Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/mjafi

Case Report

A rare constellation of imaging findings in Wolman disease

Lt Col Debraj Sen [a,*], *Brig Lovleen Satija* [b], *Col Sudhir Saxena* [c], *Lt Col Vikas Rastogi* [d], *Meenu Singh* [e]

[a] *Classified Specialist (Radiodiagnosis), Military Hospital Amritsar, C/o 56 APO, India*
[b] *Brig I/C Adm & OC Tps, Military Hospital (Cardio Thoracic Centre), Pune 411040, India*
[c] *Senior Advisor (Radiodiagnosis), Command Hospital (Central Command), Lucknow 226002, India*
[d] *Classified Specialist (Radiodiagnosis), Command Hospital (Central Command), Lucknow 226002, India*
[e] *Resident (Radiodiagnosis), Command Hospital (Central Command), Lucknow 226002, India*

ARTICLE INFO

Article history:
Received 13 June 2013
Accepted 16 February 2014
Available online 26 April 2014

Keywords:
Bilateral adrenal calcification
Infant
Radiology
Wolman disease

Introduction

Bilateral adrenal calcification in infants is an infrequent occurrence and often presents a diagnostic dilemma. Wolman disease is a very rare autosomal recessive lysosomal storage disease that is caused by severe deficiency of lysosomal acid lipase (LAL) enzyme and is fatal within the first year of life. Most literature on the subject describes the characteristic bilaterally enlarged calcified adrenals on imaging. This article presents a rare constellation of other imaging findings in Wolman disease.

Case report

A 4-month-old male infant patient, an issue of second-degree consanguineous marriage and born normally at full-term, was brought to this hospital with progressive abdominal distension, vomiting and listlessness noted over the last one month. There was no history of fever, diarrhoea or jaundice. The first three months of the baby's life were uneventful with normal weight gain and achievement of milestones. There was no history of similar illness in the family. The baby's parents came from a poor socio-economic strata and he was suspected to be suffering from protein-energy malnutrition.

On examination, the baby weighed 4.5 kg. He was pale and had a protuberant abdomen. There was evidence of hepatosplenomegaly with the liver span measuring 9.0 cm and the spleen palpable 3.0 cm inferior to the costal margin. The neurological examination and fundus were normal. Laboratory investigations revealed microcytic hypochromic anaemia with a haemoglobin of 10 g/dL, leucopaenia with a total leucocyte count of 3000/mm^3 and thrombocytopaenia with a platelet count of 75,000/mm^3. Vacuolated lymphocytes were noted in the peripheral blood smear. The serum albumin was 2.5 g/dL. The liver function tests were deranged with raised serum bilirubin (2.0 mg/dL) and elevated transaminases (alanine transaminase – 150 IU/L, aspartate transaminase – 300 IU/L). The prothrombin time (PT) and partial thromboplastin time (PTT) were prolonged and measured 23 s and 48 s,

* *Corresponding author*. Tel.: +91 (0) 9878055215 (mobile).
E-mail address: sendebraj@gmail.com (D. Sen).
http://dx.doi.org/10.1016/j.mjafi.2014.02.006

respectively. The international normalized ratio (INR) was elevated to 1.7. Hypercholesterolaemia (230 mg/dL) and hypertriglyceridaemia (240 mg/dL) were also noted. Faecal fat was evident on 'Sudan staining'. Radiograph of the chest and abdomen revealed a protuberant abdomen with suggestion of hepatosplenomegaly and bilateral paraspinal triangular calcific lesions (Fig. 1). Ultrasonography of the abdomen revealed hepatosplenomegaly, a contracted calcified gallbladder and bilaterally enlarged calcified adrenals (Fig. 2). A subsequent computerized tomography (CT) scan of the abdomen showed hepatomegaly with steatosis, calcified contracted gallbladder, splenomegaly, retroperitoneal lymphadenopathy and ascites apart from the calcified adrenal glands (Figs. 3 and 4). The enlarged adrenal glands maintained their triangular configuration and revealed dense peripheral calcification. Based on the clinical presentation, laboratory investigations and constellation of radiological findings, the diagnosis of Wolman disease was arrived at. The infant's poor health and deranged coagulation profile precluded any attempts at corroborative liver or bone marrow biopsy. Despite supportive therapy, the infant died after a week of admission. Post-mortem liver biopsy revealed 'foamy' histiocytes and 'cholesterol clefts' in the Kupffer cells, which confirmed the diagnosis. The parents were counselled about the genetic nature of the disease and actions to be taken at the next conception.

