Journal of Community Hospital Internal Medicine Perspectives

COACTION PUBLISHING

CASE REPORT

Starvation marrow – gelatinous transformation of bone marrow

Eric Osgood, MD[1]*, Salman Muddassir, MD[2], Minal Jaju, MBBS[1], Robert Moser, MD[3], Farwa Farid, MBBS[4] and Nishith Mewada, MBBS[1]

[1]St. Francis Medical Center, Department of Internal Medicine, Seton Hall University School of Graduate Medical Sciences, South Orange, NJ, USA; [2]St. Francis Medical Center, Department of Medicine, Seton Hall University School of Graduate Medical Sciences, South Orange, NJ, USA; [3]St. Francis Medical Center Department of Pathology, Johns Hopkins University, South Orange, NJ, USA; [4]Rawalpindi Medical College, Department of Radiology, Holy Family Hospital, Rawalpindi, Pakistan

Gelatinous bone marrow transformation (GMT), also known as starvation marrow, represents a rare pathological entity of unclear etiology, in which bone marrow histopathology demonstrates hypoplasia, fat atrophy, and gelatinous infiltration. The finding of gelatinous marrow transformation lacks disease specificity; rather, it is an indicator of severe illness and a marker of poor nutritional status, found in patients with eating disorders, acute febrile illnesses, acquired immunodeficiency syndrome, alcoholism, malignancies, and congestive heart failure. We present a middle-aged woman with a history of alcoholism, depression, and anorexia nervosa who presented with failure to thrive and macrocytic anemia, with bone marrow examination demonstrative of gelatinous transformation, all of which resolved with appropriate treatment. To our knowledge, there are very few cases of GMT which have been successfully treated; thus, our case highlights the importance of proper supportive management.

Keywords: *gelatinous infiltration*; *anemia*; *erythropoiesis*; *mucopolysaccharide*

*Correspondence to: Eric Osgood, 22101 Cornerstone Drive, Yardley, PA 19067, USA, Email: edoajo@gmail.com

Received: 30 April 2014; Revised: 11 July 2014; Accepted: 21 July 2014; Published: 29 September 2014

Gelatinous bone marrow transformation (GMT) was identified in twentieth century in autopsy specimens of patients suffering from starvation; hence, the alternate diagnostic terms 'starvation marrow' or 'serous atrophy of fat' (1–3). GMT, a rare clinicopathologic entity, involves bone marrow hypoplasia, fat atrophy, and infiltration by gelatinous material (1–8). While the exact etiology remains unclear, the reviewed literature associates GMT with protein catabolic conditions and severe malnourishment, including anorexia nervosa, acute febrile states; young patients (<40) with acquired immunodeficiency syndrome (AIDS), alcoholism, malabsorption; middle-aged patients with lymphoma; and elderly patients with carcinomas, lymphomas, and congestive heart failure (1–8). The degree of a patient's weight loss may be the predominant risk factor (8, 9). This report details the presentation of a middle-aged woman with history of alcoholism, depression, and anorexia nervosa presenting with weight loss, confusion, failure to thrive, and macrocytic anemia with gelatinous transformation of bone marrow, and reversibility of the condition upon receiving treatment.

Case report

A 40-year-old African American woman with a medical history of anorexia nervosa, depression, and a documented history of iron overload syndrome presented to the emergency department with a self-reported weight loss of 150 lbs, confusion, ambulatory dysfunction, and generalized weakness, all of which progressed over a period of 1 year. Approximately 5 months earlier, she had been hospitalized for 8 weeks, having presented at that time with weakness, weight loss (stated her baseline weight was 234 lbs and at that time weighed 118 lbs) and dysphagia, and was diagnosed with vitamin D deficiency, niacin deficiency, myopathy, as well as esophageal ulceration, gastritis, and duodenal ulcer which were demonstrated on esophagogastroduodenoscopy (EGD). She had been discharged home with planned follow-up in 3 weeks; however, she did not present for follow-up. She stated she was eating an unrestricted oral diet; however, she had previously received both enteral and parenteral nutrition due to the severity of her malnourishment. Further review of systems revealed absent menses for the past 3 years. Aside from her personal history of alcohol abuse disorder,

Citation: Journal of Community Hospital Internal Medicine Perspectives 2014, **4**: 24811 - http://dx.doi.org/10.3402/jchimp.v4.24811

she denied abuse of licit or illicit substances including tobacco, and was in remission from alcoholism at the time of presentation for more than 6 months.

