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CASE REPORT

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# Spleen localization of light chain deposition disease associated with sea blue histiocytosis, revealed by spontaneous rupture

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**Abstract** Splenic involvement by a light chain deposition disease (LCDD) associated with sea-blue histiocytosis occurred in a 55-year-old man presenting with LCDD of the kidney without myeloma. Lambda light chain deposits were demonstrated by immunohistochemistry in vessel walls and along the ring fibres of the red pulp sinuses. Accumulation of sea blue histiocytes in the cords was also present. Stiffness of the walls of the red pulp sinuses resulting from light chain deposits may have induced accumulation and destruction of circulating blood cells. Lipid catabolism with production of ceroids may have resulted in lipidic histiocytosis with a sea blue histiocyte pattern.

**Key words** Spleen · Light chain deposition disease · Sea blue histiocytes · Ceroids · Spontaneous rupture

## Introduction

Light chain deposition disease (LCDD) is a relatively rare condition characterized by the deposition of monoclonal light chain in multiple organs [13, 18], associated either with myeloma or lymphoproliferative disease [11, 13], or with monoclonal gammopathy of unknown significance (MGUS) [5, 13] or no detectable gammopathy. The most commonly involved site in LCDD is the kidney, and splenic involvement has rarely been reported [12, 13, 18].

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We report a case of LCDD with spleen involvement associated with another rare lesion, sea blue histiocytosis, representing an accumulation of lipopigments, particularly ceroids, in macrophages.

## Clinical history

In 1996, a 55-year-old man who had been monitored for 30 years for hypertension was admitted for evaluation of moderate renal failure, severe hypertension and pancytopenia. Laboratory data included a haematocrit of 21.1%, a white cell count of 1900 per $mm^3$ and a platelet count of 51 000 per $mm^3$. Abnormal serum chemistry included blood urea nitrogen of 2.52 g/l and creatinine of 58 mg/l. Blood calcium was normal. Serum protein immunoelectrophoresis showed a monoclonal free lambda chain component, but both bone marrow aspirate and biopsy and radiological evaluation failed to reveal any evidence for myeloma. The diagnosis of LCDD of the kidney (Randall's disease) was established in the renal biopsy, which revealed deposits of lambda light chain in the glomerular mesangium and along the tubular basement membranes. The patient was then treated by haemodialysis. One year later he suffered spontaneous splenic rupture and underwent surgery with splenectomy.

## Materials and methods

Spleen tissue was fixed in 4% formalin followed by conventional processing and embedding in paraffin wax. Sections 3 µm thick were stained with haematin-eosin-safran (HES), Giemsa, periodic acid–Schiff (PAS), Perls and Gordon-Sweet's silver stain. Ultraviolet illumination was used on unstained slides to analyse autofluorescence and after thioflavine T staining. Immunohistochemistry on paraffin-embedded sections was performed with an avidin–biotin peroxidase detection system for CD20, CD3, kappa and lambda light chains and immunoglobulin heavy chain expression (Dakopatts). In situ hybridization was performed on paraffin slides using kappa and lambda oligonucleotides (Dakopatts).

## Pathological findings

The spleen weighed 1220 g and showed laceration of the capsule with haemorrhage. The underlying parenchyma showed no macroscopic abnormality. No adenopathy was found in the hilus.

Histologically, the splenic parenchyma was found to be destroyed in some places by haemorrhagic foci relating to the spontaneous rupture of the spleen. In areas where the splenic tissue was preserved, the white pulp showed somewhat atrophic follicles with no germinal centre. The wall of trabecular arteries and arterioles was thickened, with scattered nodular eosinophilic deposits that did not stain with thioflavine T. Upon HES staining, the most striking observation was the accumulation of clear histiocytes in the red pulp. These cells had foamy cytoplasm and were prominent in the splenic cords. Histiocytes containing lipochromic pigment in the form of yellow-brown, small round granules were also present. These granules were PAS positive and had a sea blue colour varying intensity with Giemsa staining (Fig. 1). They were also autofluorescent when studied under UV light. They did not contain haemosiderin in the Perls-stained sections. These aggregates of histiocytes were accompagnied by small clusters of plasma cells and rare polymorphonuclear leucocytes, mainly neutrophils.

Immunohistochemistry demonstrated a typical pattern of light chain disease of the lambda isotype. Deposition, mainly nodular, was found in the media of many trabecular arteries and in arterioles present in the white pulp (Fig. 2). The most striking finding was the deposition of light chains along the ring fibres of the red pulp sinuses. On immunohistochemistry with an anti-lambda chain antibody, the framework of the sinuses was visible, as it was in silver impregnation (Figs. 2, 3). The nests of plasma cells were polytypic with no evidence of a predominant lambda chain population. In situ hybridization confirmed this polytypia. PCR did not disclose any immunoglobulin heavy chain gene rearrangement at the *FR3* locus.

