CORRESPONDENCE

Gelatinous Transformation of Bone Marrow: A Prospective Tertiary Center Study, Indicating Varying Trends in Epidemiology and Pathogenesis

Sneh Singh · Monica Gupta · Gajender Singh ·
Ashima Batra · Pratibha Dhiman · Abhinav ·
Sonia Chhabra · Rajeev Sen

Received: 15 February 2014 / Accepted: 3 February 2015 / Published online: 17 February 2015
© Indian Society of Haematology & Transfusion Medicine 2015

Abstract Gelatinous bone marrow transformation (GTBM) also known as serous atrophy is a degenerative change in the hematopoietic bone marrow and is a rare well recognized pathological entity. It was earlier described mainly in association with anorexia nervosa and psychiatric eating disorders, but recently it has been reported in ulcerative colitis, tuberculosis, chronic renal diseases, immuno suppressed states (mainly HIV infection), malignancies and Kala azar. Treatment is based on treating the underlying disease. Our objective was to study the epidemiology and pathogenesis of diseases causing gelatinous transformation of bone marrow, at a tertiary center level. A

prospective study was conducted on 732 samples of bone marrow aspirate with the aim of identifying gelatinous transformation in bone marrow aspirates which was confirmed by Alcian blue stain at pH 2.5. The presence of this material was correlated with the hematological profile of the patient, the presenting signs and symptoms and provisional clinical diagnosis at initial visit. Incidence of gelatinous transformation was calculated to be nearly 4.8 % and the condition was more common in males (23) as compared to females (12) (Male:Female = 2:1). Forty percent of the cases were seen in children followed by 37 % in adolescents and young adults. The older individuals comprised only 23 % of the cases. The bone marrow was hypocellular in 21 (60 %), normocellular in 10 (28.5 %) and hypercellular in four cases (11.5 %). Five cases with GTBM progressed to aplastic anaemia of which three were in children.

S. Singh
General Hospital, Rohtak, India
e-mail: dr.sneh.singh@gmail.com

M. Gupta · G. Singh · A. Batra (✉) · S. Chhabra · R. Sen
Department of Pathology, Pt B.D. Sharma PGIMS, H No. 901
Ward No. 22, Jhang Colony, Rohtak, Haryana, India
e-mail: drashimabatra@gmail.com

M. Gupta
e-mail: monikashashwat@hotmail.com

G. Singh
e-mail: drgajender@rediffmail.com

S. Chhabra
e-mail: ashub611@yahoo.in

R. Sen
e-mail: drrajeevsen@gmail.com

P. Dhiman
GMC, Kolkata, India
e-mail: dhimandrpratibha@yahoo.com

Abhinav
Government College for Women, Khanpur kalan, Sonapat, India
e-mail: abhi67@gmail.com

Keywords Gelatinous transformation · Bone marrow · Alcian blue · Pathogenesis

Gelatinous transformation of bone marrow (GTBM) characterized by fat cell atrophy, focal loss of hematopoietic cells and deposition extracellular gelatinous material is regarded as a disorder of unknown pathogenesis [1]. Earlier described mainly in association with anorexia nervosa and psychiatric eating disorders, it has recently been reported in ulcerative colitis, tuberculosis, chronic renal diseases, immuno suppressed states, malignancies and Kala azar, systemic lupus erythematosus, and in one patient maintained on chronic intravenous nutrition [2–6]. The presenting hematological symptoms may be that of monocytopenia, bicytopenia or pancytopenia in most cases. Treatment is based on treating the underlying disease. The gelatinous

substance may disappear following treatment or may persist [1, 2, 7].

A prospective study was conducted with the aim of identifying GTBM aspirates which was confirmed by Alcian blue stain at pH 2.5. This was correlated with the hematological profile of the patient, clinical presentation and provisional clinical diagnosis at initial visit. The positive cases were followed up with serial hemograms and a repeat bone marrow aspiration or trephine bone marrow biopsy in a few selected cases. The smears were screened for presence of lymphocytes, plasma cells, mast cells and stromal cells, along with evidence of increased vascularity in the form of capillary cores. Granulomas, necrotic foci and storage cells and basophilic or orangish material were also looked for.

Bone marrow aspirates submitted to clinical hematology section from different clinical departments from 01/09/2011 up to 31/08/2012 (1 year) were examined. No separate criteria was used to select cases with suspicion of gelatinous transformation. The smears were routinely stained by Leishman's stain. Alcian blue pH 2.5, Toluidine blue, Giemsa, Congo red, Ziehl Nelson using 20 % sulphuric acid and Perl's iron stain was used where needed. Reticulocyte count was also done and high performance liquid chromatography (HPLC) was performed to confirm cases with thalassemia. Histologically GTBM was confirmed by its positivity for Alcian Blue at an acidic pH. The differential diagnosis include marrow edema, necrosis and amyloid which were excluded by using special stain including Congo red and Phosphotungstic acid haematoxylin (PTAH).

A total of 732 samples of bone marrow aspirate were received, of which 35 (4.8 %) showed GTBM. It was more common in males (23) as compared to females (12) (Male:Female = 2:1). Fourteen patients (40 %) were in pediatric age group (<15 years), 13 patients (37 %) were adolescents and young adults (15–40 years), four patients were in 5th decade and four in 6th and 7th decades respectively.

The bone marrow was hypocellular in 21 (60 %), normocellular in 10 (28.5 %) and hypercellular in four cases (11.5 %). It was observed that the presence of capillary fronds in the bone marrow aspirates was associated with infectious conditions including TB, Leptospirosis, HIV, Hepatitis B. In these cases the bone marrow was mostly normocellular or hypercellular and occasionally hypocellular. Parvovirus infected patient did not show increased vascularity and the marrow was markedly hypocellular (Figs. 1, 2).