On general examination, she appeared emaciated and cachectic despite being within normal range of body weight for her height, suggesting underlying obesity with marked weight loss and malnutrition. She weighed 97 lbs and was 5 feet tall, with a body mass index of 18.9 (based on her self-reported baseline weight, this is a 137 lb weight loss). Vital signs demonstrated only mild sinus tachycardia with heart rate of 105 without orthostatic changes noted. Cephalic examination revealed sunken orbits. Keratoconjunctivae were pale, and sclerae appeared muddy. Oropharyngeal exam demonstrated dental erosions. Cardiopulmonary and lymphatic examinations were unremarkable. Abdominal examination initially revealed only a well-healed percutaneous endoscopic gastrostomy (PEG) scar. Bilateral lower extremity edema was present. Neurologic exam disclosed decreased muscle tone and evidence of cognitive decline (SLUMS [Saint Louis University mental status] score was 20/30), consistent with dementia.

Laboratory studies revealed macrocytic anemia (hemoglobin 7.8 g/dL MCV [mean corpuscular volume] 125 fL, reticulocyte 2.3%, red blood cell [RBC] 1.82×10^{12}/L, with normal white blood cell [WBC] and platelet counts, normal folate and vitamin B12, normal iron and transferrin studies, and elevated ferritin being 1,491 ng/mL [normal 15–200 ng/mL]). Serum chemistries were unremarkable. Total 25 hydroxy vitamin D was extremely low at 4 ng/mL, deficient range <20 ng/mL. 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, slightly elevated total bilirubin of 1.2 mg/dL, elevated aspartate transaminase of 94 U/L (normal range 0–32 U/L), slightly elevated alanine transaminase of 36 (normal range 0–33 U/L), and elevated alkaline phosphatase of 167 U/L (normal range 35–104 U/L). Serum ammonia was measured due to her confused status and history of hepatic disease, which was slightly above normal range at 54 μmol/L (normal range 11–51 μmol/L). Subsequent direct bilirubin measured 2 days later was 0.4 mg/dL (normal range 0.0–0.3 mg/dL) indicating a primarily indirect hyperbilirubinemia. A viral hepatitis profile demonstrated hepatitis A IgM antibody positivity, indicative of active hepatitis A infection.

Neurologic investigation initially included structural neuroimaging specialty consultation with neurology and psychiatry services, as well as evaluation of systemic etiologies (Lyme disease, Wilson's disease, B12 and/or folate deficiency, syphilis, vasculitides and rheumatologic disease, etc.). A non-contrast CT of the head at the time of admission showed age-inappropriate diffuse cerebral atrophy. Magnetic resonance imaging (MRI) with fluid attenuated inversion recovery (FLAIR), in addition to age-inappropriate atrophy already demonstrated on CT, showed a few scattered foci of increased T2 and FLAIR (Fig. 1) signal in the subcortical white matter bilaterally which are non-specific. Erythrocyte sedimentation rate (ESR) was significantly elevated at 130 mm/h (normal range 0–20 mm/h), and rheumatoid factor was positive with a titer above 1:4, suggesting an inflammatory or possibly autoimmune process. Other biomarkers including anti-nuclear antibodies (ANA), lyme titer, RPR, folate, vitamin B12, serum copper and ceruloplasmin, as well as human immunodeficiency virus (HIV) 1 and 2 ELISA were non-reactive. Electromyelography (EMG) with nerve conduction studies (NCS) demonstrated bilateral lower extremity myopathy without evidence of demyelinating disease.

