GAUCHER'S DISEASE

Report of a Case

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Abstract. Panich, Vicharn, et al. : Gaucher's Disease : Report of a Case. Siriraj Hosp. Gaz. 1970, 22: 27-34.

The first adult case of Gaucher's disease in Thailand was reported. The diagnosis was based on hepatosplenomegaly and Gaucher's cells in the bone marrow without any evidence of leukaemia. The manifestation of the disease was very mild with neither any skin change, pingueculae nor elevated serum acid phosphatase.

Introduction

Gaucher's disease or cerebroside lipidosis was first described by Gaucher[1] in 1882. In 1924, Lieb[2] isolated large amounts of cerebrosides from the tissue of a patient suffering from this disease. Suomi and Agranoff[3] were the first to demonstrate that in Gaucher's disease the lipids accumulating in the tissue were glucocerebrosides. The disease is now believed to be due to the deficiency of glucocerebrosidase,[4, 5] resulting in accumulation of glucocerebrosides in reticuloendothelial cells and consequent destruction of organs. A reticuloendothelial cell with large amount of glucocerebrosides in cytoplasm has a characteristic appearance and is called a " Gaucher's cell ".

About four hundred cases have been reported so far in the world. Most of the cases have been reported from Europe and America. A high incidence in Jews especially Ashkenazi has been noted.[6] The disease has also been reported in Negroes,[7, 8] Indians,[9] Japanese,[10] and Maori.[11] In Thailand this disease was first detected in 1966[12] by Tuchinda et al., in two sibling children. The patient presented in this paper is the first chronic case, of an adult from this country. Recently, Tuchinda et al.[13] encountered another childhood case.

Case Report

The patient was an 18 years old male with Chinese ancestry. He had had epigastric pain for 4 years. The pain was relieved by meal. A few episodes of " black stool " were noticed one year previously but he did not seek medical attention for all these symptoms. He was admitted to the Department of Medicine and Siriraj Hospital on October 12, 1968 because of melena and pallor for

one week. On the day of admission he vomited black content and fainted.

His parents were non – related Chinese immigrants from the southern part of China. His 63 – year – old mother is now living and healthy but the father died 13 years ago of an unknown cause at the age of 53. Family history will be discussed in detail later.

On physical examination the patient was severely anaemic without jaundice. There was no sign of bleeding on the skin. Liver and spleen were 5 cm. and 10 cm. respectively below costal margins. No other abnormal physical sign was detected.

Blood examination revealed haemoglobin concentration of 5.2 gm. per cent, packed cell volume 14 per cent, white blood count 4,200 per c.mm., platelets slightly decreased in number and red blood cells markedly hypochromic. Anisocytosis, poikilocytosis and polychromasia were also noticed in his peripheral blood film. Bone marrow showed slight increase in cellularity, the elements increased being megakaryocytic and erythroid series. Myeloid series was normal. Numerous Gaucher's cells were seen (Fig. 1). Urine examination was normal, stool tarry in appearance and benzidine test strongly positive.

Upper gastro – intestinal roentgenographic examination revealed neither ulcer nor esophageal varices. Bone survey showed a slight expansion of lower end of shafts of femurs (Fig. 2). Chest roentgenogram was normal.

Serum albumin was 3.1 gm. per cent, globulin 1.5 gm. per cent, creatinine 1.0 mg. per cent, uric acid 4.9 mg. per cent. Direct and total bilirubin were 0.3 and 0.6 mg. per cent, respectively, cephalin – cholesterol flocculation test negative, thymol turbidity test 4.2 units, zinc turbidity test 4.6 units, iodine test negative, aspartate transaminase 21 sigma units, alanine transaminase 10 sigma units, bromsulfalein retention 4.0 per cent, cholesterol 133.3 mg. per cent, acid phosphatase 0.8 units and alkaline phosphatase 1.6 Bodansky units.

The Cr^{51} red cell survival revealed a rather shortened half life of 17 days. There was an excessive spleen count of 13.7 K (normal spleen activity was less than 5 K). Coagulogram was normal except for prolonged plasma thromboplastin generation test of 125 seconds which could be corrected by fresh normal human plasma. Serum iron was 32 microgram per cent, and UIBC, 387 microgram per cent.

