

## Gelatinous Transformation of the Bone Marrow: A Rare Presentation

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### ABSTRACT

Gelatinous bone marrow transformation (GMT) is a rare disorder of unknown pathogenesis. It is characterized by fat cell atrophy, focal loss of hematopoietic cells and deposition of extracellular gelatinous substances, which histochemically are mucopolysaccharides and rich in hyaluronic acid. GMT occurs more often in adults males than in females. The spectrum of underlying diseases is heterogeneous and age dependent. Anorexia nervosa, acute febrile states and AIDS in younger ages (<40 years), alcoholism and lymphomas in middle ages, and carcinomas, lymphomas, and chronic heart failure in older ages (>60 years) were most commonly associated with GMT. GMT may be reversible if the underlying disorder can be eliminated. In conclusion, GMT represents an indicator of severe illness in a patient but is not specific for a particular disease.

**Keywords:** Gelatinous transformation, Bone marrow, Mucopolysaccharides.

### INTRODUCTION

Gelatinous bone marrow transformation is a rare disorder of unknown pathogenesis, characterized by the presence of extracellular "gelatinous" material, fat atrophy and associated focal marrow hypoplasia.<sup>1</sup> Histochemical nature of the extracellular substance is hyaluronic acid which appears as pink-purple material on Romanowsky stained bone marrow preparation.<sup>2,3</sup> The lesion is usually associated with severe weight loss and cachexia, but factors other than malnutrition also play a significant role in the pathogenesis of gelatinous transformation.<sup>3,4</sup>

GMT is also referred to as starvation marrow or serous fat atrophy and seen exclusively in adults with male preponderance. The condition is reversible if underlying disorder is eliminated.<sup>4,5</sup>

### CASE SUMMARY

A 40-year-old woman presented to the medicine clinic with a history of generalized weakness and weight loss for the last 12 months. She had been hospitalized for 4 weeks with similar complaints of weakness, weight loss and dysphagia 4 months prior to the present illness and was diagnosed with gastritis. She had previously received both enteral and parenteral nutrition due to her severe malnourishment.

On general examination, she appeared emaciated and cachectic. Vital signs demonstrated only mild sinus tachycardia. Cardiopulmonary examinations revealed mild dyspnoea. Abdominal examination revealed mild tenderness in the right iliac fossa. Bilateral lower extremity edema was present. X ray chest showed mild cardiomegaly with ill-defined cavitary lesion in the right lung apex. A non-contrast CT of the abdomen showed diffuse bowel wall thickening with focal ulceration. Endoscopy guided biopsy revealed multiple degenerate epithelioid cell granulomas in a caseous background, suggestive of tubercular infection.

Laboratory studies revealed haemoglobin 7.2 g/dl with decreased red cell indices, red blood cell count of 1.82 million/cc with normal white blood cell and platelet counts, normal folate and vitamin B12 and normal iron studies. Erythrocyte sedimentation rate was significantly elevated at 130 mm/hr with normal range of rheumatoid factor, suggesting an inflammatory process. Other biomarkers like human immunodeficiency virus (HIV) 1 and 2 ELISA were non-reactive. Thyroid studies were within normal limits. Hepatic profile demonstrated a normal total protein of 7.1 g/dl, low albumin of 2.4 g/dl and normal serum total bilirubin. Bone marrow aspirate showed severe pancytopenia. Bone marrow biopsy was performed. Microscopically, bone marrow

smears showed reduced hematopoietic cells and fat cells with many shrunken fat cells (Figure 1). The hypocellular marrow was filled with amorphous gelatinous substances, which stained red-pink with periodic acid-Schiff (Figure 2). The GMT areas showed a low content of reticulin fibers (Figure 3).

Her management consisted primarily of supportive care with plenty of fluids and 4 drug anti tubercular treatment. She also received anabolic steroid megestrol in dosage of 800 mg daily, and multivitamin and zinc supplements, with significant improvement in her appetite. Her treatment was properly maintained for the next 12 months, and her follow-up examination demonstrated marked clinical improvement.

