

## Case Report

## Wolman Disease in an Egyptian Patient

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## ABSTRACT

Lysosomal acid lipase deficiency leads to accumulation of cholesteryl esters and triglycerides in different body tissues. This disorder is manifested in two clinical forms; cholesteryl ester storage disease which is a benign adult form and Wolman disease (WD), a fatal autosomal

recessive form. We present an Egyptian infant with WD whose diagnosis was based on clinical, laboratory and imaging features. This is the first reported patient with WD from Egypt.

KEYWORDS: acid lipase deficiency, adrenal calcification, cholesteryl ester, Wolman disease

## CASE REPORT

A 15-week old Egyptian baby girl presented with a history of failure to thrive and abdominal distension. She was the first baby to first cousin parents. Pregnancy and delivery were uneventful. On physical examination, the baby was pale with hypotonia and massive hepatosplenomegaly. Her complete blood count showed anemia with thrombocytopenia (Hb was 6.6 gm/dl and platelets  $35 \times 10^9/L$ ). Radiological examinations (plain abdominal and skeletal radiographs, abdominal ultrasonogram, non enhanced CT scan, and MRI of the abdomen and brain) were done. Vacuolated lymphocytes were detected in peripheral blood as well as foamy cells on bone marrow examination. The patient developed fever during her hospital stay. She gradually deteriorated and died from progressive hepatic failure and assumed septicemia, in spite of negative cultures, at age of five months.

Plain radiograph of the abdomen (Fig. 1) showed calcification in the suprarenal regions, large liver and splenic shadows, and dilated bowel loops. In addition, a generalized diminished bone density was noted on skeletal survey (Fig. 2).

Ultrasonography (US) demonstrated large hyperechoic adrenal glands with posterior shadowing consistent with bilateral adrenal calcification. Moreover, a markedly enlarged liver with diffusely increased echopattern, simulating fatty liver, a massive splenomegaly and ascites were also seen (Fig. 3).

Non-enhanced computed tomography (CT) of the abdomen revealed bilateral dense calcification of adrenal glands with preserved configuration. CT also demonstrated low attenuation of the enlarged liver (20 HU) indicating fatty infiltration (Fig. 4).

This finding was confirmed on magnetic resonance imaging (MRI) with high signal intensity of the liver on T1-weighted images with very low signal intensity on both T2 and fat suppression STIR (short time inversion recovery) images (Fig. 5: a, b). Massive splenomegaly, minimal ascites and low signal intensity of calcification of large adrenal glands were also identified on MRI. Dilated bowel loops were also noted on abdominal radiograph, CT and MRI examinations. MRI of the brain was unremarkable.

## DISCUSSION

An abnormal accumulation of cholesteryl esters and triglycerides in many tissues results from lysosomal acid lipase deficiency. This is expressed in two forms, namely, Wolman disease (WD) and cholesteryl ester storage disease. The latter is a mild form that usually manifests itself in adulthood while WD is fatal, nearly always before the age of one year. Both are autosomal recessive disorders<sup>[1]</sup>. WD has been found in various ethnic groups in several European countries, Canada, North America and Turkey<sup>[1]</sup>. Several reported cases from the Middle-East region have been related to Jews of Iraq and Arabs of the Galilee and Gulf Area<sup>[2]</sup>. To the best of our knowledge, no Egyptian patient with WD has been reported before.

WD affects many organs and tissues including liver, spleen, intestinal mucosa and lymph nodes<sup>[3]</sup>. It must be considered in an infant presenting with hepatomegaly, gastrointestinal symptoms and failure to thrive. The presence of bilateral adrenal calcification, hepatosplenomegaly and gastrointestinal symptoms strongly supports the diagnosis of WD<sup>[1]</sup>. Detection of vacuolated macrophages in the bone

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Fig. 1: Plain abdominal radiograph shows bilateral faintly calcified adrenal glands, notably the left and dilated bowel loops