He was first thought of as having upper gastrointestinal haemorrhage, probably from peptic ulcer or ruptured oesophageal varices with secondary iron deficiency anaemia. Two units of blood were given, peptic ulcer regimen and iron medication were administered. After bone marrow examination was done, Gaucher's disease with secondary hypersplenism was diagnosed. The cause of upper gastro – intestinal haemorrhage was still not clear. This might be due to a minute peptic ulcer which was not visualized by barium meal or due to thrombocytopenia and coagulation defect. The chronic upper gastro – intestinal haemorrhage caused secondary iron deficiency anaemia.

He responded very well to antacid and iron therapy and has been in good health presently with normal haemoglobin level, low white blood cell count and moderately decreased number of platelets.

Upon inquiry of the past history in detail, the patient had never noticed the mass in his abdomen. But his mother

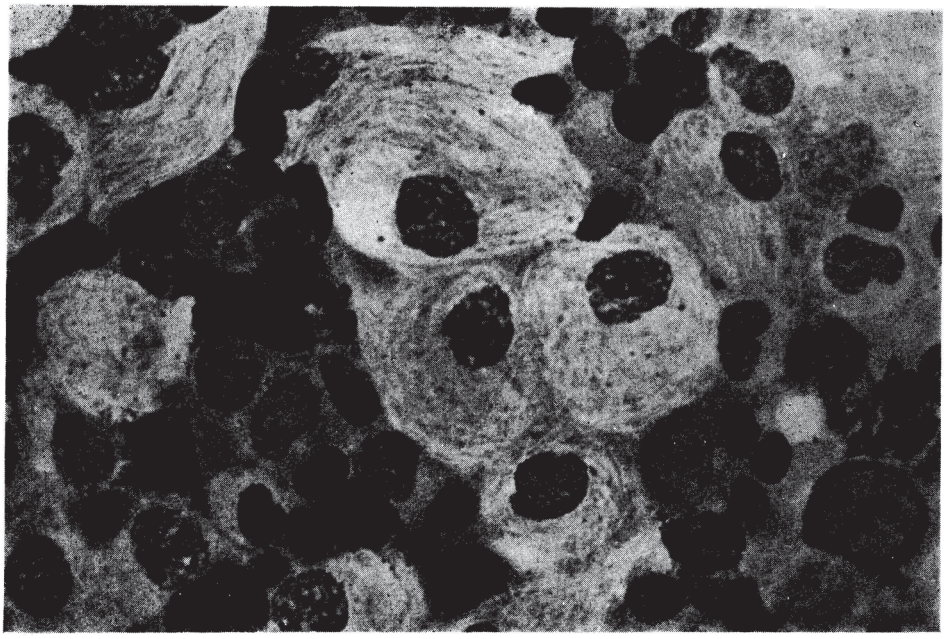


Fig. 1. Gaucher's cells in bone marrow (x 1000).