## DISCUSSION

Gelatinous bone marrow transformation (GBM) also known as serous atrophy is a degenerative change in the hematopoietic bone marrow.<sup>4</sup> Gelatinous bone marrow transformation is a rare complication of unknown pathogenesis related to several underlying diseases.<sup>5,6</sup> It was earlier thought to be associated with anorexia nervosa and psychiatric eating disorders, but recently it has been reported in tuberculosis, chronic renal diseases, immunosuppression with HIV infection and cancers.<sup>2,3</sup> GMT is more often seen in adult men than in women, with a mean age of 53.7 years.<sup>3</sup>

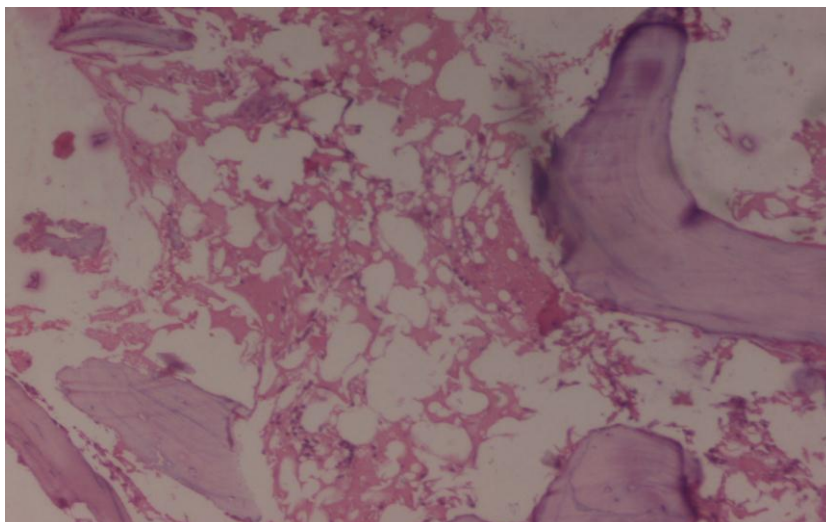
It is described as a focal loss of hematopoietic cells, atrophy of fat cells and deposition of eosinophilic gelatinous substance rich in hyaluronic acid.<sup>4,5</sup> It has been well documented that chronic malnutrition such as anorexia nervosa, starvation, alcoholism, vegetarianism and in some psychotic and geriatric patients with disturbed food intake may be the source of GMT.<sup>6,7</sup> Also malignant tumors lead to emaciation and induce metabolic derangements leading to GMT. Several severe metabolic disorders, such as type I diabetes mellitus and hypothyroidism and severe generalized infectious diseases such as AIDS may also induce GMT. It has been reported that dysfunction of the gastrointestinal tract, leading to celiac disease and ulcerative colitis may precipitate into GMT. Many solid pediatric tumors like neuroblastomas and leukemias have been studied to show gelatinous changes in bone marrow biopsies.<sup>8,9</sup> To date there has been only a single case of GMT in a child, reported from India with severe weight loss and anaemia.<sup>5</sup>

GMT may act as an indicator of severe illness in a patient but is not indicative of a particular disease. The wide range of diseases in which GMT may occur suggests that the gelatinous changes may be the result of basic bioregulatory processes that are activated in different pathologic conditions but lead to morphologically similar lesions in the bone marrow.<sup>4,5</sup> Treatment is based on treating the underlying disease.<sup>5</sup> Tavassoli et al reported a complete disappearance of GMT changes in patients with anorexia nervosa and in experimentally starved animals after normalization of their nutritional status.<sup>4</sup> These findings indicate that GMT is reversible lesion if the underlying disorder can be eliminated.

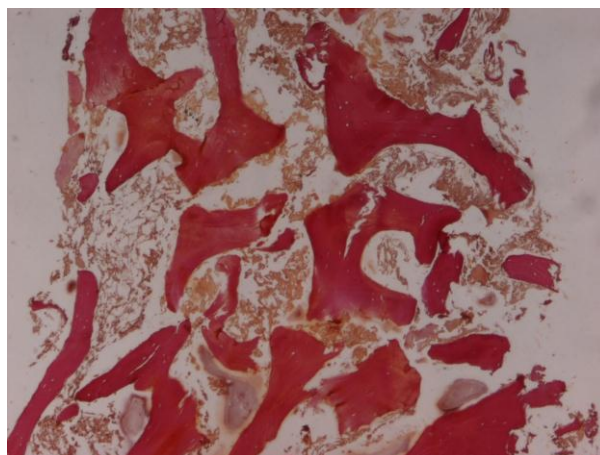
GMT may be confused with marrow edema, amyloid and marrow necrosis. Marrow edema shows fat cells of normal size surrounded by alcian blue-negative substance. Unlike GMT, amyloid deposits in the bone marrow characteristically stain with Congo red and show apple-green birefringence on examination with polarized light. In advanced marrow necrosis, necrotic debris has a heterogeneous, granular appearance and lacks the staining properties of GMT. Moreover, marrow necrosis is accompanied frequently by necrosis of the adjacent bone.<sup>8,9</sup> Diagnosis is based on bone marrow core biopsy with microscopic examination, in correlation with clinical presentations. Radiologic studies may reveal focal lesions with non-specific findings of "hot spot" on PET/CT scan and patchy areas on MRI.<sup>10</sup> On electron microscopy, the gelatinous substances in GMT shows randomly aggregated non-amyloid fibrillar and granular material.<sup>4</sup> Bone marrow microscopic examination shows focal hypoplasia of fat cells and hematopoietic cells with accumulation of extracellular gelatinous substances that appear as pink-purple material on Romanowsky stained bone marrow preparation.<sup>6</sup>

