

Gelatinous Degeneration of the Bone Marrow in Anorexia Nervosa

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Anorexia nervosa is a chronic psychiatric process characterized by a restrictive disorder in alimentary habits. Hematologic alterations in the peripheral blood include cytopenias involving one or more hematopoietic lineages. Morphologic changes in the bone marrow and stereologic alterations in bone marrow adipocytes may also be observed in anorexia nervosa. We present a 12-year-old girl who had chronic anorexia and one third of body weight loss during an 8-month period. She was apathetic and had missed several menstrual cycles. The sex maturity rating was Tanner stage IV. There was no lymphadenopathy, no hepatosplenomegaly, and no identifiable tumor mass. She was not anemic, but was found to have leukopenia, neutropenia and a low level of triiodothyronine. Sections of the bone marrow biopsy showed almost complete serous atrophy (gelatinous degeneration) of the bone marrow. In this patient, the bone marrow alteration is related to nutritional deprivation of anorexia nervosa. (*Chang Gung Med J* 2004;27:845-9)

Key words: gelatinous degeneration, serous atrophy, bone marrow, anorexia nervosa.

Anorexia Nervosa (AN) is a chronic psychiatric illness that involves a reduction in calorie and fat intake. Hematologic alterations in the peripheral blood include cytopenias involving one or more hematopoietic lineages. Morphologic changes in the bone marrow and stereologic alterations in bone marrow adipocytes may also be observed in anorexia nervosa. The association of hematological abnormalities in patients with AN have been reported in only a few cases, probably because AN is uncommon and because notable hematologic abnormalities only rarely complicate the patients' courses.⁽¹⁾ We herein present such a case.

CASE REPORT

A 12-year-old girl had had anorexia and a decrease in body weight from 40 kg to 27 kg during an 8-month period. She had had constipation, and

insomnia, but no vomiting. Her menarche had occurred about 8 months prior to the onset of anorexia and she had no further cycles since the onset of anorexia. Laboratory examination results at a local hospital revealed the blood urea nitrogen (BUN) was 36.2 mg/dL, cholesterol level was 225 mg/dL and triglyceride level was 154 mg/dL. The triiodothyronine (T3) level was low at 22 ng/dL. Thyroxine (T4), serum alpha-fetoprotein, carcinoembryonic antigen, and beta-human chorionic gonadotropin levels were all normal. Computerized axial tomography of abdomen revealed no gross abnormalities. Reviewing her personal and social history, she lived in a restrained family. She had been incommunicative and docile since childhood. She performed well in school but was anxious about being separated with her close girl friends because they will be going to different junior high school.

On admission, she appeared apathetic and very

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thin. Her body weight was 27 kg (< 3rd percentile) and her body height was 155.2 cm (75th ~ 90th percentile). She had mild bilateral periorbital swelling. The neck was supple without palpable lymph nodes. The heart rate was 50-60/min with regular rhythm and a fixed split S2. There was no hepatosplenomegaly. An increased number of thin hairs were noted on her back. Breast and pubic hair development were at Tanner stage IV.

Laboratory examination results revealed a hemoglobin (Hb) of 15.5 g/dL, hematocrit of 39.0%, mean corpuscular volume (MCV) of 85.9 fL, and white cell count (WBC) of 4,200/ μ L with 40% neutrophils, 52% lymphocytes, 7% monocytes, and 1% eosinophil. Platelet count was 152,000/ μ L. Urinalysis was normal with specific gravity 1.010 and pH 7. The BUN was 21 mg/dL, creatinine was 0.7 mg/dL, albumin/globulin was 4.3/2.4 g/dL, aspartate aminotransferase was 55 U/L, and alanine aminotransferase was 85 U/L. The cholesterol level was 232 mg/dL, uric acid was 5.5 mg/dL, and lactate dehydrogenase was 102 U/L. The T3 level was 45 ng/dL (range, 60-181 ng/dL), T4 was 4.8 μ g/dL