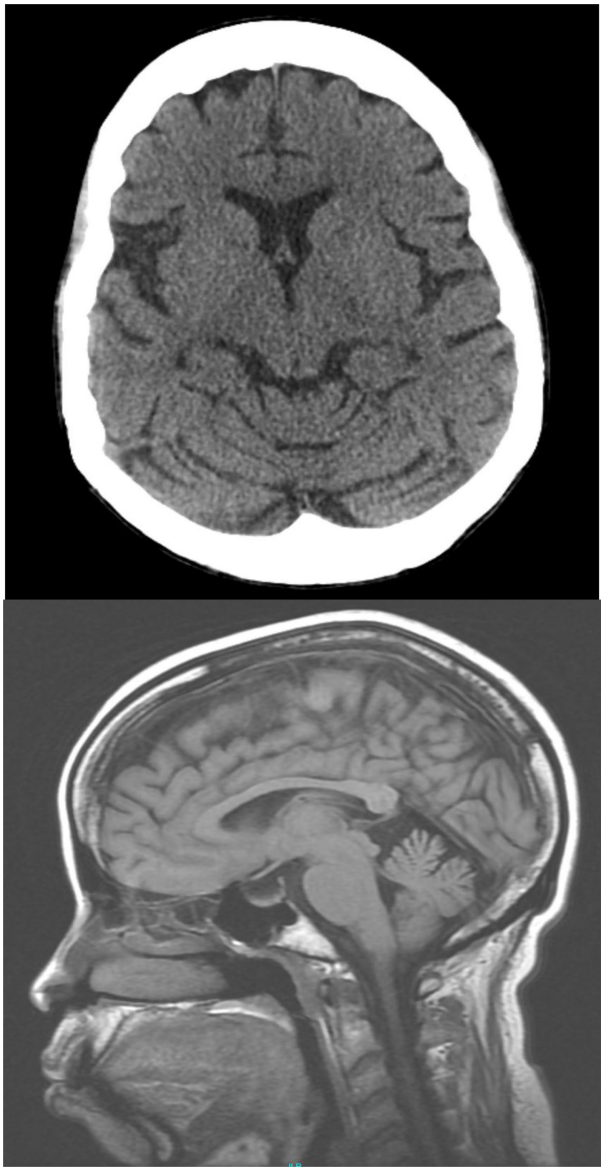

Fig. 1. Axial CT and Sagittal MRI of the brain show significant age-inappropriate diffuse cerebral atrophy.

Citation: Journal of Community Hospital Internal Medicine Perspectives 2014, **4**: 24811 - http://dx.doi.org/10.3402/jchimp.v4.24811

Additional diagnostic modalities were pursued, which included functional neuroimaging and genetics testing. Single photon emission computer tomography (SPECT) imaging was done, but revealed no additional diagnostic findings. Testing for early Alzheimer's associated gene mutations was also negative.

Abdominopelvic CT without IV contrast (Fig. 2) was obtained, which demonstrated marked ascites with anasarca, and a small fatty liver. Further laboratory studies included serum alpha-fetoprotein, human hemochromatosis protein (HFE) gene, ceruloplasmin, anti-liver–kidney–muscle (anti-LKM) antibody, and serum prealbumin, all of which were unremarkable except low prealbumin (14 mg/dL [normal = 18–45 mg/dL]), which is a more specific marker of protein malnutrition than albumin. During the hospital course, the patient gradually manifested significant ascites on physical examination. Further research into the patient's medical chart from her previous hospitalization at another facility

