Association of sickle cell anemia and glycogen storage disease type 1a.

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We report an unusual case of sickle cell anemia (SCA) associated with glycogen storage disease (GSD) type 1a. A 4-year-old boy was diagnosed with SCA at the age of 2 months after an episode of chest infection. At the age of one year he developed hand and foot syndrome followed by acute chest syndrome and one episode of aplastic crisis. He required several blood transfusions and exchange transfusion. There was no history of jaundice, abdominal pain, joint pain or seizures.

Developmental history revealed a motor delay in which he walked at the age of 2-years, while other aspects of development were normal. Parents were first cousins. He had a brother who died at the age of 9-months due to an unidentified metabolic disease associated with hepatomegaly, hypoglycemia and developmental delay. Another living, younger brother who experienced hypoglycemia and convulsions, and thereafter he was diagnosed with GSD. Both brothers were not sicklers. Upon examination the child looked stunted, pale, not jaundiced with a dull's face, protuberant abdomen and thin upper and lower limbs. His growth parameters were all below the fifth percentile of the growth chart, while vitals were normal. Chest examination was normal, with hyperdynamic precordium. Abdomen was hugely distended with a liver span of 16 cms, but no splenomegaly, ascites or renal masses. Central nervous system examination was normal. Laboratory investigations showed hemoglobin 6.2 g/dl, platelets 306x10^9/L corrected white blood cells 17 x 10^9/L predominantly neutrophils and reticulocytes of 15%. Peripheral blood film showed sickle cells, polychromasia, target cells and neutrophilia. Hemoglobin electrophoresis revealed homozygous S/S band. ABG, during chest infection, pH was 7.2; PCO_2 10.26; BE 16.37 with O_2 saturation of 95%. Urea and electrolytes were normal. Tests for toxoplasmosis, rubella, cytomegalovirus, syphilis, hepatitis B and C, human immunodeficiency virus, repeated bacterial and virology cultures were negative. Asymptomatic hypoglycemia was noticed on several occasions of illnesses where random glucose levels were 2.7, 1.4, 1.8, 0.7, 1.3 mmol. LFT showed a total bilirubin of 19 mcmol/l with the direct portion of 4 mcmol/l, alanine aminotransferase 277u/l; aspartate transaminase 375u/l; GGT 225u/l; total protein, 77g/l; albumin fraction, 38g/l and serum lactic acid 4.3 (↑) (NR 0.4 -2), serum triglycerides 6.61 mmol/l (↑), serum cholesterol 4.34 mmol/l (N) and serum uric acid 475 mcmol/l (↑).

Chest x-ray showed cardiomegaly, with residuals of pneumonic changes. Electrocardiogram revealed sinus rhythm at a rate of 150 and left ventricular hypertrophy. Echocardiogram, showed dilated cardiomyopathy involving mainly the left atrium, left ventricle, with no evidence of pericardial effusion. Abdominal ultrasound revealed hyper echoic enlarged liver, possibly due to metabolic disease. No evidence of gall stones. Computerized tomography scan of the abdomen revealed the same findings in addition to bilaterally enlarged kidneys with no evidence of acute or chronic Budd-Chiari syndrome. Liver biopsy showed normal architecture, unremarkable portal tracts; the parenchyma showed swollen hepatocytes full of glycogen as shown by para-aminosalicylic acid (PAS) and nuclear inclusion positive for PAS were also seen. Electron microscopy showed centrally located nucleus of hepatocytes with prominent nucleoli in some. The cytoplasm is largely occupied by glycogen particles, rosettes which are not membrane bound. Glycogen nuclear inclusions are also seen. There are a few other cytoplasmic organelles such as mitochondria, smooth and rough cytoplasmic reticulum. Some hepatocytes exhibit large lipid droplets. The diagnosis was consistent with GSD most likely type 1a. The patient was treated with the usual protocols for sickle cell patients in addition to uncooked corn starch overnight, which will improve his growth, liver size and correct hypoglycemia. Both sickle cell anemia and GSD are autosomal recessive conditions; however the ß-globin gene cluster on chromosome 11 and the GSD type 1-a gene is located on chromosome 17q21; therefore, there is a little chance of linked inheritance. The unusual co-occurrence of sickle and GSDs prompt speculation regarding the effect of one disease on the course of the other and the effect of both diseases on one child. Although, hepatomegaly is found in more than 90% of patients with SCA and sickling crisis can affect the liver in approximately 10% of patients,[1] this was not the condition in our case.

We have excluded all other diseases which cause such a huge liver especially hepatic sequestration, Budd-Chiari syndrome, other metabolic storage disorders such as Niemann-Pick disease,

malignancy and congestive heart failure as a contributing factor to the existing hepatomegaly. However, the recognition of GSD was delayed in our patient because all symptoms were initially attributed to underlying SCA. Both SCA and GSD could present with repeated infections, failure to thrive, hepatomegaly with abnormal liver enzymes and cardiomegaly. Therefore, when symptoms change in SCA or acquires an atypical clinical course a concurrent illness should be considered in the differential diagnosis; as early recognition of a co-existing disease such as GSD is important to institute appropriate therapy and prevent potential complications.[2] The clinical presentation, biochemical derangement and liver biopsy were supportive of GSD; in addition, the absence of neutropenia excludes GSD-1b[3] and the presence of lactic acidemia and hyperuricemia makes GSD type III a remote possibility.[4] Since enzymatic assay was not available in our institute, our management plan was directed towards the most common form GSD-1a, in addition to conventional management of sickle cell disease.

In conclusion, since SCA is commonly seen by pediatricians, it is important to have a high index of suspicion when a common disorder has an atypical presentation in order to avoid preventable complications.

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Omphalitis and necrotizing fasciitis in neonates

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Although, the incidence of infective umbilical cord /periumbilical tissue has decreased in the developing countries,[1-3] but a spectrum of complication related to infection of unhealthy umbilical stump including neonatal omphalitis (NO) and necrotizing fasciitis (NF) is still seen. We present the experience of these infections during the last 5 years at the Royal Hospital (RH), Muscat, Sultanate of Oman the only tertiary center with facility of pediatric surgery. During the recent years (January 2000 to January 2004), a total of 15 cases with the diagnosis of NO/NF were admitted to RH. Out of the 15 cases, 8 had NO while 7 had NF. The differentiation is made according to the severity[3] (Category 1: Umbilical discharge/ malodorous unhealthy umbilical stump, Category 2: Omphalitis with periumbilical erythema, Category 3: Omphalitis with systemic sepsis, Category 4: Omphalitis with fasciitis and systemic sepsis). The case summaries are depicted in **Table 1**.

All babies were born at term and all received parenteral antibiotics. Blood cultures were negative in all cases except in case 12 (*Staphylococcal epidermidis*). Majority of the cases was referred from other hospitals (60%). Only one case was born at home (case 13). The mean age at presentation was 5 days and the mean hospital stay was 8 days. There were 8 males and 7 females. Out of 7 serious stage/category 4 NF cases, 3 died, giving a mortality of 42% (overall mortality was 20%, 3 out of 15), which shows a reduction by 50% from our previous experience a decade back.[4] The improvement noted could be a reflection of better maternal and child health care, decreased home birth, early recognition, inpatient care with use of parenteral antibiotics and following baby friendly hospital initiative, as suggested by Sawardekar.[3] However, further improvement could be achieved by more aggressive approach, as shown by Garner et al.[5] The use of local agents may also have potential role. A recent randomized clinically trial has also shown the benefits of triple dye/alcohol regime in comparison to dry cord care.[6]

In conclusion, it is evident from the data presented that incidence and mortality related to