Megaloblastic erythroid hyperplasia was seen in two cases in children and five in adults. Iron deficiency anaemia, sideroblastic anaemia and anaemia of chronic diseases was also reported in the cases with GTBM. Out of the cases

Fig. 1 GTBM in trephine biopsy in malabsorption $\times 1000$ (Alcian blue). (Color figure online)

Fig. 2 GTBM in trephine biopsy in leptospirosis $\times 400$ (Alcian blue). (Color figure online)

associated with malignancies, four of them were on chemotherapy three of the cases were of acute myeloid leukaemia and one had embryonal rhabdomyosarcoma.

Five of our cases progressed to aplastic anaemia, of which three were children. Retrospectively we tried to presume that the presence of GTBM along with relative increase in lymphoid, plasma, mast and stromal cells along with the paucity of capillary fronds may be sign of impending aplastic anaemia, more so in children.

GTBM, also known as serous atrophy is a degenerative change in the hematopoietic bone marrow and is a rare well recognized pathological entity. It is characterized by accumulation of gelatinous substance of mucopolysaccharides and hyaluronic acid which stains positive by Alcian Blue at an acidic pH. The differential diagnosis include marrow edema, necrosis and amyloid [1, 2].

GTBM, in the past, was usually described mostly in adult males. In our study, the majority of patients were in

the pediatric age group, a fact that indicates changing epidemiological trends. The incidence and male:female ratio was, however in concordance with previous studies [1]. Fifty percent of the pediatric patients were cachectic at the initial visit and most of them showed dramatic improvement after treatment. However three children progressed to aplastic anaemia and two died. There is danger of mistaking the associated marrow aplasia of GTBM as aplastic anaemia of immune origin [2].

Sen et al. in their study found 48.05 % of patients with GTBM having infective pathology, 7.6 % showing evidence of nutritional depletion, 26.15 % had evidence of aplastic anaemia and toxic marrow suppression and 4.6 % had underlying malignant disorder [8]. In HIV/AIDS patients, GTBM is known to occur which can be treated by controlling the disease with HAART [9, 10]. The single HIV positive case in our study was a female who revealed hypercellular marrow showing megaloblastic reaction with abundant lymphoplasmacytic infiltrate. Bohm J in his study found that GTBM occurred exclusively in adults, more often in males and the spectrum of underlying diseases was heterogeneous and age dependent [1, 11].

Jain et al. studied 43 cases of GTBM in a period of 4 years and found 14 patients to be in pediatric age group. All the patients presented with anaemia and had preceding history of anorexia, malnutrition and chronic debility [12].

In our study majority of patients are in pediatric group with more than 14 % of the patients progressing to aplastic anaemia, which is alarming since with improved health care and socioeconomic status the overall prevalence of malnutrition is declining in our country [13]. We conclude that (1) increase lymphocytes plasma cells, mast cells and stromal cells along with absence of capillary proliferation and presence of gelatinous transformation indicates impending aplastic anaemia (2) patients presenting with aplastic conditions should be carefully screened for GTBM and (3) increase vascular cores were associated with infectious pathology and resulted in good hematological recovery. Prospective studies for longer time periods have to

undertaken jointly by hematologists, pathologists and pediatricians to prove this hypothesis of etiopathogenesis.

References

1. Bohm J (2000) Gelatinous transformation of the bone marrow: the spectrum of underlying diseases. *Am J Surg Pathol* 24:56–65
2. Yamamoto M, Belmont HM, Utsunonmiya M et al (2009) Gelatinous transformation of the bone marrow in systemic lupus erythematosus. *Lupus* 18:1108–1111
3. Chen S, Hung I, Jaing T, Sun C (2004) Gelatinous degeneration of the bone marrow in anorexia nervosa. *Chang Gung Med J* 27: 845–849
4. Wagner S, Wood S, Amess JAL (1988) Pancytopenia in a patient receiving home intravenous nutrition. *Eur J Clin Nutr* 42: 1029–1034
5. Yamamoto M, Belmont HM, Utsunonmiya M et al (2009) Gelatinous transformation of the bone marrow in systemic lupus erythematosus. *Lupus* 18:1108–1111
6. Sasaki Y, Yamagishi F, Yagi T, Mizutani F (1999) A case of pulmonary tuberculosis case with pancytopenia accompanied to bone marrow gelatinous transformation. *Kekkaku* 74:361–364
7. Mathew M, Mathews I, Manohar C et al (2001) Gelatinous transformation of bone marrow following chemotherapy for myeloma. *Indian J Pathol Microbiol* 44:53–54
8. Sen R, Singh S, Singh H, Gupta A, Sen J (2003) Clinical profile in gelatinous bone marrow transformation. *J Assoc Phys India* 51:585–588
9. Leguit RJ, van den Tweel JG (2010) The pathology of bone marrow failure. *Histopathology* 57:655–670
10. Stroup JS, Stephens JR, Baker DL (2007) Gelatinous bone marrow in an HIV-positive patient. *Proc (Bayl Univ Med Cent)* 20(3):254–256
11. Bohm J, Schmitt-Graff A (2000) Gelatinous bone marrow transformation in a case of idiopathic myelofibrosis: a morphological paradox. *Pathology* 196:775–779
12. Jain R, Singh ZN, Khurana N, Singh T (2005) Gelatinous transformation of bone marrow: a study of 43 cases. *Indian J Pathol Microbiol* 48:1–3
13. Meshram II, Arlappa N, Balakrishna N, Mallikharjuna Rao K, Laxmaiah A, Brahmam GN (2012) Trends in the prevalence of undernutrition, nutrient and food intake and predictors of undernutrition among under five year tribal children in India. *Asia Pac J Clin Nutr* 21(4):568–576