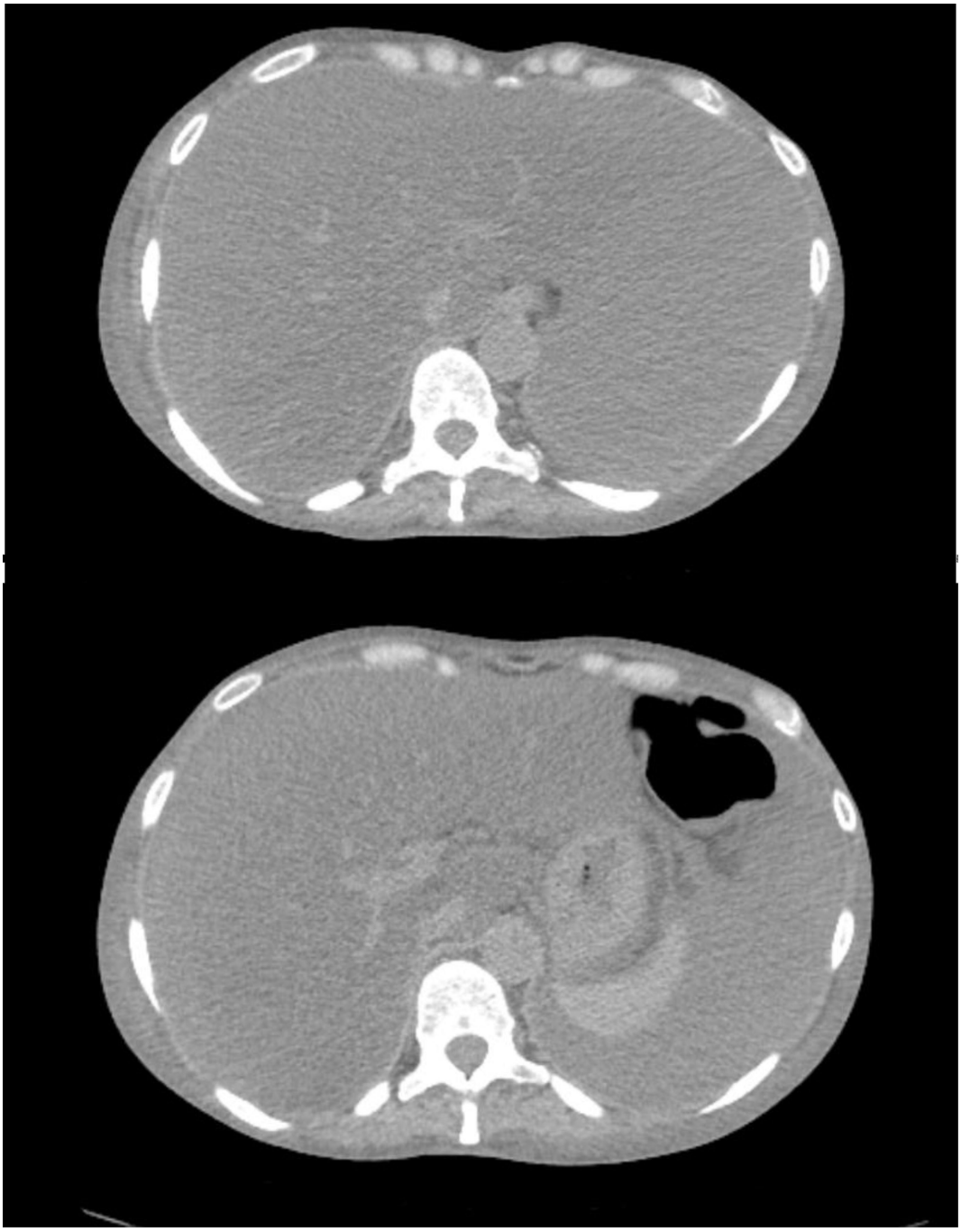

Fig. 2. CT of the abdomen with oral contrast shows marked hepatic steatosis and ascites.

revealed that a liver biopsy had been done. Histologic examination had not revealed any additional diagnosis, and the hepatic iron index was 1.9 (hepatic iron index above 1.9 in a patient without liver failure suggests hemochromatosis – given the abnormalities noted in hepatic function, an index of 1.9 was not considered diagnostic for hemochromatosis).