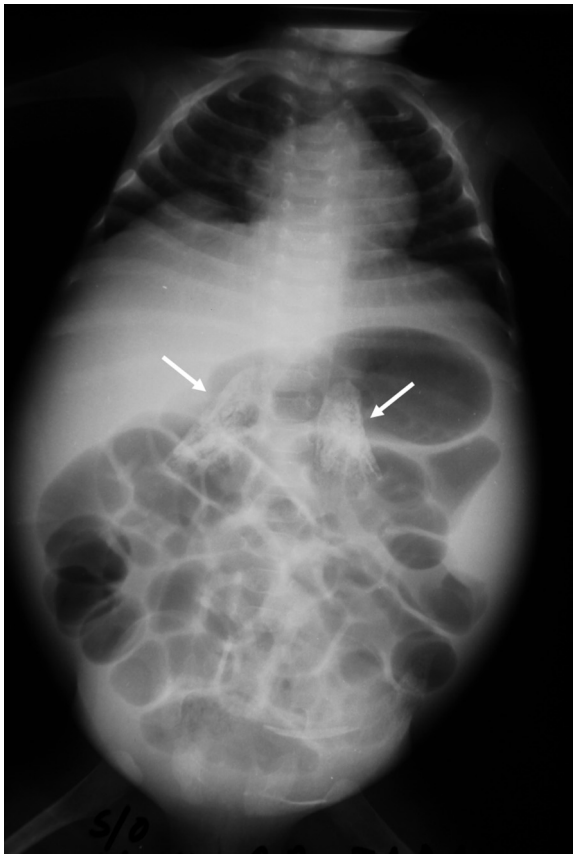

Fig. 1 – Radiograph of the chest and abdomen reveals a protuberant abdomen with bilaterally enlarged calcified adrenal glands (white arrows).

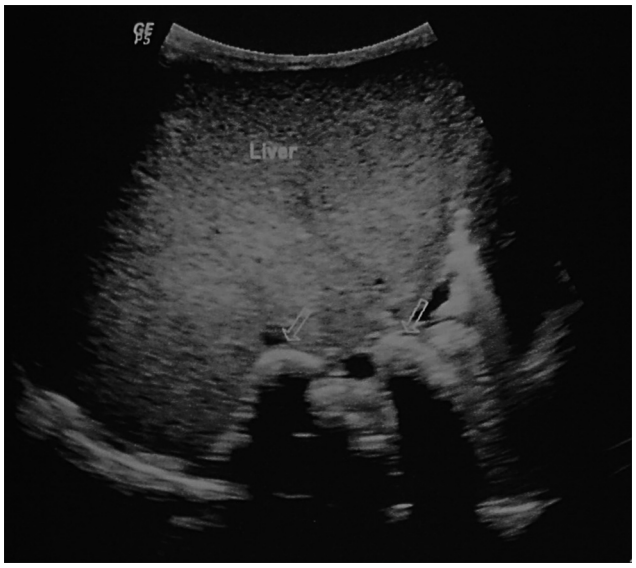

Fig. 2 – Ultrasonographic image showing hepatomegaly. Also note the enlarged calcified adrenal glands casting distal acoustic shadowing (arrows).

Discussion

Wolman disease is a very rare autosomal recessive lysosomal storage disease that is caused by severe deficiency of the lysosomal acid lipase (LAL) enzyme and is fatal within the first year of life. It is named after Moshe Wolman, an Israeli neuropathologist.[1] The disease is characterized by lipid deposition in multiple organs and was first described in 1956 in an infant who presented with vomiting and pallor and had calcified adrenal glands.[1–3] About 80 cases have been reported globally till 2008 and only 5 cases from India till date.[4–6]

The gene for LAL is located on chromosome 10q23.2-q23.3 and it contains 10 exons.[3] The type of defect in the LAL genotype determines the residual enzymatic activity and consequently the severity of the phenotype – residual acid lipase activity within 3–8% of normal LAL leads to the more benign cholesteryl ester storage disease (CESD) and absence of any residual activity leads to Wolman disease.[7] The exact pathogenesis of Wolman disease is unclear. In tissues rich in LDL-receptors, there is efficient uptake of plasma LDL with liberation of cholesterol by LAL. This cholesterol in turn down-regulates the LDL receptor. In Wolman disease, the downregulation of LDL-receptors does not occur, leading to accumulation of LDL cholesteryl esters in lysosomes. The over-uptake of LDL-associated toxic molecules and oxidation of LDL in these tissues (e.g. adrenals, reticuloendothelial system) leads to cytotoxity.[8]

A characteristic feature of Wolman disease is bilaterally enlarged calcified adrenal glands. This occurs due to the saponification of fatty acids and their subsequent calcification.[2,3] The calcified adrenals may be detected on plain radiography, ultrasonography and computerized tomography. On magnetic resonance imaging (MRI), the enlarged fatty adrenal glands reveal signal intensity similar to abdominal fat on T1- and T2-weighted images and the calcifications are seen in the