Virchows Arch [Pathol Anat] (1986) 409:119–124

Virchows Archiv A

Case report

Lipofuscin accumulation in the human spleen with an unusual distribution

A case report

L. Jonathan Zwi and Irvin A. Lampert

Departments of Histopathology, Ealing Hospital and Royal Postgraduate Medical School, Uxbridge Road, Southall, Middx UB1 3HW, Great Britain

Summary. Lipofuscin granules were found in an unusual distribution in an atrophic human spleen. The pigment was confined to the sinus littoral cells and was absent from the splenic histiocytes. The lipofuscin differed from the ceroid-type of lipofuscin found in the various conditions associated with the 'syndrome of the sea-blue histiocyte' in its distribution, ultrastructure and its association with splenic atrophy rather than splenomegaly.

Key words: Spleen – Pigments – Atrophy

Introduction

Lipofuscin has been found in many organs and tissues in humans and animals as a normal concomitant of ageing and atrophy, due to genetic or acquired metabolic abnormalities, or due to exposure to exogenous substances (Pearse 1985; Ghadially 1982). Lipofuscin is not, however, a normal constituent of the human spleen, and ultrastructural studies of the spleen in humans (Hirasawa and Tokuhiro 1970; Bishop and Lansing 1982) and also in rabbits (Burke and Simon 1970a) make no mention of its presence. A less oxidised form of lipofuscin, sometimes referred to as ceroid, is found in the histiocytic cells of the human spleen in a number of different conditions, giving rise to the so-called 'syndrome of the sea-blue histiocyte' (Silverstein et al. 1970; Rywlin et al. 1971a; Golde et al. 1975). Splenic histiocytic lipofuscin has also been found in certain strains of mice (ceroid type) (Crichton et al. 1980) and in trout (Tischendorf 1969).

We report a case in which typical lipofuscin was encountered in an incidentally removed atrophic spleen. In this case, the distribution of the pigment was most unusual, being confined to the sinus littoral cells.

Offprint requests to: I.A. Lampert at the above address

Case history

A 69 year old female patient was admitted to hospital for investigation of epigastric and back pain and symptoms of large bowel obstruction. She had had a Polya gastrectomy 27 years previously for a perforated gastric ulcer and she had been relatively well since then. She commented that she had been thin since the operation. Radiological investigations showed herniation of the splenic flexure of the colon through a left diaphragmatic hernia. At surgery, the spleen was noted to be small and was adherent to the diaphragm close to the hernia. It was damaged during mobilisation and removed.

Methods

The spleen was fixed in 10% formalin. Blocks were processed for routine histology and the sections examined after staining with haematoxlin and eosin and a reticulin stain. PAS, Schmorl's stain, Perls' stain and a long Ziehl-Neelsen stain were then done to identify the pigment found. The alcoholic picric acid procedure for the removal of formalin pigment was performed. Blocks from the formalin-fixed tissue were post-fixed in 1% O_8O_4, embedded in epoxy resin and semi-thin sections were stained with toluidine blue. Thin sections were stained with lead citrate and uranyl acetate and examined with an AE1 801 electron microscope.

Results

Macroscopic appearance

The spleen was small and weighed only 45 g, but was of normal shape and colour. The capsule was smooth and vessels appeared normal.

Light microscopy

Splenic arterioles showed mild peri-arteriolar fibrosis and splenic cords were slightly thickened. An unexpected finding was the presence of numerous small brown granules in the majority of the sinus littoral cells (Fig. 1). The pigment granules were absent from splenic cord histiocytes, the cells of the white pulp and the endothelial and smooth muscle cells of arterioles. Occasional granules were present extracellularly in the peri-arteriolar collagen, possibly due to previous incorporation of pigment-containing littoral cells into the growing cuff of collagen, with subsequent death of the cells. The pigment was stained by the Schmorl's stain and the long Ziehl-Neelsen stain, and was negative by the PAS and Perls' stain, identifying it as a lipofuscin. The pigment was resistant to alcoholic picric acid.

Electron microscopy

Ultrastructural preservation was fair, despite initial fixation in unbuffered formalin, but membrane and cell matrix loss was evident. The various cells of the red pulp appeared normal, except for the presence of ovoid osmiophilic bodies in most sinus littoral cells. Occasional remnants of limiting membranes were identified around these bodies and the globular, variably electron-dense contents were characteristic of typical lipofuscin (Figs. 2, 3). Myelinoid bodies, as seen in human ceroid accumulations and in murine lipofuscinosis, were not present in this case.

