

Gelatinous Marrow Transformation (GMT): A Disease or a Symptom of Underlying Disorders

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ABSTRACT

Introduction: Gelatinous marrow transformation (GMT) is a rare condition characterized by fat cell atrophy, focal hypoplasia of haematopoietic cells and an accumulation of extracellular gelatinous substances. The purpose of this study was to study the spectrum of underlying disorders associated with GMT in our setup.

Methods: This study reviews 109 cases of GMT with bone marrow aspirate, biopsies, haematological and clinical profile of all patients diagnosed with GMT over a period of 10 years. GMT was diagnosed in BM biopsy based on characteristic morphological appearance and was confirmed by alcian blue positive staining pattern at pH levels of 2.5.

Results: The age of the patients with GMT ranged from 7 months to 68 years. Twenty four (24) out of one hundred and nine (109) cases were in paediatric age group (less than 15 years). Mean age was 27.05 years. Most common association was seen with nutritional deficiency followed by post-chemotherapy and HIV cases.

Conclusions: GMT is a relatively uncommon condition, an indicator of severe illness and often underdiagnosed. A high index of suspicion is required to diagnose this condition.

Key Words: Gelatinous marrow transformation (GMT), fat cell atrophy, focal hypoplasia, haematopoietic cells.

INTRODUCTION

Gelatinous marrow transformation (GMT) is characterized by fat cell atrophy, focal hypoplasia of haematopoietic cells and an accumulation of extracellular gelatinous substances. [1-3] GMT has been classically observed in association with chronic debilitating disorders, such as anorexia nervosa, starvation, malignancy, chronic infections, systemic lupus erythematosus, and myxoedema. [1,3-5] This report presents our findings in 109 cases of GMT and describes a spectrum of underlying disorders with emphasis on possible underlying mechanism.

MATERIALS AND METHODS

A retrospective study was carried out on 109 cases of GMT over a period of 10 years. All samples were processed using standard techniques. Aspirate smears were fixed in methanol and stained by Giemsa. Trepine biopsy specimens were stained with haematoxylin and eosin.

Cases showing focal or diffuse deposition of pink purple (metachromatic) material on Giemsa stained Bone Marrow Aspirate (BMA) and/or Bone marrow Biopsy (BMB) smears were included in the study. The BMA and BMB slides were in

addition stained with Periodic Acid Schiff (PAS) &/or Alcian blue at pH 2.5, which demonstrated blue staining acid mucopolysaccharides. Clinical profile of each case was evaluated.

RESULTS

GMT involved all age groups. The age of the patients with GMT ranged from 7 months to 68 years. Twenty four out of 109 cases were in pediatric age group (less than 15 years). Mean age was 27.05±16.08 years. There was a slight male preponderance with a male to female ratio of 1.6:1. Approximately 2.7% of the marrow aspirates and biopsies received in the department of Pathology for evaluation from all age groups demonstrated GMT. However, there was a slight increase in the incidence of GMT amongst the patients in the age group of 20 to 29 years with 3.5% of the marrow biopsies showing GMT. A severe and extended GMT was observed in younger ages, especially in young men.

In majority of the cases, a single definite disease was identified in association with GMT. The spectrum of underlying diseases was heterogeneous. (Table 1)

The hemoglobin level was available in 101 cases (approximately 92.6%) and all of them were found to be anemic. The degree of anemia, however, did not correlate with the extent of GMT in the marrow. The hemoglobin levels in cases with diffuse GMT lesions (mean hemoglobin level, 9.5g/dL; n 36) were not much different from that seen in focal GMT (mean hemoglobin level, 10.0g/dL; n 65). The total leukocyte and platelet blood counts of the patients showed no correlation with the grades of GMT.