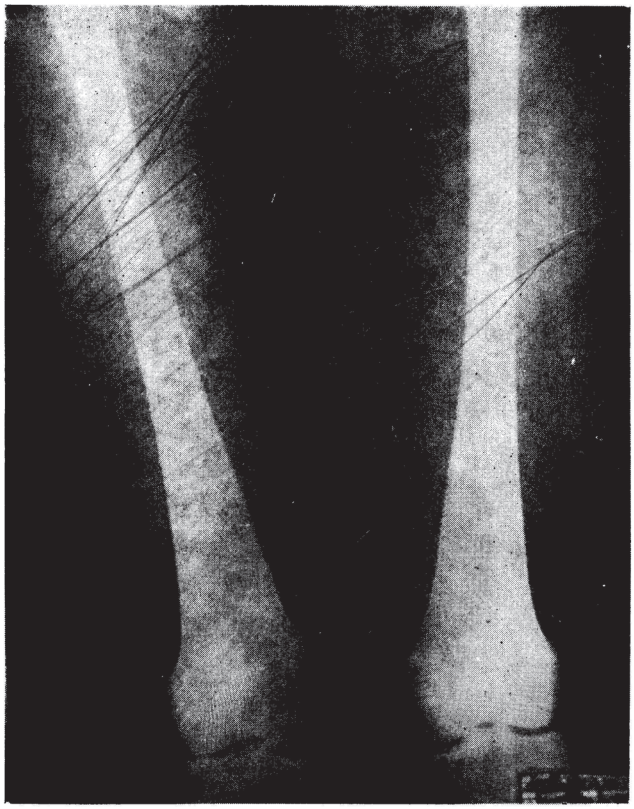


Fig. 2. Roentgenograph of femurs, showing slight expansion of lower ends and thinning of cortices.

said that she began to feel a mass over his left hypochondriac region since he was four or five years old.

The patient's pedigree is shown in Fig. 3. His parents were not related. The mother had 6 pregnancies with one resulting in abortion at about 3 months of gestation. His eldest sister died at the age of 21 from an unknown cause in this hospital. Case history could not be traced; although the mother said that the daughter was operated on for a mass in the left side of abdomen. The latter has a daughter (III – 1) who is now healthy. Her second and third siblings died in childhood without apparent cause. The patient's 28 – year – old brother was normal on physical and routine haematological examination.

Discussion

Detailed family history could not be obtained so the mode of inheritance of Gaucher's disease in this case cannot be discussed. According to the history of the illness of his eldest sister, the diagnosis of Gaucher's disease is suspected but cannot be confirmed. In most cases, Gaucher's disease is inherited as autosomal recessive,[14] but families indicating autosomal dominant mode of inheritance have also been reported.[15]

If the history of onset in this case informed by the mother is correct the disease must have begun before the age of four or five. The progress of the disease in this case must have been very slow. This is well in accordance with the very few positive physical signs detected.

The diagnosis of Gaucher's disease in this patient was based upon hepatosplenomegaly and Gaucher's cells in the bone marrow without any stigma of leukaemia. Recently, there are reports of Gaucher's cells in bone marrow and spleen of some patients with chronic

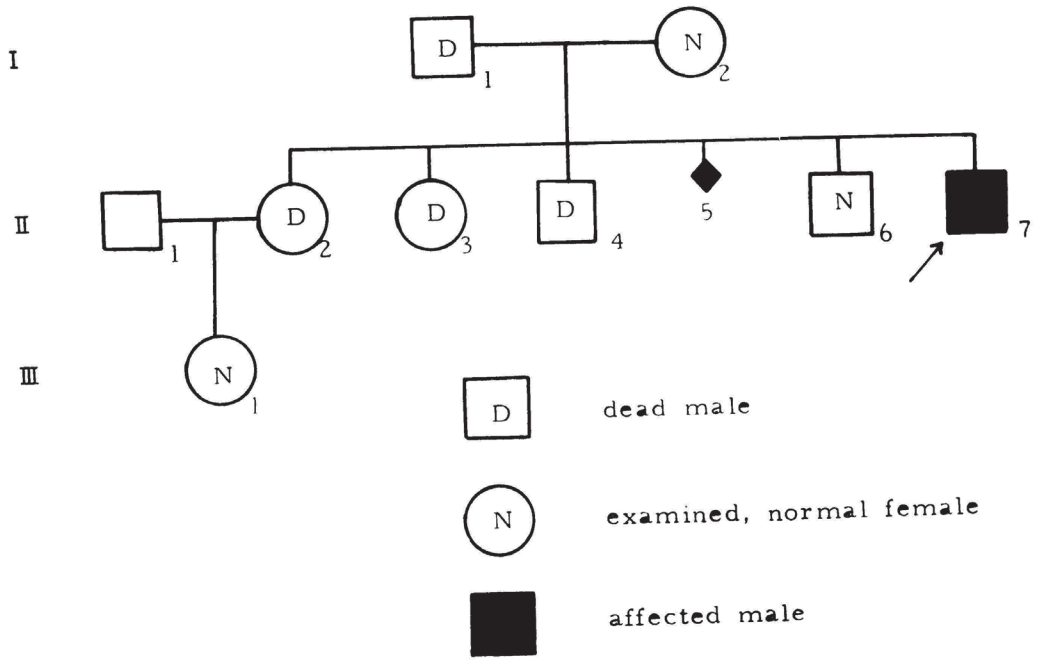


Fig. 3. Pedigree of the patient.