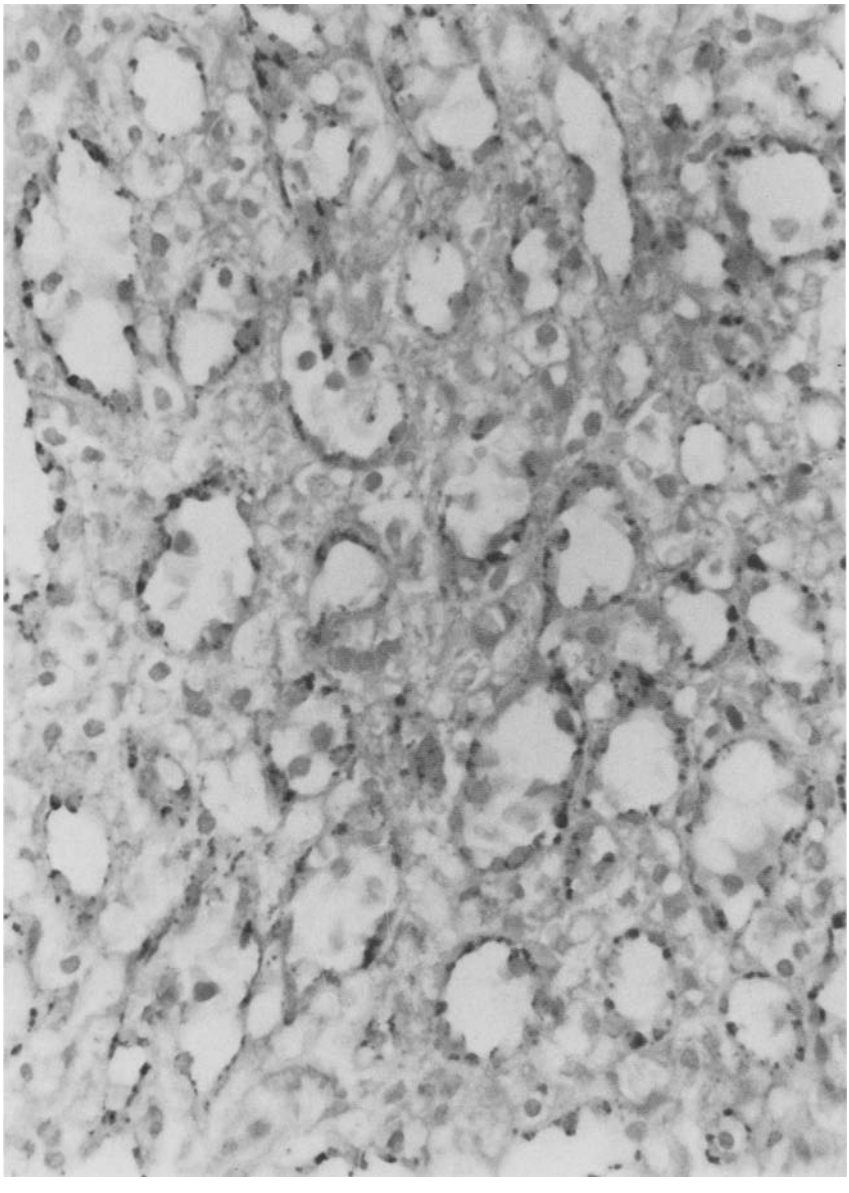

Fig. 1. Red pulp of spleen. Lipofuscin is present in most sinus littoral cells. Schmorl's stain × 300

Discussion

The pigment found in this case was typical lipofuscin, and as such represents a new finding in the human spleen, different to the ceroid-type lipofuscin of the 'syndrome of the sea-blue histiocyte'. Both types of lipofuscin result from lysosomal accumulation of indigestible oxidised lipidic material and

