Autopsy Case Reports

Image in Focus

Gelatinous transformation of bone marrow

Flavia Fazzio Barbin[a], Cristiano Claudino Oliveira[a]

How to cite: Barbin FF, Oliveira CC. Gelatinous transformation of bone marrow. Autops Case Rep [Internet]. 2017;7(2):5-8. http://dx.doi.org/10.4322/acr.2017.013

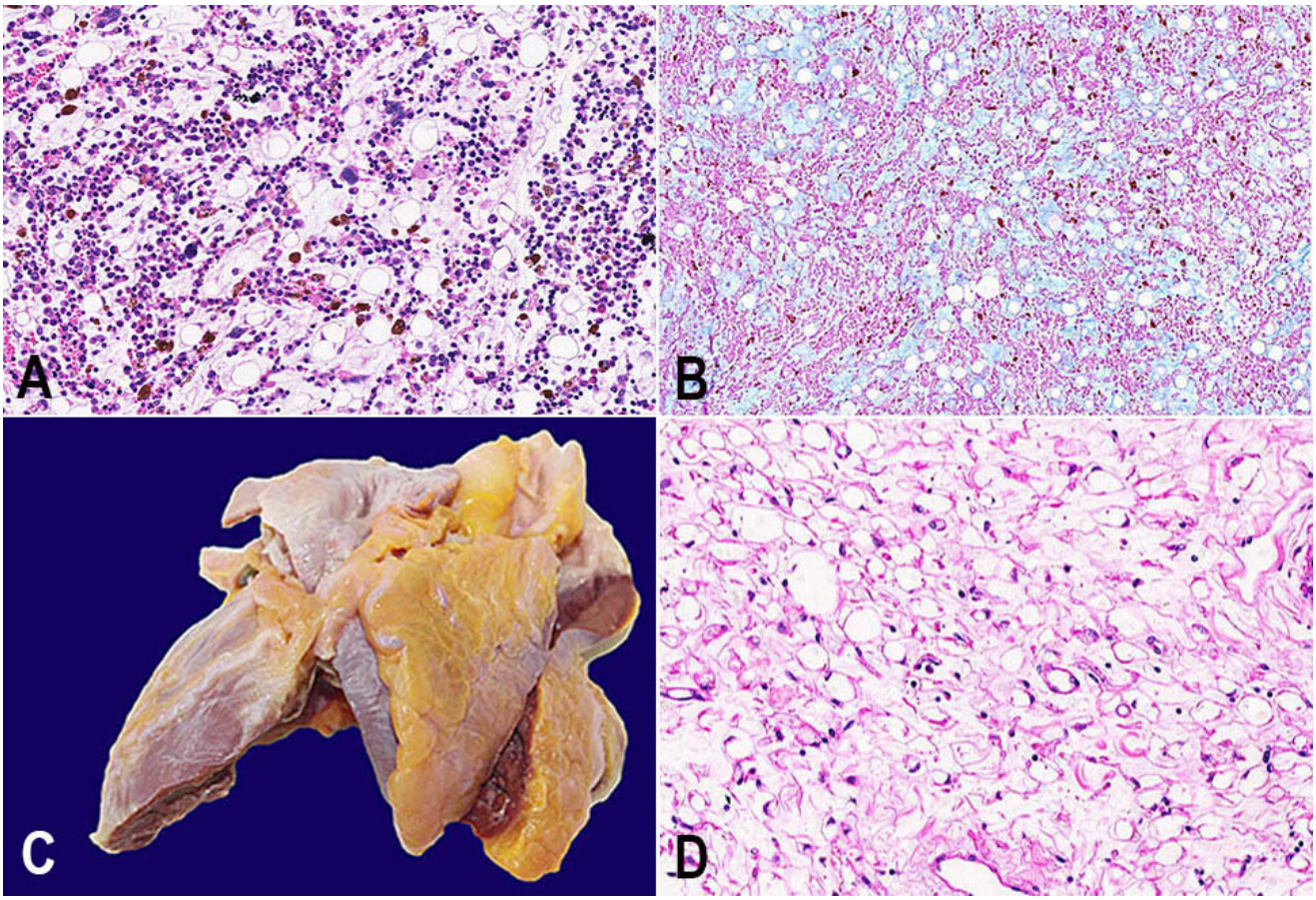

Image courtesy Dr. Cristiano Claudino Oliveira

Figure 1. A - Bone marrow with severe hypoplasia and gelatinous material in interstice (H&E, 400X); **B** - Bone marrow tissue stained with Alcian Blue showing the gelatinous material in interstice, which is an alcianophilic deposit of mucin (Alcian Blue, 400X); **C** - Gross examination of the heart showing the bright appearance of pericardial adipose tissue, which is an example of gelatinous transformation outside the bone marrow; **D** - Pericardial adipose tissue with the same histological aspect noted in the bone marrow, which is consistent with the macroscopic aspect of the heart (H&E, 400X).