The patient's significant macrocytic anemia was also investigated. The folate, vitamin B12, and normal thyroid studies were all normal, and the patient reported being completely abstinent from alcohol in the recent past; therefore, the etiology was unclear. During the hospitalization, her anemia became increasingly severe, falling below 7 and requiring transfusion of packed RBCs. No evidence of a bleeding source or intravascular erythrocyte destruction was found. Hematology performed a bone marrow biopsy. Bone marrow histopathology and flow cytometry revealed infiltration by gelatinous substance, fat atrophy and marrow hypocellularity (Fig. 3), with normal female karyotype and no evidence of occult malignancy.

During the hospital course, her management consisted primarily of supportive care. She was hydrated intravenously until she became euvolemic and was able to achieve adequate oral intake of fluids. Her macro and micronutrient deficiencies were addressed and repleted. She received megestrol, which works through various hormonal pathways including glucocorticoid and gonadotropic stimulation, and at doses between 400 and 800 mg daily has been shown to improve appetite and oral intake in patients with anorexia. There was significant improvement in her appetite, and she tolerated a calorically adequate oral diet, which was supplemented by multivitamins, zinc, folic acid, and vitamin D. She was also treated pharmacologically with sertraline 100 mg daily, and non-pharmacologically with physical therapy and counseling. Her caloric intake improved as evidenced by improved prealbumin and body weight.

Once she became medically stable, she was transferred to the psychiatric unit, as her depression and severe cognitive deficits had only minimally improved and was not suitable for discharge. Over the next month and a half, she slowly improved, and appropriate outpatient support services were arranged. Her treatment was properly maintained for the next 6 months, and her follow-up examination at this time demonstrated marked clinical improvement, significant resolution of her neurocognitive deficits, as well as a rise in hemoglobin to 11.5 g/dL with normalization of RBC indices (i.e., MCV).

Discussion

The above case represents a young female with severe malnutrition presenting with hypoproliferative macrocytic anemia, as well as hepatic disease and neuropsychiatric impairment. The pathologic lesion ultimately identified was GMT. Her severe anemia improved once she received appropriate nutritional and supportive management.

Interestingly, the patient's body mass index was not particularly low on presentation. However, she did apparently lose 137 lbs in less than a year (53% weight loss). A small retrospective study published in 2002 correlating bone marrow changes and clinical factors in patients with eating disorders found that the amount of weight loss alone correlated with bone marrow changes, with no

