Type 1 Gaucher disease with fatal outcome in a 17 year old girl from Kazakhstan

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A 17 year old girl was referred to the National Research Center for Maternal and Child Health of the Nazarbayev University Medical Center in Astana, Kazakhstan in June 2016 with a 4 month history of easy fatigability, dyspnea, abdominal distension, and episodic fainting.

The family history showed only an unspecified hematological disease as the cause of death of her grandmother. The patient had been anemic since the age of 2 years, and was then found to have massive splenomegaly with pancytopenia. She had been splenectomised at the age of 4 years for symptomatic relief of pancytopenia. At that time, patent foramen ovale and a slightly enlarged left ventricle were detected and left untreated. At 6 years of age the patient had been admitted to the hospital with a closed fracture in the upper third of the left femur, and anemia (Hb 8.9 g/dl) was still present. From the age of 7 years the patient had complained of recurrent bone pain especially in the spine. At 11 years of age compression fractures of the T3, T4, T5 and T6 vertebrae had been found. A provisional diagnosis of Kummell disease had been made and the patient had undergone non-operative treatment to stabilize the vertebral column.

Physical examination revealed a critical condition with grade 4 dyspnea, low oxygen saturation (89% on O_2 through face mask), pallor, abdominal distension, and massively enlarged liver extending into the pelvis. Blood tests showed Hb 7.7 g/dl, WBC 6.51 × 10^9/L, platelets 206 × 10^9/L, prothrombin time 18 sec, AST 71 IU/L (normal < 59), and ALT 41 IU/L (normal < 29).

A chest X-ray [Figure 1] showed cardiomegaly, dilated pulmonary artery and elevation of the right diaphragmatic dome secondary to massive hepatomegaly. An ECG demonstrated sinus tachycardia (106 bpm) and right axis deviation. An echocardiogram revealed 58% ejection fraction, atrial septal defect with pronounced right atrium, right ventricle and pulmonary trunk dilatation.

A bone marrow aspiration showed numerous cells suggestive of Gaucher cells, with eccentric nuclei, abundant bluish, fibrillary cytoplasm resembling wrinkled tissue paper [Figure 2].

The patient was transferred to the cardiovascular intensive care unit where she died 12 hours later.

Enzymatic and genetic analysis confirmed Gaucher disease. β-glucocerebrosidase

Figure 1. Chest X-ray

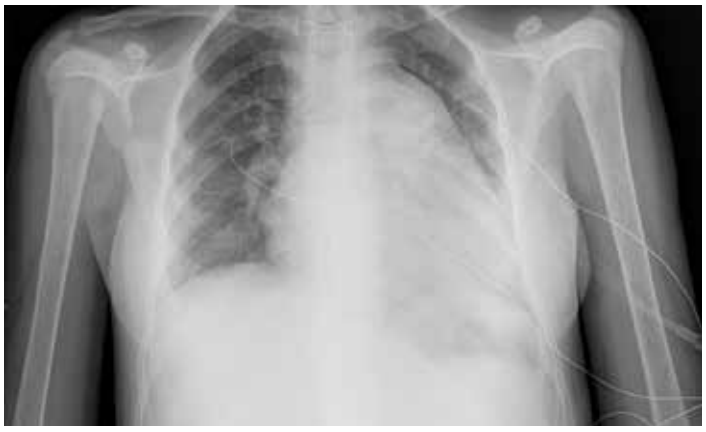
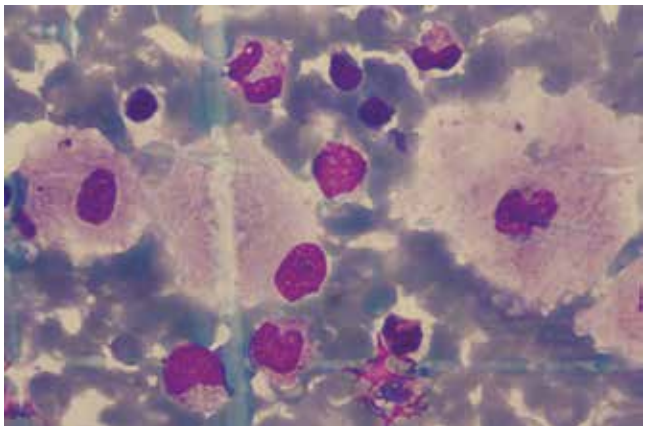


