterized by localized growth of clonal plasma cells and restriction of light chain deposits to sites adjacent to the precursor cell proliferation. A less aggressive clinical course can probably be expected than in the usual form of LCDD, but a long-term follow-up is necessary to establish the clinical significance of this variant of LCDD.

References

1. Lin J, Markowitz GS, Valeri AM, Kambham N, Sherman WH, Appel GB et al (2001) Renal monoclonal immunoglobulin deposition disease: the disease spectrum. J Am Soc Nephrol 12:1482–1492
2. Pozzi C, Locatelli F (2002) Kidney and liver involvement in monoclonal light chain disorders. Semin Nephrol 22:319–330
3. Pozzi C, D'Amico M, Fogazzi GB, Curioni S, Ferrario F, Pasquali S et al (2003) Light chain deposition disease with renal involvement: clinical characteristics and prognostic factors. Am J Kidney Dis 42:1154–1163
4. McKenna RW, Kyle RA, Kuehl WM, Grogan TM, Harris NL, Coupland RW (2008) Plasma cell neoplasms. In: Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J, Vardiman JW (eds) WHO classification of tumours of haemopoietic and lymphoid tissues, 2nd edn. IARC, Lyon, pp 200–213
5. Popović M, Tavčar R, Glavač D, Volavšek M, Pirtošek Z, Vizjak A (2007) Light chain deposition disease restricted to the brain: the first case report. Hum Pathol 38:179–184
6. Piard F, Yaziji N, Jarry O, Assem M, Martin L, Bernard A et al (1998) Solitary plasmacytoma of the lung with light chain extracellular deposits: a case report and review of the literature. Histopathol 32:356–361
7. Rostagno A, Frizzera G, Ylagan L, Kumar A, Ghiso J, Gallo G (2002) Tumoral non-amyloidotic monoclonal immunoglobulin light chain deposits ('aggregoma'): presenting feature of B-cell dyscrasia in three cases with immunohistochemical and biochemical analyses. Br J Haematol 119:62–69
8. Bellotti V, Merlini G (1996) Toward understanding the molecular pathogenesis of monoclonal immunoglobulin light-chain deposition. Nephrol Dial Transplant 11:1708–1711
9. Randall RE, Williamson WC Jr, Mullinax F, Tung NY, Still WJ (1976) Manifestations of systemic light chain deposition. Am J Med 60:293–299
10. Buxbaum JN, Genega EM, Lazowski P, Kumar A, Tunick PA, Kronzon I et al (2000) Infiltrative nonamyloidotic monoclonal immunoglobulin light chain cardiomyopathy: an underappreciated manifestation of plasma cell dyscrasias. Cardiology 93:220–228
11. Toor AA, Ramdane BA, Joseph J, Thomas M, O'Hara C, Barlogie B et al (2006) Cardiac nonamyloidotic immunoglobulin deposition disease. Mod Pathol 19:233–237
12. Rivest C, Turgeon PP, Senécal JL (1993) Lambda light chain deposition disease presenting as an amyloid-like arthropathy. J Rheumatol 20:880–884
13. Bhargava P, Rushin JM, Rusnock EJ, Hefter LG, Franks TJ, Sabnis SG et al (2007) Pulmonary light chain deposition disease: report of five cases and review of the literature. Am J Surg Pathol 31:267–276
14. Colombat M, Mal H, Copie-Bergman C, Diebold J, Damotte D, Callard P et al (2008) Primary cystic lung light chain deposition disease: a clinicopathologic entity derived from unmutated B cells with a stereotyped IGHV4-34/IGKV1 receptor. Blood 112:2004–2012
15. Khoor A, Myers JL, Tazelaar HD, Kurtin PJ (2004) Amyloid-like pulmonary nodules, including localized light-chain deposition: clinicopathologic analysis of three cases. Am J Clin Pathol 121:200–204
16. Weichman K, Dember LM, Prokaeva T, Wright DG, Quillen K, Rosenzweig M et al (2006) Clinical and molecular characteristics of patients with non-amyloid light chain deposition disorders, and outcome following treatment with high-dose melphalan and autologous stem cell transplantation. Bone Marrow Transplant 38:339–343
17. Lorenz EC, Gertz MA, Fervenza FC, Dispenzieri A, Lacy MQ, Hayman SR et al (2008) Long-term outcome of autologous stem cell transplantation in light chain deposition disease. Nephrol Dial Transplant 23:2052–2057
18. Dores GM, Landgren O, McGlynn KA, Curtis RE, Linet MS, Devesa SS (2009) Plasmacytoma of bone, extramedullary plasmacytoma, and multiple myeloma: incidence and survival in the United States, 1992–2004. Br J Haematol 144:86–94