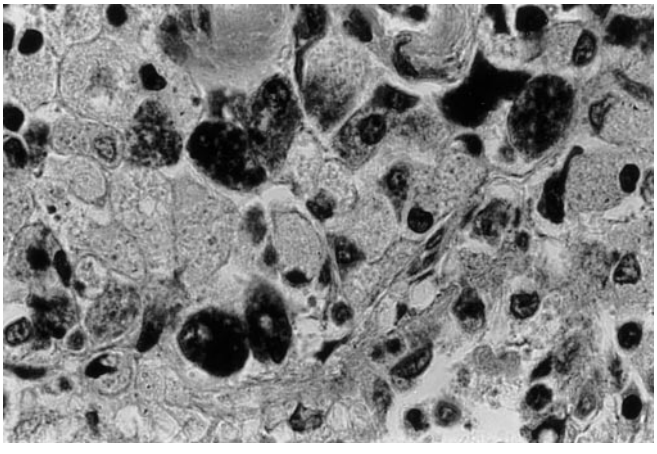
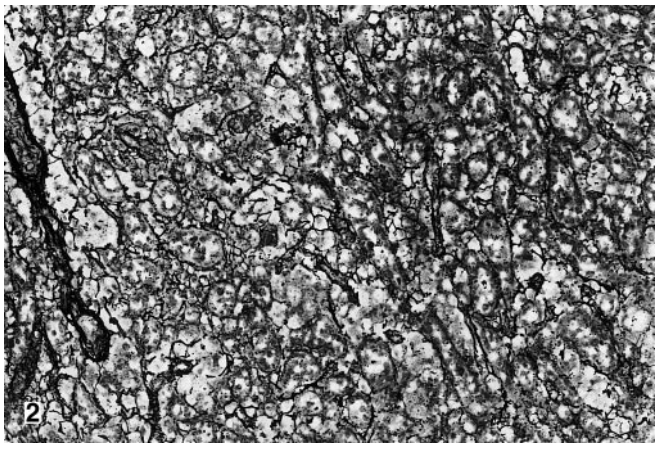


**Fig. 1** Cluster of histiocytes with deep blue granules in the splenic cords (Giemsa, original magnification ×100)



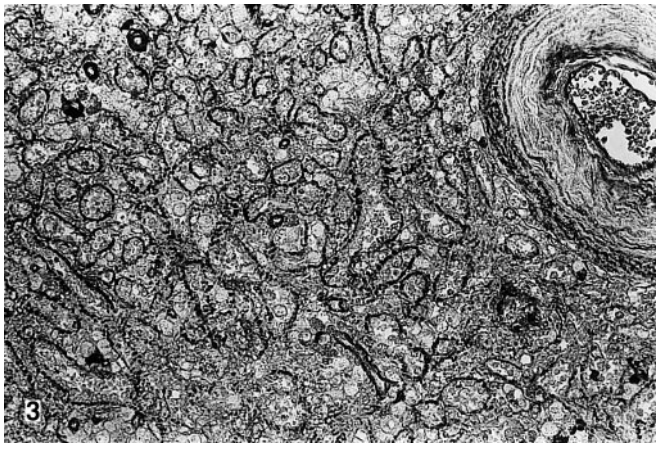




**Fig. 2, 3** Framework of the sinuses underlined with silver impregnation (**2** Gordon-Sweet, original magnification ×20) and with the nodular deposits of lambda light chain (**3** antibody antilambda light chain, avidin-biotin peroxydase, original magnification ×20)

## Discussion

Splenic involvement is rare in LCDD [1, 13], although splenomegaly has been described in this disease. Histopathological reports are scarce and mostly concern autopsy material [12, 14, 18]; they mention severe deposits around the sinuses [11, 12] and atrophy of the white pulp [14]. Multinucleated giant cells around deposits have been reported, but no mention has been made formerly of foamy or sea blue histiocytes.

In reported cases of LCDD, the deposits are usually kappa light chain [13]. Deposits of lambda light chain, as in our case, are less common [11].

Idiopathic sea blue histiocytosis syndrome was described by Silverstein [3, 9, 22], but masses made up of sea-blue histiocytes owing to accumulation of ceroids can also be seen in various other diseases, including the chronic myeloproliferative disorders [8, 10], idiopathic thrombocytopenic purpura (ITP) [4, 8, 16, 17, 21], hyperlipoproteinaemia type V [20], and various storage diseases such as Gaucher's or Nieman Pick's disease [2, 6, 9], and with protracted parenteral nutrition [2]. All these conditions are associated with a disorder of the normal

destruction of circulating blood cells by macrophages in the splenic red pulp. The presence of these abnormal cells in the cords or their death may attract histiocytes. The death of the cells accumulating in the cords produces a large amount of cell membrane lipoproteins, which are normally digested by histiocytes, but perhaps as a result of a partial deficit of catabolic enzymes in the macrophages in some cases, these cells are unable to catabolize the cell lipoproteins totally. Accumulation of both soluble and insoluble (lipopigments) lipids in the macrophage system results in lipidic histiocytosis. In some cases, lipopigments, and especially ceroids, accumulate in such amounts that sea blue histiocytosis can result [19].

In the present case, the association of two rare and apparently unrelated diseases could be explained by the following hypothesis. Light chain deposits along the annular fibres circling the red pulp sinuses form an obstacle to blood cell migration through the sinus walls, resulting in accumulation and death of cells within the cords. Histiocytes are attracted locally [15]. In somes patients this increase in lipoprotein uptake by macrophages might overcome the capacity of the cells to catabolize these lipids. A postulated impairment of macrophage function could result in lipidosis with ceroidosis. In keeping with this hypothesis is the fact that lipid histiocytosis with sea blue histiocytes has been described in association with other microvascular diseases of the spleen, such as peliosis and splenoma [7, 8].

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