CASE REPORT

Gelatinous bone marrow transformation secondary to unusual eating habits and drastic weight loss

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SUMMARY

Gelatinous bone marrow transformation (GMT), also known as starvation bone marrow, has been reported in a number of chronic illnesses, eating disorders (anorexia nervosa) and malignancies. We report the case of a 37-year-old man with a history of bipolar disorder and obesity (weighing >300 pounds) who presented due to recently developing a deep yellow colour to his skin. Over the past 2 years, through diet and exercise, he lost over 150 pounds. He reported running 6–8 miles per day and eating 'lots of squash'. We made the diagnosis of starvation hepatitis and bone marrow degeneration, and referred the patient to a dietician and haematologist/oncologist, where improvements were observed at 4 weeks follow-up.

BACKGROUND

Gelatinous bone marrow transformation (GMT), also known as starvation bone marrow, has been associated with cachexia in a number of chronic illnesses (such as AIDS), eating disorders (anorexia nervosa), malnutrition and malignancies.^{1–2} Bone marrow adipose tissue (BMAT) is markedly increased in conditions of global calorie restrictions, chronic protein-energy malnutrition (especially in children with Kwashiorkor) and negative energy balance.^{3–6} GMT is more common in men, with one study showing the male to female ratio as 6:4.⁷ As more and more individuals become motivated to lose large amounts of weight, GMT secondary to drastic weight loss programme deserves further attention. Drastic weight loss programmes can be harmful and may lead to GMT. Most of the literature regarding GMT related to nutritional deficiency has described with anorexia nervosa, but literature is silent regarding unusual eating habits for intentional weight loss leading to GMT. Unusual eating habits combined with a strenuous exercise-based weight loss programme leading to bone marrow stress have very rarely been reported in the literature. We are reporting this interesting case of GMT resulting from such a programme.

CASE PRESENTATION

A 37-year-old man with a medical history bipolar disorder, not currently on any medications, and who usually avoids going to doctors because of lack of insurance, presented with weakness, nausea and a deep yellowish colour to his skin. He reported that he had weighed over 300 pounds 2 years ago, but through diet and exercise, he got down to 145 pounds. He discovered that he could eat lots of squash, feel full and therefore be able to lose

weight. He had been eating at least 1000 g of squash, rich in vitamin A, every day for the past 2 years. He also admitted to eating 6–10 ounces of carrots every day, as well as a lot of salad. For the past 2 years, he had been running 6–8 miles per day, all year around. Recently, he reported a deeper yellowish discolouration of his skin that was not going away. He also noted that his lips started to swell up and feeling very weak and nauseated. He stated that his face also felt puffy, and he gained 30 pounds in the last 6 weeks. He reported taking naproxen occasionally for body aches. He denied any fever, and denied any alcohol use in the past 5 years and no tobacco abuse. He had not been sexually active for 5 years, and never had male or multiple partners. Family history is noteworthy for his mother who has non-alcoholic steatohepatitis and chronic kidney failure.

On physical examination, the patient had a strange affect, sinus bradycardia, non-icteric, pale mucous membranes and mild tenderness in right upper quadrant. Bowel sounds were present and no organomegaly appreciated. The patient's skin was deep yellow in colour with no scleral icterus.

Laboratory examination revealed white cell count (WBC) of $3.0 \times 10^3/\mu\text{L}$ (reference range 4.1– $10.9 \times 10^3/\mu\text{L}$) and haemoglobin 8.1 g/dL (reference range 12.9–17.31 g/dL). Mean corpuscular volume (MCV) and platelet count were within normal limits. There was biochemical evidence for iron deficiency (ferritin 8 ng/mL (range 26–388 ng/mL), iron 14 $\mu\text{g/dL}$ (range 40–160 $\mu\text{g/dL}$), total iron binding capacity 417 $\mu\text{g/dL}$ (range 250–450 $\mu\text{g/dL}$), iron saturation 3% (range 14–48%). His vitamin B₁₂ level was normal. The patient exhibited transaminitis with aspartate aminotransferase as high as 928 U/L (range 12–70 U/L); alanine aminotransferase was 501 IU/L (range 12–46 U/L) and alkaline phosphatase was highly elevated at 297 U/L (40–125 U/L).

A bone marrow biopsy showed hypocellular bone marrow with appearance of gelatinous transformation with no convincing morphological evidence for neoplastic appearance (figures 1 and 2). Bone marrow karyotype was normal.

The patient was started on ferrous sulfate and folic acid and advised to begin a regular (balanced) diet, with a dietician involved in the care. After 7 weeks, his WBC count was $8.4 \times 10^3/\mu\text{L}$, haemoglobin 10.2 g/dL, MCV 85 g/dL and normal platelet count.

After 7 weeks, aspartate aminotransferase trended down to 43 IU/L. Total alkaline phosphatase trended down to 72 U/L and alanine aminotransferase trended down to 48 U/L. Antihepatitis

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Figure 1 Bone marrow showing gelatinous transformation/serous fat atrophy; low cellularity due to large, pinkish areas lacking haematopoiesis (low magnification, $\times 100$; H&E stain.).