[a] São Paulo State University, Botucatu School of Medicine, Department of Pathology. Botucatu, SP, Brazil.

Gelatinous transformation of bone marrow (GTBM) was recognized in the 20th century in the autopsy specimens of patients with prolonged starvation and cachexia.[1,2] GTBM is a rare hematological condition associated with numerous etiologies, and represents a marker of underlying severe disease.

The main feature is adipose cell atrophy, hematopoietic tissue hypoplasia, and the deposition of an eosinophilic substance, which consists of a material similar to mucopolysaccharide hyaluronic acid.[3-5] This substance stains for Alcian Blue at pH 2.5, but loses its positivity after pretreatment with bovine testicular hyaluronidase.[2]

GTBM is a histological pattern, which is mainly presented in the context of nutritional deprivation, such as anorexia nervosa, severe malnutrition, or cachexia.[6] Other clinical scenarios are malabsorption, alcoholism,[7] severe infections,[3] congestive heart failure, and acute febrile states.[1]

Böhm[2] studied 155 patients with GTBM and realized that the etiologies varied according to the age of the patient. For patients under 40 years old, the most common causes were anorexia nervosa, acute febrile states, and acquired immunodeficiency syndrome (AIDS). Patients between 40 and 60 years old presented neoplasms, such as carcinomas and lymphomas, and congestive heart failure as the main documented etiologies. The study also detected that 81% of the patients exhibited weight loss and 78% presented anemia.[2]

According to Böhm[2], neoplasms were present in 37.5% of the cases, malnutrition in 16.8%, infections in 11.8%, digestive disorders in 10.1%, heart failure in 7.0%, and metabolic disorders in 5.4%. About 11.4% of the etiologies were represented by other causes, such as iron deficiency, renal failure, psychoses, and myelodysplastic syndrome. Etiologies mentioned by other studies[2-6,8] include renal failure,[3] disseminated tuberculosis, alcoholic pancreatitis,[5] systemic lupus erythematosus,[2,4] excessive physical activity,[6] and non-specified eating disorders.[8]

The possibility of other hypotheses to explain the physiopathology of this phenomenon[1,3] include the existence of GTBM in other diseases without the obligatory association with malnutrition, and patients with severe anorexia nervosa whose bone marrow does not develop this transformation.

The central physiopathological aspect of this condition is the depletion of fat cells due to a state of severe catabolism, with the subsequent deposition of a gelatinous substance on the bone marrow, which is mainly comprised of a hyaluronic acid-like material. This deposit renders the bone marrow as an adverse microenvironment for hematopoiesis[1] by inhibiting the interaction between the hematopoietic cells and the signalizing molecules.[9] Moreover, studies in vivo show that fat cells are important to maintain hematopoietic progenitor cells.[10]

The secretion of a huge number of cytokines, such as interleukin-1, interleukin-2, and the tumor necrosis factor, are part of the pathogenesis of GTBM in contexts of severe infections. During the seroconversion of AIDS, or when the disease is in the early phase, the multiple failure of organs or the presence of cancer are situations where there are a higher number of cytokines.[11]

Apparently, protein-caloric malnutrition is involved in the pathogenesis, because GTBM is never found in patients with specific protein nutritional deficiency (i.e. kwashiorkor, marasmus).[11] Differential diagnosis is important for GTBM with other conditions; namely, bone marrow edema, bone marrow necrosis, aplastic anemia, and amyloidosis.[2,4]

Edema normally shows hypocellular areas in which fat cells are of a normal size and in a normal quantity. A fluid-like material, which is not stained with Alcian Blue, surrounds these cells. Bone marrow necrosis is defined as the necrosis of myeloid tissue and medullary stroma, consisting of cellular debris with an irregular and indistinct cell margin with cytoplasmic shrinkage and nuclear pyknosis, karyorrhexis, and karyolysis. Aplastic anemia is characterized by a loss of myeloid tissue, the absence of fat cell atrophy, and a negative Alcian Blue stain.[4] Amyloids on the bone marrow are often found on the vessel walls, but sometimes these deposits are interstitial. Bone marrow shows an increase in atypical monotypic plasma cells in amyloidosis associated with light-chain protein. Secondary amyloidosis may have an increased number of polyclonal plasma cells and other characteristics of chronic inflamation.[12] Amyloid deposits in the bone marrow characteristically stain with Congo Red stain, and show apple-green birefringence on examination with polarized light.[2]

Generally, recovery of the bone marrow is expected when the underlying cause of GTBM is treated. However, according to the etiology, there are different types of treatment. Patients with anorexia nervosa showed peripheral blood count recovery after the administration of cautious nutritional therapy, and another treatment was refractory. It was then necessary to administer granulocyte colony-stimulating factor (G-CSF) and erythropoietin.[10,13] Combining erythropoietin and G-CSF results in rapid and sustained hematopoietic recovery. There is also a reduction of 91% in the cost of health care delivered to the patient. However, addressing nutritional deficiencies is also necessary to recovery normal marrow function.[10]