myeloid leukaemia.[16 – 19] The possibility of chronic myeloid leukaemia in our patient could be ruled out by the findings in peripheral blood and bone marrow reported.

Sallow yellow skin pigmentation has been reported in some patients with this disease;[20, 21] the nature and mechanism of occurrence are not yet known. There is no abnormal pigmentation in our patient.

Brill[22] was the first to describe pingueculae in Gaucher's disease and Medoff[23] found that pingueculae were present in about 25 per cent of cases. This was absent in our patient.

Bone changes have been described in patients with Gaucher's disease,[24] but the most common site is the lower end of femur. The normal concavity is lost along the medial border of the bone, which becomes convex. The cortex at lower end of femurs show thinning. All these changes cause the lower ends of femurs look like an Erlenmeyer flask. Bone change in our patient, if present, was found only at lower end of femur and was very mild.

Tuchman et al.[25] were the first to demonstrate that serum acid phosphatase might be elevated in Gaucher's disease. They examined the serum of 8 patients and found that acid phosphatase was elevated in all of them. Enzyme acid phosphatase in the serum of these patients was found to be different from the enzyme found in another disease, for example, carcinoma of the prostate, in that acid phosphatase in Gaucher's disease was non – tartrate – inhibitable.

The difference in age at onset and progress of the disease in chronic adult and infantile form can be explained on the basis of enzyme glucocerebrosidase level in the patient's spleen. This was found to be 15 per cent in chronic adult form, but only 1 per cent in infantile form.[26]

Reference

1. Gaucher, P. : De l'épithélioma primitif de la rate. These de Paris, 1882.

2. Lieb, H. : Cerebrosidspeicherung bei Morbus Gaucher. Ztschr. physiol. Chem. 1924, 140 : 305.

3. Suomi, W.D., and B.W. Agranoff : Lipids of the Spleen in Gaucher's Disease. J. Lipid Res. 1965, 6 : 211.

4. Brady, R.O., J.N. Kanfer, and D. Shapiro : Metabolism of Glucocerebrosides. II. Evidence of an Enzymatic Deficiency in Gaucher's Disease. Biochem. & Biophys. Res. Commun. 1965, 18 : 221.

5. Brady, R.O., J.N. Kanfer, R.M. Bradley, and D. Shapiro : Demonstration of a Deficiency of Glucocerebroside-cleaving Enzyme in Gaucher's Disease. J. Clin. Invest. 1966, 45 : 1112.

6. Groen, J.J. : Gaucher's Disease. Hereditary Transmission and Racial Distribution. Arch. Intern. Med. 1964, 113 : 543.

7. Herndon, C.N., and J.R. Bender : Gaucher's Disease. Cases in Five Related Negro Sibships. Amer. J. Hum. Genet. 1950, 2 : 49.

8. McClatchie, S., et al. : Gaucher's Disease in Kenya. E. Afr. Med. J. 1965, 42 : 411.

9. Spackman, W.C., and F.P. MacKie: Gaucher's Type of Splenomegaly in a Mahralta Village, with a Case Treated by Splenectomy. Ind. Med. Gaz. 1925, 40:69.