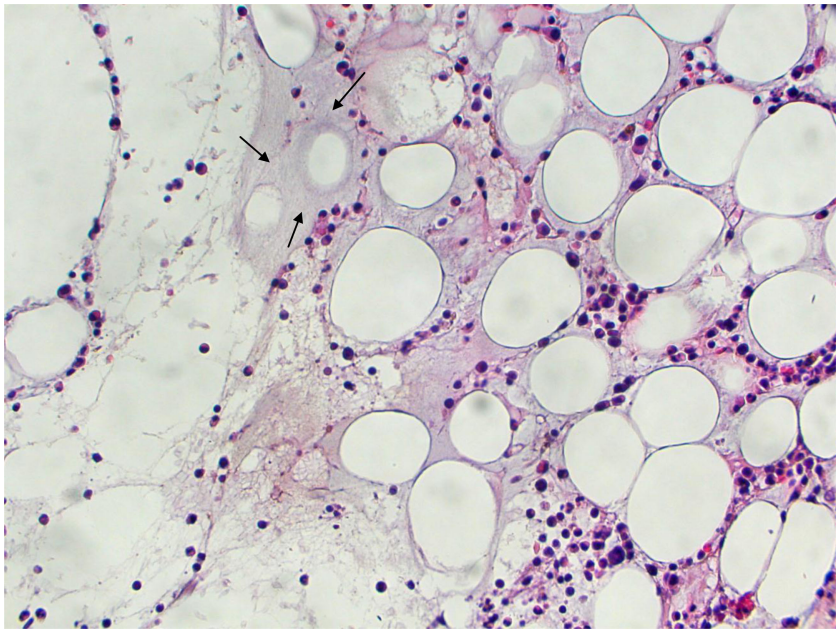

Fig. 3. Pathologic examination of bone marrow demonstrating focal gelatinous substance (arrows), consistent with 'starvation' bone marrow.

Citation: Journal of Community Hospital Internal Medicine Perspectives 2014, **4**: 24811 - http://dx.doi.org/10.3402/jchimp.v4.24811

correlation found between bone marrow changes and other clinical factors (9).

Whether GMT was fully or partially responsible for any components of the patient's hematologic, hepatic, or neurocognitive presentation is unknown. Her liver disease certainly could have been related to a self-limited hepatitis A infection, as well as being a manifestation of her severe protein malnutrition. The cause of her severe cerebral atrophy is unclear. Macrocytic anemia has been described in the literature as associated with GMT; however, causality versus association has not been clearly elucidated. Nevertheless, GMT is a very rare finding, and typically occurs in young adult males with severe malnutrition (1, 4). While still unclear, the purported pathophysiology involves deposition of gelatinous substance in bone marrow to replace adipose cells which are systemically depleted due to severe catabolism (1, 3, 5). Mucopolysaccharides enriched with hyaluronic acid comprises this gelatinous substance deposition, rendering the bone marrow microenvironment unfavorable for erythropoiesis, (3, 5, 6) although degree of GMT and severity of anemia have not been shown to be concordant (1, 2). Though the lesion is mostly associated with chronic wasting diseases, few patients with malnutrition develop GMT, therefore, additional factors likely play a role in its pathogenesis (1, 3). While the condition should theoretically reverse upon adequately treating the underlying cause (1, 2, 4, 5, 7), few cases of successful reversal of GMT have been published.

Conflict of interest and funding

The authors have not received any funding or benefits from industry or elsewhere to conduct this study.

References

1. Bohm J. Gelatinous transformation of the bone marrow: The spectrum of underlying diseases. Am J Surg Pathol 2000; 24(1): 56–65.
2. Boullu-Ciocca S, Darmon P, Sebahoun G, Silaghi A, Dutour-Meyer A. Gelatinous bone marrow transformation in anorexia nervosa. Ann Endocrinol (Paris) 2005; 66(1): 7–11.
3. Seaman JP, Kjeldsberg CR, Linker A. Gelatinous transformation of the bone marrow. Hum Pathol 1978; 9(6): 685–9.
4. Munfus DL, Menke DM. Case of severe serous fat atrophy. Mayo Clin Proc 2009; 84(7): 570.
5. Tavassoli M, Eastlund DT, Yam LT, Neiman RS, Finkel H. Gelatinous transformation of bone marrow in prolonged self-induced starvation. Scand J Hematol 1976; 16(4): 311–19.
6. Mehta K, Gascon P, Robboy S. The gelatinous bone marrow (serous atrophy) in patients with acquired immunodeficiency syndrome. Evidence of excess sulfated glycosaminoglycan. Arch Pathol Lab Med 1992; 116(5): 504–8.
7. Chen SH, Hung IJ, Jaing TH, Sun CF. Gelatinous degeneration of the bone marrow in anorexia nervosa. Chang Gung Med J 2004; 27(11): 845–9.
8. Stroup JS, Stephens JR, Baker DL. Gelatinous bone marrow in an HIV-positive patient. Proc (Bayl Univ Med Cent) 2007; 20(3): 254–6.
9. Abella E, Feliu E, Granada I, Millá F, Oriol A, Ribera JM, 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; 118(4): 582–8.