## CONCLUSION

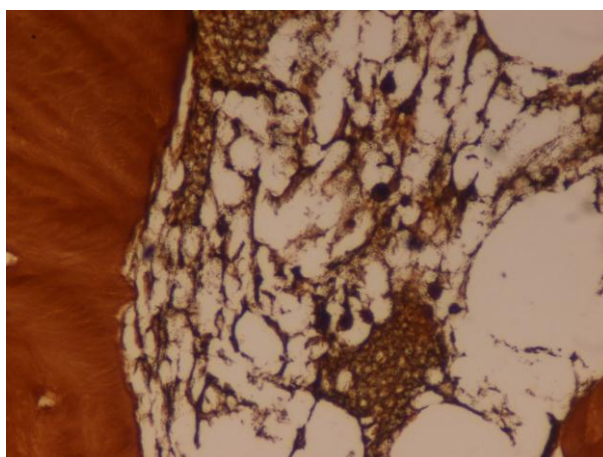
Gelatinous bone marrow transformation leads to the deposition of hyaluronic acid which probably reduces haematopoiesis. Due to a complex inflammatory process, it alters the hematopoietic microenvironment and the bone marrow stroma. Gelatinous degeneration is still a rare disorder, indicative of an advanced underlying disease and its recognition could help guide investigations and treatment.



**Fig. 1:** Microscopically, bone marrow biopsy sections showed reduced hematopoietic cells and fat cells with many shrunken fat cells. Hematoxylin and Eosin x 10 X.



**Fig. 2:** The hypocellular marrow was filled with amorphous gelatinous substances, which stained red-pink with periodic acid-Schiff. PAS x 40 X.



**Fig. 3:** The GMT areas showed a low content of reticulin fibers. Reticulin x 40 X.

## REFERENCES

1. James PS, Carl RK and Alfred L. Gelatinous transformation of the bone marrow  
Hum Pathol. 2010;6:685-692.
2. Xiangrong Z. Gelatinous transformation of bone marrow. Am J Surg Pathol. 2010;24:56-59.
3. Singh S, Gupta M, Singh G, Batra A, Dhiman P and Abhinav P. Gelatinous Transformation of Bone Marrow: A Prospective Tertiary Center Study, Indicating Varying Trends in Epidemiology and Pathogenesis. Indian J Hematol Blood Transfus. 2016;32(1):358-360.
4. Tavassoli M, Eastlund DT, Yam LT, Neiman RS and Finkel H. Gelatinous transformation of bone marrow in prolonged self-induced starvation. Scand J Hematol. 1976;16(4):311-319.
5. Sreeya D, Pritinanda M, Rakhee K and Debdatta B. Gelatinous Marrow Transformation. Turk J Hematol. 2014;31:175-179.
6. Joachim B. Gelatinous Transformation of the Bone Marrow: The Spectrum of Underlying Diseases. Am J Surg Pathol. 2000;24(1):56-65.
7. Ryota N, Mitsuaki I, Keiko H, Takashi Y, Miyuki Y and Hiroko O. Prominent gelatinous bone marrow transformation presenting prior to myelodysplastic syndrome: a case report with review of the literature. Int J Clin Exp Pathol. 2013; 6(8):1677-1682.
8. Eric O, Salman M, Minal J, Robert M, Farwa F and Nishith M. Starvation marrow - gelatinous transformation of bone marrow. J Comm Hosp Intern Med Persp. 2014;4:24-28.
9. Munfus DL and Menke DM. Case of severe serous fat atrophy. Mayo Clin Proc. 2009;84(7): 570-578.
10. Hong FS, Mitchell CA and Zantomio D. Gelatinous transformation of bone marrow as a late morphological change in imatinib mesylate treated chronic myeloid leukemia. Pathol. 2010; 42:84-85.