A (immunoglobulin M and G), antihepatitis C antibody and hepatitis B surface antigen were all negative. Antimitochondrial antibody, antinuclear antibody and antiliver kidney smooth muscle antibody were also all negative. Both vitamin K and vitamin A were within normal limits. Human immune deficiency antibodies (HIV-1 and HIV-2) were non-reactive and serum protein electrophoresis was normal.

A colonoscopy and oesophagogastroduodenoscopy and biopsies from upper and lower gastrointestinal tract did not reveal any pathology. Ultrasound of the abdomen and MRI of the liver and biliary tree revealed gall stones only. So a clinical diagnosis of starvation bone marrow hypoplasia and starvation hepatitis was made. Subsequent liver biopsy was normal.

The patient was referred to a dietician for advice on a balanced diet and had shown improvement by 7 weeks follow-up.

DIFFERENTIAL DIAGNOSIS

GMT, also known as starvation bone marrow, has been reported in a number of chronic illnesses, eating disorders (anorexia nervosa) and malignancies. Our patient presented with a deep yellowish discolouration to his skin, weakness, nausea, swelling of the lips and recent weight gain, after having lost over 150 pounds in 2 years and eating a diet containing much squash and carrots. A bone marrow biopsy showed hypocellular bone marrow with appearance of gelatinous transformation with no convincing morphological evidence for neoplastic appearance. Differential diagnoses included gelatinous bone marrow

Figure 2 Bone marrow showing gelatinous transformation/shrunken fat cells (high power, $\times 500$; H&E stain).

secondary to eating disorders, smear artefact, gelatinous bone marrow secondary to unusual eating habits and rapid drastic weight loss, gelatinous bone marrow secondary to neoplastic process and gelatinous bone marrow secondary to infectious process.

TREATMENT

1. Dietician interventions: the patient was advised by dietician during stay in the hospitals and then at the 7-week follow-up about balance diets and increased calorie intake with each increase of mileage during his exercise regime.
2. Ferrous sulfates, multivitamins and folic acid were also prescribed.

OUTCOME AND FOLLOW-UP

At 7 weeks follow-up, the patient had improved clinically and showed improvements in laboratory results.

DISCUSSION

GMT is a condition of unknown pathophysiology characterised by smooth, eosinophilic stromal material (likely hyaluronic acid), fat cell atrophy, patchy loss of haematopoietic cells and deposition of gelatinous materials. This disturbed microenvironment of the bone marrow leads to impaired haematogenesis.¹ Bone marrow adipose tissue acts as a buffer mechanism in conditions of variable nutrition availability to the body.⁸ In starvation conditions, a leptin deficiency occurs. Leptin is a stimulus for haematopoiesis, but in severe malnutrition and anorexia nervosa this stimulus is impaired.^{9–11} Research studies reveal that osteoblasts have a positive effect on haematopoiesis,¹² while fat cells suppress haematopoiesis.¹³ So, in starvation marrow this balance is disturbed in favour of excess adipocytes, resulting in suppression of haematopoiesis and leading to gelatinous transformation of the bone marrow.

In the current literature, there are 20 articles describing GMT. Mostly of these are case reports, with only three reported research studies.⁸ GMT is more common in men, and one study reports the mean age of presentation as 24 years.⁸ In this study from India, out of 1498 cases, 65 patients were identified with GMT. The most common aetiology was found to be infection (48%) (including bronchopneumonia, tuberculosis, sepsis and enteric fever), followed by haematological conditions (26%) (aplastic anaemia and toxic depression of bone marrow), nutritional disorders (7.6%) and malignancies.⁸ Anorexia nervosa and starvation are the most common causes of GMT related to malnutrition.^{14–16} Eating disorders such as anorexia nervosa or other malnutrition states have been reported in approximately 20% of the cases of gelatinous bone marrow.¹ Myelodysplastic syndrome, acute myeloblastic leukaemia, idiopathic myelofibrosis have also been associated with GMT, while no aetiology has been identified in some cases.^{17–19}

Bone marrow biopsies of the iliac crest in patients with anorexia nervosa have revealed increased adipocytes.²⁰ The degree of variation in weight correlates with bone marrow findings in those cases of anorexia nervosa, irrespective of duration of illness. These findings point toward reversibility of GMT.²⁰ In our patient leukopenia had resolved at 3 weeks follow-up, supporting the reversibility of GMT. In one study of patients with anorexia nervosa (including 10 women with anorexia nervosa and 10 normal-weight age-matched women) 1H-MR spectroscopy evaluation revealed greater bone marrow tissue in their L4 vertebrae and femoral metaphysis and diaphysis.²¹

The prognosis of GMT depends upon the aetiology. One case report of 7 years of survival with GMT of idiopathic origin with

supportive care, including blood transfusion every 2 weeks and supplemental iron therapy has been reported.²² Charania *et al*²³ reported a case of GMT secondary to anorexia nervosa successfully treated with haematopoietic growth factors in conjunction with nutritional support.