Fig. 2: Plain radiograph of the left upper limb shows diffuse osteopenic bone

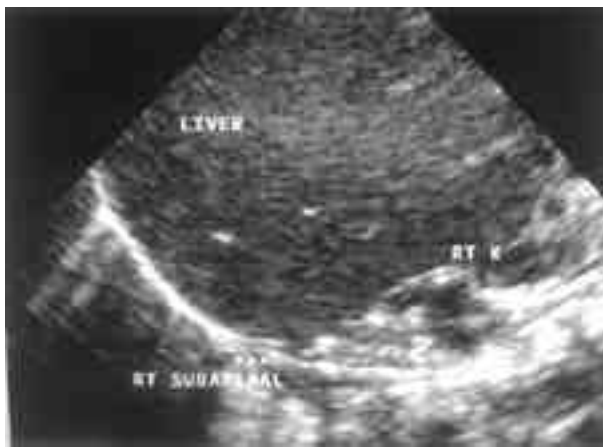


Fig. 3: Ultrasonography of upper abdomen demonstrates bright echogenicity of the liver and diffuse punctate calcification of enlarged right adrenal gland. Similar changes found in the left adrenal (not shown)



Fig. 4: Unenhanced CT scan shows hepatomegaly, diminished liver density (20HU) and calcified large adrenal glands

marrow is a characteristic feature of this disorder<sup>[1-3]</sup>.

Radiologically, bilateral punctate cortical adrenal calcification is characteristic of WD. Calcification appears to be confined to this organ, despite infiltration of all body tissues by vacuolated macrophages<sup>[1,3]</sup>. This calcification was well demonstrated in our patient on US and CT, but less appreciated on MRI. Adrenal calcifications may be seen with tumors (neuroblastoma, ganglioneuroma, teratomas, adenoma, pheochromocytoma and carcinoma), complicating a vascular lesion (hemorrhage), infections (tuberculosis and histoplasmosis) or with Addison disease<sup>[4]</sup>. However, none of these show bilateral cortical calcification with preserved configuration of enlarged adrenals<sup>[1,3]</sup>. It is believed that extensive bilateral punctate calcification throughout the adrenals, with retention of their normal triangular shape is diagnostic of WD<sup>[4]</sup>.

Skeletal survey demonstrated generalized osteopenia. This is in keeping with other reports in

the literature<sup>[1,4]</sup>. It results from excessive marrow infiltration by foamy macrophages<sup>[1]</sup>.

Involvement of the liver results in bright echo pattern noted in US, low attenuation on CT and high signal intensity on T1-weighted images and low signal intensity more than expected on both T2 and STIR images. This is explained by accumulation of lipid droplets in hepatocytes giving an appearance similar to that seen in fatty infiltration<sup>[3,5-7]</sup>.

The small bowel dilatation was identified on abdominal radiograph, CT and MRI. However, thickening of bowel wall reported by others<sup>[3,4]</sup> was not demonstrated in our case. These changes mostly affect the proximal small intestine<sup>[3]</sup>. The infiltration of lamina propria of small bowel by lipid-filled histocytes impairs absorption and results in steatorrhea<sup>[1,4]</sup>.

Lipid deposition in lymph nodes in patients with WD results in foamy lymph nodes<sup>[4,8]</sup>. Fulcher *et al*<sup>[8]</sup> described the imaging pattern of lymph nodes in a case of WD in which the fat containing



Fig. 5a: Unenhanced coronal T1-weighted (repetition time msec/echo time msec =500/23) MR image demonstrates hepatosplenomegaly displacing the dilated small bowel loops with multiple low signal intensity foci of the left adrenal calcification.



Fig. 5b: Coronal T2-weighted (3600/120) MR image demonstrates more hypointensity of the liver due to fat deposition.

lymph nodes had low attenuation on CT and were isointense to retroperitoneal fat on MRI, indicative of fat deposition. In our patient, no obvious enlargement or abnormal signal intensity of mesenteric or retroperitoneal lymph nodes could be appreciated.

Cerebral MRI studies have rarely been undertaken in patients with WD. No disorganized morphological change, atrophy or signal abnormalities of the brain were detected on MRI in our patient. This is in keeping with the findings of Al-Essa *et al*<sup>9</sup> who reported normal brain on MRI as well as normal glucose uptake in cerebral cortex, basal ganglia, white matter and cerebellum on positron emission tomography (PET).

There is no specific treatment for either WD or cholesteryl ester storage disease. The main goal of treatment in WD is to ameliorate the gastrointestinal symptoms of diarrhea and vomiting<sup>11</sup>. Bone marrow transplantation was reported to be successful in maintaining long-term remission in one patient with WD<sup>10</sup>.

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