Wolman's Disease. The First Two Cases from Bahrain

*Hassan Ali Zein Aldeen, MBchB, DCH, MRCP(UK)**
*Fayek Al-Hilli, MBChB,DPath,PhD(Path)***
*Akbar M Mohammad,MD,FAAP**
*Najeeb S Jamsheer, MD,FRCR****
*Khalil Hassan Ras Romani, MS*****

Wolman's disease, a rare autosomal recessive disorder, is reported in two Bahraini children who are not related.

Bahrain Med Bull 1999;21(1): 24-26

Wolman's disease, a familial autosomal recessive disorder first described by Wolman et al in 1956 and 1961[1] is due to deficiency of lysosomal acid lipase and characterised by the deposition of Cholesterol ester and triglycerides in most body tissues. It is clinically manifested with vomiting, intractable diarrhoea, failure to thrive, abdominal distention, hepatosplenomegaly and enlarged calcific adrenals. The disease is rare and not confined to patients of Jewish ancestry as it was thought earlier since sporadic cases have been reported in other ethnic groups including Moslem children[2,3]. We report two unrelated Moslem Arab Bahraini children with Wolman's disease.

THE CASES

Case 1

Three months old Bahraini Arab male infant admitted in 1982 to Salmaniya Medical Centre, Bahrain with history of diarrhoea, vomiting, abdominal distention and failure to thrive. He was the product of a full term pregnancy with normal home delivery. His birth weight was 2 Kg. His parents were Moslem Arab Bahraini of consanguinous marriage, they had 5 daughters and 3 other sons, one of whom had mylomeningocele. Soon after birth the child was unable to suckle but after few days he started breast feeding normally. He was admitted at the age of 20 days with 5 days history of cough, vomiting, diarrhoea and abdominal distention.

On admission the infant was marasmic, hypothermic, pale and inactive. His body temperature was 35°C, pulse rate 100/minute, respiratory rate 42/minute and weight 2.7 Kg. The abdomen was markedly distended with the liver and spleen extending 3cm and 2cm below costal margin respectively. The chest was clear, heart sound loud and rapid with an audible systolic murmur and the neurological examination showed no deficit. There were no palpable lymph nodes.

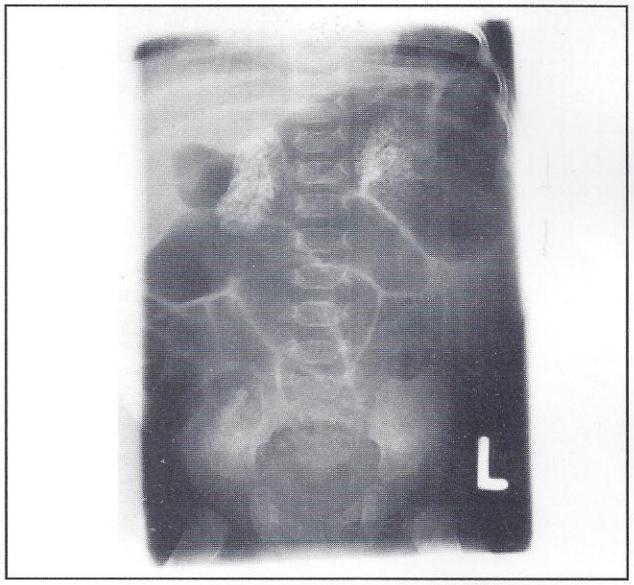

Figure 1. Plain radiograph of the abdomen showing bilateral suprarenal enlargement and calcification

Abdominal x-ray showed two massive punctate calcific triangular paravertebral shadows situated at the level of the first lumbar vertebra extending upward to the eleventh vertebra (Fig 1). The chest x-ray and skeletal survey showed osteopenia; otherwise unremarkable. The laboratory investigations are shown in Table 1.

The patient was rehydrated with intravenous half saline solution and his electrolytes corrected. He was given intravenous gentamycin 5 mg/kg, ampicillin 100 mg/kg, 25 mg hydrocortisone and multivitamins. He also received 50 ml whole blood transfusion. His condition deteriorated and died 21 hours after admission.

At postmortem the infant was poorly nourished and underdeveloped with moderate jaundice weighing 2.650 gm. The body length was 55 cm and head circumference 35

* Department of Paediatrics
** Department of Pathology
*** Department of Radiology
**** Department of Surgery
Salmaniya Medical Complex
State of Bahrain