10. Reiss, O., and K. Kato: Gaucher's Disease. Amer. J. Dis. Child. 1932, 43:365.

11. Woodfield, D.G., et al.: Gaucher's Disease in a Maori. New Zealand Med. J. 1966, 65:701.

12. Tuchinda, S., et al.: Personal Communication.

13. Tuchinda, S., et. al.: Personal communication.

14. McKusick, V.A.: Mendelian Inheritance in Man. The Johns Hopkins Press, Baltimore, 1968.

15. Hsia, D.Y-Y., et al.: Gaucher's Disease. Report of Two Cases in Father and Son and Review of the Literature. New Eng. J. Med. 1959, 261:164

16. Albrecht, M.: "Gaucher-Zellen" bei Chronisch Myeloischer Leukämie: Blut 1966, 13:169.

17. Smith, W.C., et al.: Gaucher Cell in Chronic Granulocytic Leukemia. Lancet 1968, 2:780.

18. Kattlove, H.E., et al.: Gaucher Cells in Chronic Myelocytic Leukemia: An Acquired Abnormality. Blood. 1968, 33:379.

19. Rosner, F., et. al.: Gaucher Cells in Leukemia. J.A.M.A. 1969, 209:935.

20. Bloem, T.F., et al.: Gaucher's disease. Quart. J. Med. 1936, 5:517.

21. Thannhauser, S.J.: Lipidoses, Disease of the Intracellular Lipid Metabolism. Grune & Stratton, New York, 1958.

22. Brill, N.E.: Primary Splenomegaly. Amer. J. Med. 1901, 121:377.

23. Medoff, A.S., and E.D. Bayrd: Gaucher's Disease in 29 Cases; Hematologic Complications and Effect of Splenectomy. Ann. Int. Med. 1954, 40: 481.

24. Moseley, J.E.: Bone Changes in Hematologic Disorders. A Mount Sinai Hospital Monograph. Grune & Stratton, New York, 1963, pp. 183-198.

25. Tuchman, L.R., et. al.: Elevation of Acid Phosphatase in Gaucher's Disease. J. Mt. Sinai Hosp. 1956, 23:227.

26. Brady, R.O.: Genetics of the Sphingolipidoses. Med. Clin. N. Amer. 1969, 53:827.

(เรื่องย่อจากภาษาอังกฤษข้างต้น)

โรค โกเชร์: รายงานผู้ป่วย ๑ ราย

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ได้รายงานผู้ป่วยชายจีน อายุ ๑๘ ปี มีอาการตกเลือดในทางเดินอาหารส่วนต้น. ตรวจร่างกายคลำได้ตับและม้าม ๕ และ ๑๐ ซม. ใต้ชายโครงตามลำดับ. ตรวจเลือดพบค่า ฮีโมโกลบิน และจำนวนเม็ดเลือดขาวและ เพลตเลต น้อยกว่าปรกติ. ตรวจไขกระดูกพบ เมกะคาริโอซัยท และเม็ดเลือดแดงอ่อนวัยเพิ่มขึ้นปานกลาง, และพบเซลล์ โกเชร์ จำนวนมาก. การตรวจทางรังสีไม่พบแผลในทางเดินอาหารส่วนต้นหรือมีหลอดเลือดขอด; พบความผิดปรกติเล็กน้อยที่กระดูกต้นขาส่วนล่าง. หน้าที่ตับปรกติ. ช่วงครึ่งชีวิตของเม็ดเลือดแดงที่มี โฆมเมียม ๕๑ เกาะอยู่เท่ากับ ๑๗ วัน (ค่าปรกติ ๒๕—๓๒), และมีการทำลายเม็ดเลือดแดงมากที่ม้าม.

ผู้ป่วยได้รับการวินิจฉัยโรคว่าเป็นโรคโกเชร์, ฮัยเปอร์สเปลนิสม, และภาวะเลือดจางขาดเหล็กจากการตกเลือดในทางเดินอาหารส่วนต้นที่ไม่ทราบสาเหตุ. ได้ให้การรักษาแบบสำหรับแผลเปื่อย เพ็พติค และบริหารเหล็ก. ผู้ป่วยทุเลาขึ้นมาก, มีระดับ ฮีโมโกลบิน เข้าสู่เกณฑ์ปรกติ, จำนวนเม็ดเลือดขาวและเกร็ดเลือดทวีขึ้น. ขณะเตรียมรายงานผู้ป่วยมีสุขภาพเหมือนคนปรกติ.

การส่งเงินค่าบำรุง

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