(range, 4.8-12.5 μ g/dL), and thyroid stimulating hormone (TSH) was 3.51 μ IU/mL. The serum sodium, potassium, chloride, triglyceride, creatinine kinase and 24 hours urine vanillylmandelic acid were all normal; the serum anti-nuclear antibody was negative. Abdominal ultrasound showed a little ascites in the low abdomen. Electrocardiography revealed sinus bradycardia. Echocardiography showed good left ventricular performance with ejection fraction of 68%. Trivial aortic regurgitation and pulmonary regurgitation were found. The clinical impression was that she had anorexia nervosa complicated with secondary amenorrhea and hypothyroidism. Endocrine evaluation was performed. Free-T4, TSH, follicle stimulating hormone, luteinizing hormone, prolactin, and estradiol levels were within normal limits. On the 3rd day of hospitalization, Hb value fell to 13.0 g/dL after hydration, and the WBC was 2,900/ μ L with 48% neutrophils, 41% lymphocytes, 7% monocytes, 2% eosinophils, 1% basophil, and 1% atypical lymphocyte. The platelet count was 169,000/ μ L. Blood smear showed poikilocytosis and large platelets.

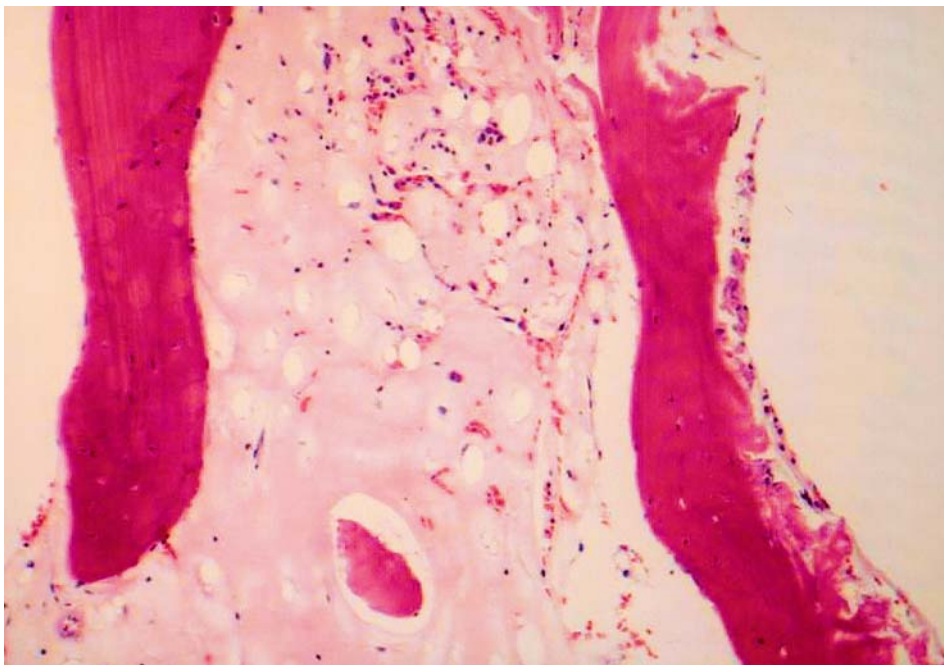


Fig. 1 Hematoxylin - Eosin stained section of bone marrow demonstrates severe hypoplasia, reduction of fat spaces, and replacement of bone marrow by amorphous ground substance ($\times 100$).

Bone marrow aspiration was done but it was a dry tap. She underwent bone marrow biopsy. The section showed serous atrophy (gelatinous transformation) of the bone marrow. Basically the marrow spaces were replaced by an amorphous ground substance. The fat cells and hematopoietic cells accounted for less than 10%, and less than 5% of the marrow spaces, respectively. Reticulin content was normal, but stainable iron content was decreased. No granulomas or other malignant cells were found (Fig. 1). Psychiatric treatment was suggested but it was refused at that time. She received psychological support and supportive treatment. Follow up blood counts 5 weeks after admission showed Hb was 12.7 g/dL, MCV was 92.8 fL, WBC was 3,300/ μ L, and platelet count was 222,000/ μ L.