Table 1. The laboratory investigation of two patients with Wolman's disease

	Patient 1	Patient 2
Haemoglobin (g/dl)	6.2	10.2
Haematocrit (%)	19	
Re. ticulocytes (%)	1.8	6
Platelets (cmm)	420	359
RBC's (cmm)	274	
Total WBC Count (cmm)	9100	8.1
Neutrophiles	30	44
Lymphocytes	48	48
Eosinophiles	3	
Monocytes (%)	8	4
Band cells (%)	9	4
Basophiles (%)	1	
Metamyelocytes (%)	1	
Sickling test	Negative	Negative
Hb Electrophoresis		AF
G6PD Activity	Reduced	Reduced
Blood group	0 Rh (positive)	
CSF examination	Unremarable	
Peripheral blood film	Foamy histiocyes, microcytic hypochromia	
Bone marrow aspirate	Foam cells	
Electrolytes (mmol)		
Na	119	138
K	2.9	4.4
Cl	101	104
HCO3	12	21
Calcium (mmol/l)	2.55	
Blood sugar (mmol/l)	7.3	
Blood urea (mmol/l)		15
Serum creatinin (umol/l)		0.3
Serum amylase (u/l)		Normal
Serum total proteins (g/l)	51	52
Albumin (g/l)	33	25
Globulin (g/l)	18	37
Total Bilirubin (umol/l)	94	<18
SGPT (u/l)		68
Gamma GT (u/l)		22
Cholesterol (mmol/l)		2.7
Triglycerides (mmol/l)		3.7
Total lipids	4.2	
Phospholipids	0.57	
Thyroid function tests		Normal
Urine examination	Unremarkable	Unremarkable
Stools examination	Unremarkable	Fat globules

cm. The abdomen was distended and there were no palpable lymph nodes. The breast and external genitalia were normal.

About 40 ml of clear ascitic fluid was collected. The spleen weighed 22 gm and was hard with pink gray cut surface showing delicate network of yellowish gray bands. The liver weighed 140 gm and was firm with golden greasy yellow homogenous cut surface. The adrenals (8 gm right and 9 gm left) were symmetrically enlarged, firm, well demarcated with gritty yellow chalky calcific cut surface. The kidneys (11 gm each) were unremarkable. The mucosa of the small intestine was white with prominent yellow granular patches. The mesenteric lymph nodes were enlarged rubbery but the mediastinal nodes were not enlarged. Minute yellow white plaques along the large blood vessels were present. The brain, upper respiratory tract, heart, lungs and gonads appeared normal. The bone marrow appeared pink and fleshy.

The dominating pattern in the microscopic sections examined was the presence of large foamy lipid-laden histiocytes. The hepatocytes were finely vacuolated and lipid-laden. The lipid-laden histiocytes were seen within the hepatic parenchyma particularly the peripheral hepatic zone as well in the Kupffer's cells, and in the connective tissue of the portal tracts; but there was no evidence of cirrhosis. In the spleen similar foamy histiocytes filled the depleted red pulp. The reticulum cells of the spleen were nearly all lipid-laden histiocytes.

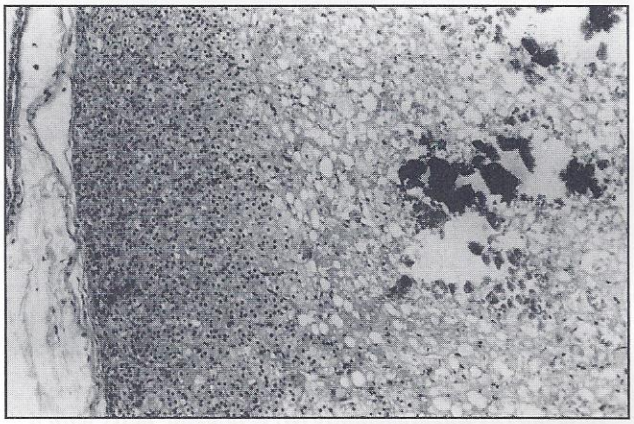

Figure 2. Adrenal tissue with preserved outer cortex and haphazardly arranged large foamy histiocytes in the deep medulla. Amorphous calcific masses are present in the cortex (H & E x 100)

The adrenal cortical cells of the zona glomerulosa and part of the fasciculata were preserved but there was complete replacement of the inner zone by haphazardly arranged large vacuolated cells. Amorphous partly calcific masses were present throughout the inner cortex (Fig 2). No other area of calcification were seen in other organs. In the kidney, vacuolated and foamy cells were also present in the mesangial cells of the glomerular tufts. The villi of the small intestine were stunted and foamy lipid-laden histiocytes filled the lamina propria and submucosa. Foam cells were also seen in the bone marrow, thymus, the mesenteric lymph nodes and the lamina propria of the oesophagus, stomach and colon. In the aorta the lipid deposition was seen between the elastic fibres especially adjacent to the intima. Few foam cells also seen within the alveolar walls of the lung or lay free within the alveolar spaces.

Case 2

Two and a half months old Bahraini Arab female infant admitted in 1993 to Salmaniya Medical Center with vomiting after feeds since the age of one month associated with abdominal distention and passage of pale stools. She was delivered normally full term after an uneventful pregnancy weighing 3.4 Kg. She was the tenth child of healthy second degree consanguineous Moslem parents with two children who had died at the age of 12 and 13 years because of gastroenteritis.