Fortunately, GMT can be reversed (as in our case) once the underlying cause is treated or corrected.^{1 2 15 16} Because GMT is not a fibrotic process, it is reversible when an adequately balanced diet is re-established or the underlying cause is treated.^{24 25}

Learning points

- ▶ Gelatinous bone marrow transformation (GMT) is a symptom of an underlying condition and can be caused by a number of aetiologies including eating disorders, rapid intentional weight loss, infections and malignancies.
- ▶ Unusual eating habits, strenuous exercise and drastic weight loss programmes can lead to GMT, so physicians should be vigilant to this entity, especially in enthusiastic younger patients.
- ▶ GMT is reversible once the underlying cause is identified and treated.

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Competing interests None.

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REFERENCES

- 1 Bohm J. Gelatinous transformation of the bone marrow: the spectrum of underlying diseases. *Am J Surg Pathol* 2000;24:56–65.
- 2 Seaman JP, Kjeldsberg CR, Linker A. Gelatinous transformation of the bone marrow. *Hum Pathol* 1978;9:685–92.
- 3 Ellison PT. *On fertile ground: a natural history of human reproduction*. Cambridge, MA: Harvard University Press, 2001:358.
- 4 Dickerson JW, John PM. The effect of protein-calorie malnutrition on composition of the human femur. *Br J Nutr* 1969;23:917–24.
- 5 Khalil M, Kaseem AS, Hafez M, *et al*. Histochemical studies of bone marrow cells in kwashiorkor. *J Trop Pediatr Environ Child Health* 1977;23:103–7.
- 6 Rao PT, Sandozi MK. Hematological findings in Kwashiorkor. *Indian J Pediatr* 1970;37:255–6.
- 7 Sen R, Singh S, Singh H, *et al*. Clinical profile in gelatinous bone marrow transformation. *J Assoc Physicians India* 2003;15:585–8.
- 8 Cahill GF Jr. Starvation in man. *Clin Endocrinol Metab* 1976;5:397–415.
- 9 Benett BD, Solar GP, Yuan JQ, *et al*. A role of leptin and its cognate receptors in hematopoiesis. *Curr Biol* 1996;6:1170–80.
- 10 Brichard SM, Delport ML, Lambert M, Adipokines in anorexia nervosa: a review focusing on leptin and adiponectin. *Horm Metab Res* 2003;35:337–42.
- 11 Fantuzzi G, Faggioni R. Leptin in the regulation of immunity, inflammation and hematopoiesis. *J Leukoc Biol* 2000;68:437–46.
- 12 Calvi LM, Adams GB, Weibrecht KW, *et al*. Osteoblastic cells regulate the haematopoietic stem cell niche. *Nature* 2003;425:861–6.
- 13 Naveiras O, Nardi V, Wenzel PL, *et al*. Bone-marrow adipocytes as negative regulators of the haematopoietic microenvironment. *Nature* 2009;460:259–63.
- 14 Basu S, Mitra S, Marwaha RK, *et al*. Gelatinous transformation of bone marrow. *Indian J Pathol Microbiol* 1997;40:383–4.
- 15 Tavassoli M, Eastlund TD, Yam LT, *et al*. Gelatinous transformation of bone marrow in prolonged self-induced starvation. *Scand J Haematol* 1976;16:311–19.
- 16 Foucar K, Reichard K, Czuchlewski D. *Bone marrow pathology*. 3rd edn. Chicago: ASCP Press, 2010.
- 17 Arranz R, Gil-Fernandez JJ, Acevedo A, *et al*. Gelatinous degeneration presenting as a preleukaemic syndrome. *J Clin Pathol* 1996;49:512–4.
- 18 Böhm J, Schmitt-Gräff A. Gelatinous bone marrow transformation in a case of idiopathic myelofibrosis: a morphological paradox. *Pathol Res Pract* 2000;196:775–9.
- 19 Niscola P, Maurillo L, Palombi M, *et al*. Gelatinous degeneration of the bone marrow: two case reports showing different hematological features and clinical outcomes. *Acta Haematol* 2007;118:165–6.
- 20 Albella E, Feliu E, Granada I, *et al*. Bone marrow changes in anorexia nervosa are correlated with the amount of weight loss and not with other clinical findings. *Am J Clin Pathol* 2002;188:582–8.
- 21 Bredella MA, Fazeli PK, Miller KK, *et al*. Increased bone marrow fat in anorexia nervosa. *J Clin Endocrinol Metab* 2009;94:2129–36.
- 22 Niscola P, Palombi M, Fratoni S, *et al*. Long-term survival of a patient with bone marrow gelatinous degeneration of idiopathic origin. *Korean J Hematol* 2012;47:309–10.
- 23 Charania RS, Kern WF, Charkrabarty S, *et al*. Successful management of gelatinous transformation of the bone marrow in anorexia nervosa with hematopoietic factors. *Int J Eat Disord* 2011;44:469–72.
- 24 Mehler PS, Howe SE. Serous fat atrophy in severe anorexia nervosa. *AMJ Hematol* 1995;49:171–2.
- 25 Steinberg SE, Nasraway S, Peterson L. Reversal of severe serous atrophy of bone marrow in anorexia nervosa. *JPEN J Parenter Enteral Nutr* 1987;11:422–3.

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