Figure 2. Bone marrow aspirate, Romanowsky-Giemsa staining, x100



activity was 2.1 μmol/L/hr (cutoff value > 2.5), and two heterozygous mutations were detected: c.[1226A>G]; [1448T>C], p.[N409S]; [L483P].

Gaucher disease is a rare lysosomal storage disorder where mutant lysosomal acid β-glucocerebrosidase fails to properly hydrolyse its substrate, glucosylceramide, which accumulates in the lysosomes in cells of macrophage lineage. Multisystem organ involvement (liver, spleen, bone marrow, lungs, central nervous system) ensues [1,2]. A high degree of suspicion is required for Gaucher disease in the presence of splenomegaly or splenectomy, anemia, bone pain and fractures secondary to light trauma. Total splenectomy accelerates bone disease in patients with Gaucher when compared with partial splenectomy [3,4], and pulmonary hypertension is so common after splenectomy in patients with Gaucher disease that some experts recommend against it if replacement therapy is available [5].

In our patient the removal of the primary reservoir of storage cells through splenectomy likely favored the migration of mononuclear phagocytes toward the bones, liver and lungs. Our case indicates that not only hematologists but also orthopedists must keep Gaucher disease in mind so patients can be diagnosed early enough in the course of the disease.

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Capsule

Gut anaerobes protect against pathogen invasion

Intestinal infections are a common problem for young animals. One explanation is the protective gut microbiota, which is not fully established in infants. How the microbiota might protect against pathogens is unclear. Kim and co-authors found that members of the group of strictly anaerobic, spore-forming bacteria known as Clostridia protect neonatal mice against diarrhea-causing pathogens. The protective effect is enhanced by giving mice the metabolite succinate in drinking water. Succinate favors colonization of the neonatal gut by cluster IV and XIVa Clostridia and concomitantly excludes *Salmonella typhimurium.*

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Capsule

Evaluation of amyloid protective factors and Alzheimer disease neurodegeneration protective factors in elderly individuals

While amyloid and neurodegeneration are viewed together as Alzheimer disease pathophysiology (ADP), the factors that influence amyloid and AD-pattern neurodegeneration may be considerably different. Protection from these ADP factors may be important for aging without significant ADP. Vemuri and colleagues tried to identify the combined and independent protective factors for amyloid and AD-pattern neurodegeneration in a population-based sample and to test the hypothesis that "exceptional agers" with advanced ages do not have significant ADP because they have protective factors for amyloid and neurodegeneration. This cohort study included a prospective analysis of 942 elderly individuals (aged 70 to ≥ 90 years) who had undergone magnetic resonance imaging and Pittsburgh compound B-positron emission tomography scans and who were enrolled in the Mayo Clinic Study of Aging, a longitudinal population-based study of cognitive aging in Olmsted County, Minnesota, USA. The authors evaluated predictors including demographics, Apolipoprotein E (APOE), intellectual enrichment, midlife risk factors (physical inactivity, obesity, smoking, diabetes, hypertension, and dyslipidemia), and the total number of late-life cardiac and metabolic conditions. The study participants included 423 (45%) women and the average age of participants was 79.7 (± 5.9) years. Apart from demographics and the *APOE* genotype, only midlife dyslipidemia was associated with amyloid deposition. Obesity, smoking, diabetes, hypertension, and cardiac and metabolic conditions, but not intellectual enrichment, were associated with greater AD-pattern neurodegeneration. In the older cohort (≥ 85 years), the Cohen *d* results showed small to moderate effects (effect sizes›0.2) of several variables except job score and midlife hypertension in predicting exceptional aging without ADP.

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