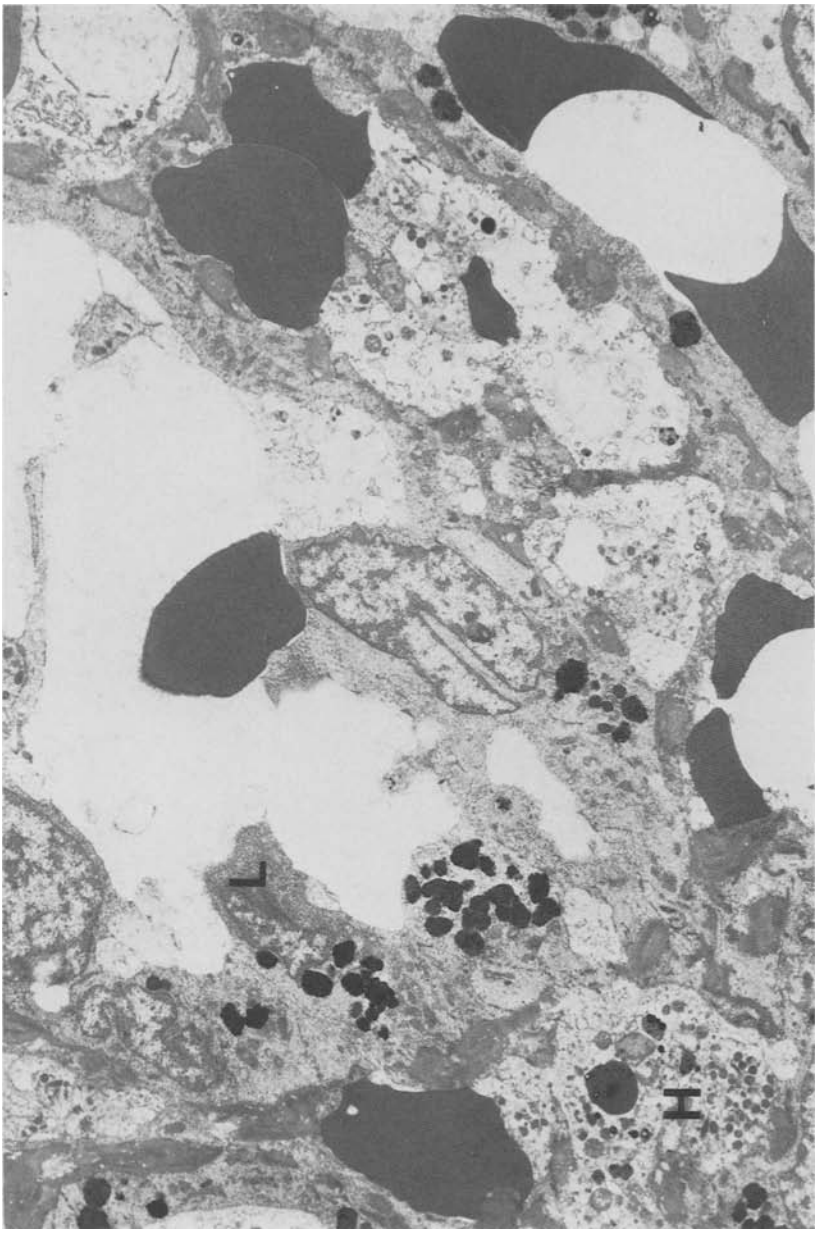

Fig. 2. Red pulp of spleen. Lipofuscin granules are seen in the sinus littoral cells (*L*), but not the histiocytic cells (*H*), which do contain lysosomes and phagocytosed material. Formalin fixed. Lead citrate and uranyl acetate ×4,800. Electron micrograph