Figure 1 refers to a 79-year-old man who was cachectic and found unresponsive in his home. He had a previous history of leprosy and was under treatment. The patient's medical record showed that he had a hemoglobin of 7.8 g/dL, a platelet count of 125,000/mm^3, and a white blood cell count of 5,500/mm^3. The bone marrow biopsy performed during the autopsy showed bone marrow hypoplasia, fat cells atrophy, and gelatinous material that stained for Alcian Blue (Figures 1A and 1B), which was consistent with the diagnosis of GTBM. The gross examination of the heart showed atrophy with the same pattern of gelatinous transformation in the pericardial adipose tissue (Figures 1C and 1D). Malnutrition was the main cause of this patient's bone marrow condition, and his cause of death was extensive bronchopneumonia.

Keywords
Bone marrow; Pathology; Cachexia

REFERENCES

1. Osgood E, Muddassir S, Jaju M, Moser R, Farid F, Mewada N. Starvation marrow: gelatinous transformation of bone marrow. J Community Hosp Intern Med Perspect. 2014;4(4):24811. PMid:25317270. http://dx.doi.org/10.3402/jchimp.v4.24811.

2. Böhm J. Gelatinous transformation of the bone marrow: the spectrum of underlying diseases. Am J Surg Pathol. 2000;24(1):56-65. PMid:10632488. http://dx.doi.org/10.1097/00000478-200001000-00007.

3. Villate A, Iquel S, Legac E. Transformation gélatineuse de la moelle osseuse: une série rétrospective monocentrique de 12 cas. Rev Med Interne. 2016;37(7):448-52. PMid:26632481. http://dx.doi.org/10.1016/j.revmed.2015.10.349.

4. Yamamoto M, Belmont HM, Utsunomiya M, Hidaka Y, Kishimoto M. Gelatinous transformation of the bone marrow in systemic lupus erythematosus. Lupus. 2009;18(12):1108-11. PMid:19762388. http://dx.doi.org/10.1177/0961203309106344.

5. Das S, Mishra P, Kar R, Basu D. Gelatinous marrow transformation: a series of 11 cases from a tertiary care Centre in South India. Turk J Haematol. 2014;31(2):175-9. PMid:25035676. http://dx.doi.org/10.4274/Tjh.2012.0151.

6. Salomo L, Salomo M, Andersen SAW, Kamper AL. How to exhaust your bone marrow. BMJ Case Rep. 2013;2013(1):21. PMid:23813507. http://dx.doi.org/10.1136/bcr-2013-009210.

7. Chang J, Park CJ. Gelatinous transformation of the bone marrow in hepatocellular carcinoma. Blood Res. 2015;50(2):71. PMid:26157774. http://dx.doi.org/10.5045/br.2015.50.2.71.

8. Schwarz D, Ponder K, Feller ER. Case delayed diagnoses: non specific findings and diagnostic challenges in eating disorders. Case Rep Med. 2009;9:3. PMid:19721704.

9. Nakanishi R, Ishida M, Hodohara K, et al. 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):1677-82. PMid:23923088.

10. Charania RS, Kern WF, Charkrabarty S, Holter J. Successful management of gelatinous transformation of the bone marrow in anorexia nervosa with hematopoietic growth factors. Int J Eat Disord. 2011;44(5):469-7. PMid:20593416. http://dx.doi.org/10.1002/eat.20833.

11. Boullu-Ciocca S, Darmon P, Sébahoun G, Silaghi A, Dutour-Meyer A. Transformation gélatineuse de la moelle osseuse au cours de l'anorexie mentale. Ann Endocrinol. 2005;66(1):7-11. PMid:15798582. http://dx.doi.org/10.1016/S0003-4266(05)81680-4.

12. Bain BJ, Clark DM, Wilkins BS. Bone marrow pathology. 4th ed. London: Wiley-Blackwell; 2010. 153 p. chap. 3. Infection and reactive changes.

13. Morii K, Yamamoto T, Kishida H, Okushin H. Gelatinous Transformation of Bone Marrow in Patients with Anorexia Nervosa. Intern Med. 2013;52(17):2005-6. PMid:23995005. http://dx.doi.org/10.2169/internalmedicine.52.0912.

Author Contributions: The manuscript was produced, reviewed, and approved by both authors. Barbin FF undertook the autopsy, interpreted the results, wrote the manuscript and approved the manuscript's final version. Oliveira CC designed the study, oriented the autopsy, interpreted the results, supervised the manuscript preparation, revised, and approved the manuscript's final version.

Conflict of interest: None

Financial support: None

Correspondence
Cristiano Claudino Oliveira
Department of Pathology - Botucatu School of Medicine (FMB) - São Paulo State University (UNESP)
Distrito de Rubião Junior, s/n – Botucatu/SP – Brazil
CEP: 18618-687
Phone: +55 (14) 3811-6238
cristiano_c_oliveira@hotmail.com