Table 1: The spectrum of underlying diseases in GMT

Clinical disease	Number
Nutritional Deficiencies	23
Megaloblastic anemia	
Iron deficiency anemia	
Multiple deficiency anemia	04
09	
10	
Post chemotherapy	19
HIV/AIDS	18
Parvovirus B19	15
Aplastic Anemia	08
Chronic Infections	06
Tuberculosis	
KalaAzar	04
02	
Lymphoma	03
Unknown	17
Total	109

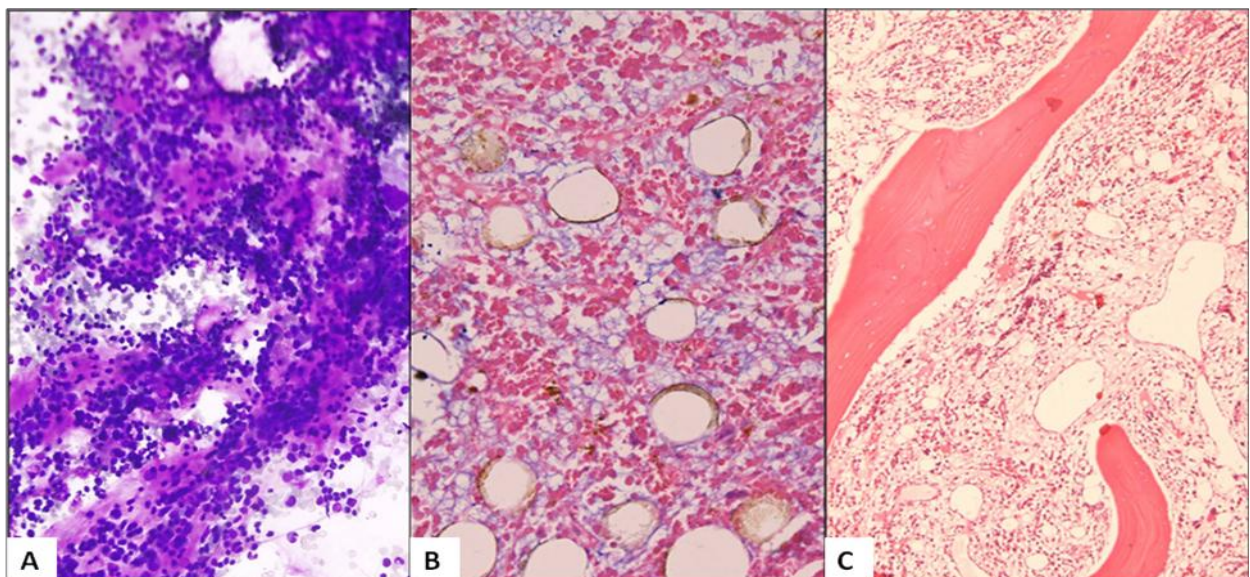


Figure 1 A Bone marrow aspirate showing marrow spaces with deposition of mucoid gelatinous material (Giemsa x 400) **B)** Gelatinous material staining strongly with Alcian blue (x 400) **C)** BMB showing deposition of mucoid gelatinous material and atrophy of fat (H&E x 2)

Microscopically, majority of the cases revealed a focal lesion easily

discernable on low-power magnification because of its low cell content. In diffuse

lesions, the marrow changes were distributed diffusely in the marrow spaces. On higher magnification, a decrease in the number of haematopoietic and fat cells in the lesions was observed along with shrinkage of many fat cells. The hypocellular spaces were filled with an amorphous gelatinous material, which stained pink with Giemsa stain and could also be observed in some of the marrow aspirates. (Fig. 1A) The gelatinous material stained weakly with periodic acid-Schiff, but strongly with alcian blue at a pH of 2.5 (Fig.1B). Cases who had received chemotherapy showed haematopoietic cell hypoplasia and extensive GMT (Fig.1C).