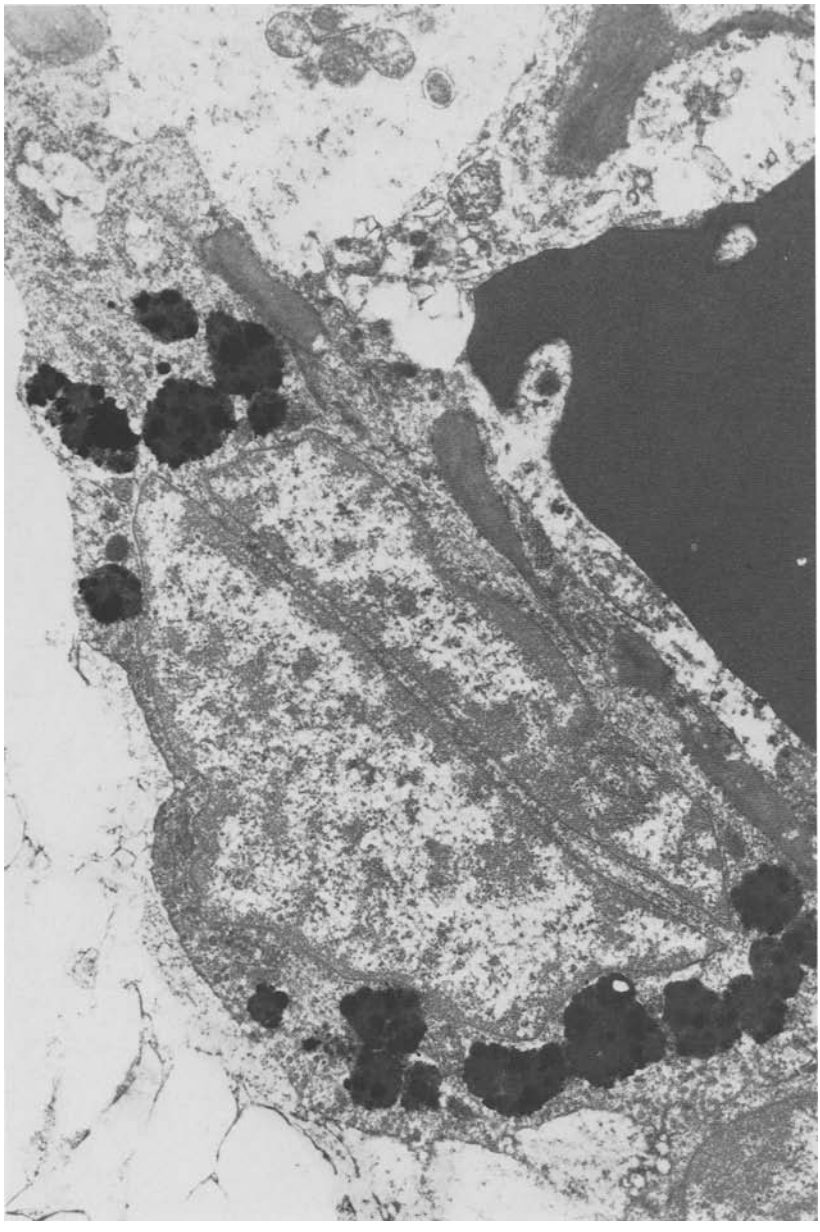

Fig. 3. Sinus littoral cells containing typical lipofuscin. Formalin fixed. Lead citrate and uranyl acetate ×12,600. Electron micrograph

have approximately similar light microscopic appearances and staining properties (Pearse 1985). However, they differ in their ultrastructure and origin. Typical lipofuscin appears as irregular, mainly electron-dense globular material, thought to originate from autophagocytosis of cell organelles (Ghadially 1982), increasing in amount when tissues undergo atrophy (Cole

et al. 1971). In contrast, ceroid type lipofuscin granules appear as myelinoid bodies ultrastructurally (Ghadially 1982) and accumulate in the spleen or other organs, mainly with excessive extracellular phagocytosis (heterophagocytosis), such as in idiopathic thrombocytopoenic purpura or hyperlipidaemia (Rywlin et al. 1971a; 1971b) or when inadequate lysosomal digestion of lipids results from a metabolic abnormality such as sphyingomyelinase deficiency or vitamin E deficiency (Golde et al. 1975; Schnitzer and Loesel 1968).

Lipofuscin has not been previously reported in the sinus littoral cells. The confinement of the pigment to these cells makes a heterophagocytic aetiology very unlikely since littoral cells show minimal phagocytic activity compared with splenic cord histiocytes (Burke and Simon 1970b). This unusual distribution of the pigment and the small size of the spleen further distinguish this case from those of splenic ceroid accumulation.

Acknowledgements. We wish to acknowledge the help of Mr A Westmacket for his help with electron microscopy, Mr W Hinks for light photomicrography and Miss K Emmott for her secretarial help.

References

Burke JS, Simon GT (1970a) Electron microscopy of the spleen I. Anatomy and microcirculation. Am J Pathol 58:127–155

Burke JS, Simon GT (1970b) Electron microscopy of the spleen II. Phagocytosis of colloidal carbon. Am J Pathol 58:157–181

Bishop MB, Lansing LS (1982) The spleen: a correlative overview of normal and pathologic anatomy. Hum Pathol 13:334–342

Cole S, Matter A, Karnovsky MJK (1971) Autophagic vacuoles in experimental atrophy. Exp Mol Pathol 14:158–175

Crichton DN, Busuttil A, Ross A (1980) An ultrastructural study of murine splenic lipofuscinosis. J Ultrastruct Res 72:130–140

Ghadially FN (1982) Ultrastructural pathology of the cell and matrix. 2nd ed. Butterworths, London

Golde DW, Schneider EC, Bainton DF, Penchev PG, Brady RO, Epstein CJ, Cline MJ (1975) Pathogenesis of one variant of sea-blue histiocyte. Lab Invest 33:371–373

Hirasawa Y, Tokuhiro H (1970) Electron microscopic studies on the normal human spleen: especially on the red pulp and the reticulo-endothelial cells Blood 35:201–212

Pearse AGE (1985) Histochemistry, theoretical and applied ed 4. Churchill Livingstone Inc New York

Rywlin AM, Hernandez JA, Chastain DE, Pardo V (1971a) Ceroid histiocytosis of spleen and bone marrow in idiopathic thrombocytopenic purpura. Blood 37:587–593

Rywlin AM, Lopez-Gomez A, Tachmes P, Pardo V (1971b) Ceroid histiocytosis of spleen in hyperlipemia. Am J Clin Pathol 56:572–579

Silverstein MN, Ellefson RD, Ahern EJ (1970) The syndrome of the sea-blue histiocyte. N Engl J Med 282:1–4

Schnitzer B, Loesel LS (1968) Brown bowel. Am J Clin Pathol 50:433–439

Tischendorf F (1969) Handbuch der mikroskopischen Anatomie des Menschen VI/6. Die Milz. Springer, Berlin Heidelberg New York

Accepted October 21, 1985