On admission the child was emaciated weighing 3.9 Kg (<

third percentile) and measuring 58.5 cm in length (<fiftieth percentile). There were no dysmorphic features. Her abdomen was distended and the bowel sounds were audible. The liver and spleen were each felt 3 cm below costal margin. There were no palpable lymph nodes. She was mildly hypotonic with normal deep tendon reflexes.

Abdominal plain x-ray showed bilateral adrenal calcification. Abdominal ultrasound showed hepatosplenomegally, calcific adrenals and thickened intestinal loops (Fig 3). The laboratory investigations are shown in Table 1.

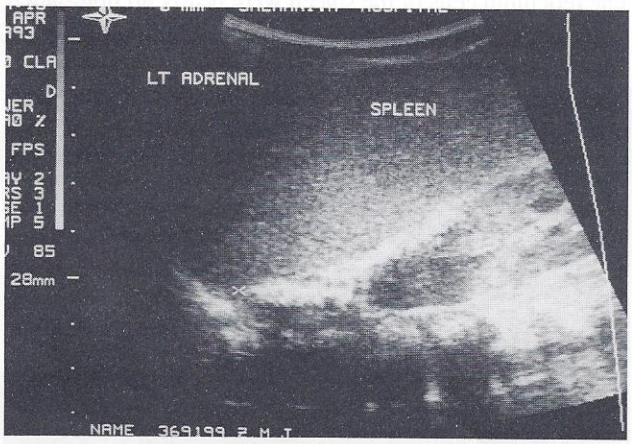

Figure 3. Ultrasound longitudinal through the spleen showing (a) splenomegallly (b) echogenic mass with a length of 2.8 cm with slight posterior shadowing in the left suprarenal area

The patient was continued on breast feeding and refused protein hydrolysate formula. She developed septicaemia with coagulopathy and received parentral ampicillin, gentamycin in addition to general supportive measures. Her condition deteriorated rapidly and died of septic shock. Postmortem examination was not done.

DISCUSSION

Two forms of acid lipase deficiency are now known with different phenotype expression; the classical Wolman's disease is fatal and typically occurs after the first month of life with vomiting, diarrhoea, failure to thrive, abdominal distention and hepatosplenomegally. The other is cholesterol ester storage disease (CESD) which takes a milder form and usually presents in adulthood[4]. Both patients in this report presented with features of Wolman's disease after birth and died soon afterward. Malabsorption and intractable diarrhoea are the common causes of death within the first year of life but other complications such as cirrhosis and respiratory failure due to cholesterol ester storage in the liver and lung tissue have been implicated.

The disease is characterised by triglyceride and cholesterol ester deposition in many tissues and these may store lipids as high as 100 times that of the normal range. The lipid profile however may be very heterogeneous in the affected infants and most reported cases have normal or slightly increased plasma triglycerides and cholesterol levels4 as in the case of our patients.

Most cases of Wolman's disease reported in the literature have familial inheritance while in the present cases there is no clear familial evidence of such transmission. It is possible here that a Wolman's disorder without familial tendency may exist.

The diagnosis of Wolman's disease can be made by demonstrating the bilateral adrenal calcification, a pathognomonic feature of this disorder. Abdominal x-ray and ultrasound will also reveal hepatomagally with normal echogenicity along with thickened bowel loops[5].

Prenatal diagnosis of families at risk can also be made by examining the acid lipase activity of cell culture obtained from chorionic villi[4,5]. Even heterozygosity for Wolman's disease can be identified by this method.

There is no specific treatment for Wolman's disease and although sustained caloric balance can be maintained by total parentral nutrition, this has not altered the eventual course of the disease. However the acid lipase deficiency of leukocytes can be corrected by bone marrow transplantation[6] and it would seem that in the future recombinant DNA technology will allow the isolation and purification of acid lipase and then direct infusion of the missing enzyme6.

REFERENCES

1. Wolman M, Sterk VV, Gatt S, et al. Primary familial xanthomatosis with involvement and calcification of the adrenals. Pediatrics 1961;28:724-57.
2. Raafat F, Hashemian MP, Abrishmai MA. Wolman's disease. Report of two new cases with review of the literature. Am J Clin Pathol 1973;59:490.
3. Al Essa M, Nounou R, Sakati N, et al. Wolman's disease: The King Faisal Specialist Hospital and Research Centre experience. Ann Saudi Med 1998;18:120-4.
4. Bona G, Gallina MR, Lavarone A, et al. A case of acid lipase deficiency; Wolman's disease. Panminerva Med 1989;31:49-53.
5. Bona G, Ozmen MN, Augun N, et al. Wolman's disease. Ultrasonographic and computed tomographic findings. Pediatr Radiol 1992;22:541-2.
6. Krivit W, Freese D, Chan KW, et al. Wolman's disease. A review of treatment with bone marrow transplantation and considerations for the future. Bone Marrow Transplan 1992;10 [Suppl 1]:97-103.