DISCUSSION

Morphologic changes in the bone marrow that combine an atrophy of fat cells and a loss of haematopoietic cells with the deposition of gelatinous substances in the marrow spaces have been described by pathologists for decades, but under different terms. Most often these lesions have been referred to as “gelatinous transformation” or “serous fat atrophy” or “starvation marrow.”^[1,6] Previous histochemical studies have shown that the gelatinous substances in GMT consist of acid mucopolysaccharides, mainly of hyaluronic acid, which strongly stain with alcian blue at pH 2.5 but lose alcian blue positivity after pretreatment with bovine testicular hyaluronidase.^[2,7] An increased incidence of GMT was observed in the age group of 20-29 years old, by various authors.^[8] In the present study the mean age of the patients was 27.5 years. The mechanisms leading to GMT have not yet been understood however; disruption of the haematopoietic microenvironment plays an important role in gelatinous degeneration. Of particular significance are the proteoglycans of the extra-cellular matrix which may regulate haematopoietic activity by influencing the diffusion of large macromolecules, including haematopoietic growth factors, by direct binding of haematopoietic growth factors and by effects on cell adhesion and detachment.^{[9-}

^{12]} An increase in the quantity of hyaluronic acid may contribute to the inhibition of haematopoietic activity by restricting the diffusion of haematopoietic growth factors or by preventing the adhesion of haematopoietic progenitor cells to stromal components leading to anemia and pancytopenia which are the most common presenting features in patients with GMT.^[8]

GMT has been observed in association with chronic debilitating disorders, but it has been most commonly reported in cases of chronic malnutrition secondary to anorexia nervosa and starvation.^[2-4] In the present study, the most common clinical association was nutritional deficiency (23 cases) followed by post-chemotherapy (19 cases) and HIV (18 cases). The increased association of GMT with chronic malnutrition may be attributed to mobilization of marrow fat in order to meet the energy requirements of the body.

^[2] The space created by depletion of fat gets filled with acid mucopolysaccharides. Cachexia from chronic debilitating illnesses such as infections (AIDS, tuberculosis, leishmaniasis), malignancy (carcinoma, leukemia/lymphoma), lupus, hypothyroidism, renal or heart failure, celiac disease, intestinal lymphangiectasia, and alcoholism and has been found at irradiated sites. Das et al^[8] in their study reported HIV to be the most common association with GMT. However, in a larger case series of 43 cases by Jain et al.^[13] none of the cases were associated with HIV infection. In another study by Sen et al.^[6] of 65 cases, GMT was most commonly associated with infections.

The proliferation of macrophages may be implicated in gelatinous degeneration of the marrow along with impaired haematopoiesis in cases of chronic infections. Macrophages produce a wide variety of secretory products, including TNF which inhibits haematopoietic progenitor cell growth in vitro and may contribute to the anaemia by promoting dyserythropoiesis and erythrophagocytosis.^[14]

Reactive oxygen intermediates also inhibit haemopoietic progenitor cell growth in vitro; both in short and long term bone marrow culture systems, and may therefore be a further factor implicated in the development of impaired haematopoiesis. [15]

In the present study 8 cases of aplastic anemia and 19 post chemotherapy cases of ALL/AML were found to be associated with GMT without fat cell atrophy. Similar findings have been reported in the literature by various authors. It is suggested that the gelatinous degeneration in these cases may be attributed to the local microenvironment factors of the marrow. [16,17] Post chemotherapy, there is a depletion of the malignant cells from the marrow along with depletion of the hematopoietic cells and these hypocellular areas are filled with gelatinous material leading to GMT. [14] GMT by its inhibitory effect on haematopoiesis results in cytopenias. Management of such cases requires amelioration of the pathogenic cause, leading to fat cell regeneration and haematopoietic regeneration.

CONCLUSION

Based on the heterogeneity of associated clinical disorders, we suggest that GMT acts as an indicator of severe illness in a patient but is not indicative of a particular disease and it is reversible if underlying disorder can be eliminated. GMT may be a result of basic bioregulatory processes that are activated in different pathologic conditions but result in similar lesions in the bone marrow.

Compliance with Ethical Standards: This article does not contain any studies with human participants or animals performed by any of the authors.

The authors declare that they have no conflict of interest.

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