DISCUSSION

After intensive investigations, malignancy was not found in this patient. The findings of 32.5% loss of body weight, chronic anorexia, constipation, insomnia, amenorrhea, bradycardia, mild hypercholesterolemia and low T3 syndrome⁽²⁾ made anorexia nervosa the most likely diagnosis. Anorexia nervosa associated with bone marrow atrophy has rarely been observed in pediatric practice. Patients with AN have an increased prevalence of anemia, leukopenia and thrombocytopenia.⁽³⁾ In a retrospective study of 67 patients, anemia (Hb<12 g/dL) was found in 27%, leukopenia (<4,000/ μ L) in 36%, neutropenia (<1,500/ μ L) in 17%, and thrombocytopenia (<150,000/ μ L) in 10% of patients. Only two patients (3%) had pancytopenia.⁽³⁾ The bone marrow findings in AN are consistently hypoplastic with some unique features. There is a reduction of bone marrow fat, associated with a notable accumulation of an amorphous ground substance consistent with acid mucopolysaccharide.⁽¹⁾ In a recent analysis of bone marrow changes in 44 consecutive patients diagnosed with AN, the marrow was classified as normal in 11%, hypoplastic or aplastic in 39%, with partial or focal gelatinous degeneration in 30%, or with complete gelatinous degeneration of the bone marrow (GDBM) in 20%. Peripheral blood cell counts may not reflect the extent of bone marrow damage.⁽⁴⁾ Bone marrow adipocytes were studied morphometrically on these patients. The hypoplastic or aplastic bone marrow showed an increase in bone marrow fat

fraction due to an increase in adipocyte diameters, while in GDBM, fat fraction and adipocyte diameters decreased.⁽⁴⁾ Starvation of carbohydrate and calories cause hypoplasia and reduction of adipose tissue in the marrow, which adversely affects hematopoiesis.⁽⁵⁾ This is not a fibrotic process and is found to be reversible with the reestablishment of adequate nutritional intake.^(5,6) In our patient, neutropenia had resolved within 3 weeks after conservative treatment, and the platelets increased. It was the total body fat mass, not lean tissue mass, which was highly correlated with the levels of total leukocytes, neutrophils and red blood cell counts. The magnetic resonance imaging (MRI) showing high intensity patterns suggestive of serous atrophy of bone marrow were correlated with total body fat mass depletion.⁽⁷⁾

In addition to AN, GDBM has also been observed in association with other chronic debilitating disorders, such as starvation, human immunodeficiency virus infection, malignancy, systemic lupus erythematosus (SLE), and postchemotherapy aplasia.⁽⁸⁻¹¹⁾ About 20% of cases of GDBM may be related to anorexia nervosa or other malnutritional states.⁽¹²⁾ In summary, we present a case of anorexia nervosa and GDBM. The initial peripheral blood counts did not reflect the extent of the bone marrow damage. The hematologic abnormalities due to GDBM recovered gradually after the nutritional status improves. Other chronic illness such as malignancy or SLE should be excluded.

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神經性厭食症的骨髓膠質變性

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神經性厭食症是種心理失調狀況，它的特色是一種會限制飲食習慣的疾病。在血液學方面的表現包括一種或多種血球數低下。骨髓型態改變與骨髓脂肪細胞的結構改變也可在神經性厭食症患者身上發現。我們報告一位12歲女孩患有長期厭食且在過去8個月內減輕了三分之一體重。她變得非常冷淡，且她的月經週期已經延遲很久。性徵發育是Tanner stage IV。並無明顯淋巴結種大，肝脾腫大，或腫塊。血液檢查發現並無貧血現象，但有白血球低下，中性球低下，以及甲狀腺素低下。骨髓切片可看到幾近全部的漿液性萎縮（膠質變性）。這個病人的血液系統已經被神經性厭食症影響了。（長庚醫誌 2004;27:845-9）

關鍵字：膠質變性，漿液性萎縮，骨髓，神經性厭食症。

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