

DR. JORDAN K SCHAEFER (Orcid ID : 0000-0002-7166-386X)

DR. SARAH M CHOI (Orcid ID : 0000-0002-7028-7313)

DR. MOSHE TALPAZ (Orcid ID : 0000-0003-3361-3981)

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Primary myelofibrosis evolving to an aplastic appearing marrow

Authors:

Jordan K. Schaefer,¹ Sarah M. Choi,² Gary D. Luker,^{3,4,5} Thomas L. Chenevert,³ Brian D. Ross,^{3,6} and Moshe Talpaz¹

¹Department of Internal Medicine, Division of Hematology/Oncology, University of Michigan, Ann Arbor, MI; ²Department of Pathology, University of Michigan, Ann Arbor, MI; ³Center for Molecular Imaging, Department of Radiology, University of Michigan, Ann Arbor, MI; ^{4,5}Departments of Biomedical Engineering and Microbiology and Immunology, University of Michigan, Ann Arbor, MI; ⁶Department of Biological Chemistry, University of Michigan, Ann Arbor, MI

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Corresponding Author:

Moshe Talpaz, MD
University of Michigan Health System
Comprehensive Cancer Center
1500 East Medical Center Drive
4302 CCC- SPC 5936
Ann Arbor, MI 48109-5936
Phone: 734-764-8195
Fax: 734-647-9654
mtalpaz@med.umich.edu

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Key Clinical Message

Our case highlights a series of bone marrow biopsies from a patient with primary myelofibrosis. Over time, this patient developed an unusual fatty appearance to his marrow, confirmed on multiple biopsies. This finding was supported by a quantitative fat MRI sequence that also shows a fatty appearance to the marrow.

Case

A 54-year-old man was diagnosed with *MPL* mutated, primary myelofibrosis in 2004 with a hypercellular marrow, MF-2 fibrosis with megakaryocyte atypia, peripheral leukoerythroblastosis, splenomegaly and an elevated lactate dehydrogenase. He was observed until 2010, when he was started on hydroxycarbamide for increasing symptoms. Prior to his 2011 enrollment in a clinical trial utilizing a novel JAK2 inhibitor, fedratinib, a bone marrow biopsy (Figure 1, Panel A; hematoxylin and eosin stain above, reticulin stain below, 10x) showed progressive megakaryocytic atypia and MF-3 fibrosis. Nearly one year into the trial, a repeat bone marrow (Figure 1, Panel B; hematoxylin and eosin stain above, reticulin stain below, 20x) was hypocellular with MF-3 fibrosis only in the cellular areas. The patient was taken off trial in 2013 and started on ruxolitinib. Repeat bone marrow biopsies in 2016 (Figure 1, Panel C; hematoxylin and eosin stain above, reticulin stain below, 10x) show a marrow comprised entirely of adipose tissue with osteosclerosis. Quantitative fat magnetic resonance (MR) imaging, utilizing methods reported separately,¹ shows replacement of the marrow with fat. Representative transaxial MR images of the pelvis show water-only, and fat-only (Figure 2, top row) constituents. Arrows show the iliac crests. A representative pseudocolor display that depicts 100% fat as dark red and 0% fat as dark blue is shown (Figure 2, bottom row). The percent fat evident in the bone marrow imaging approximates that in the subcutaneous fat. After three bone marrow biopsies and the MR demonstrating this unusual transition of primary myelofibrosis to a fatty, aplastic appearing marrow, a repeat bone marrow in 2017 (Figure 1, Panel D; hematoxylin and eosin stain above, reticulin stain below, 20x) now showed a hypocellular marrow with histopathologic findings consistent with his marrow at the time of diagnosis. To our knowledge, this is the first case of a fibrotic marrow developing such an aplastic appearance in a patient treated with a JAK2 inhibitor.

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Conflicts of interest

Dr. Talpaz is on the advisory board for CTI Biopharma and Gilead. He has received travel support from Ariad. The remaining authors have no relevant conflicts of interest.

Authorship

JKS and MT: compiled the clinical information and wrote the manuscript. SMC: provided the photomicrographs and descriptions of the bone marrow biopsies. GDL, TLC, and BDR provided the MRI images and descriptions. GDL, TLC, BDR, MT developed and wrote IRB amendments to include advanced MRI protocols. All authors reviewed and approved the manuscript.

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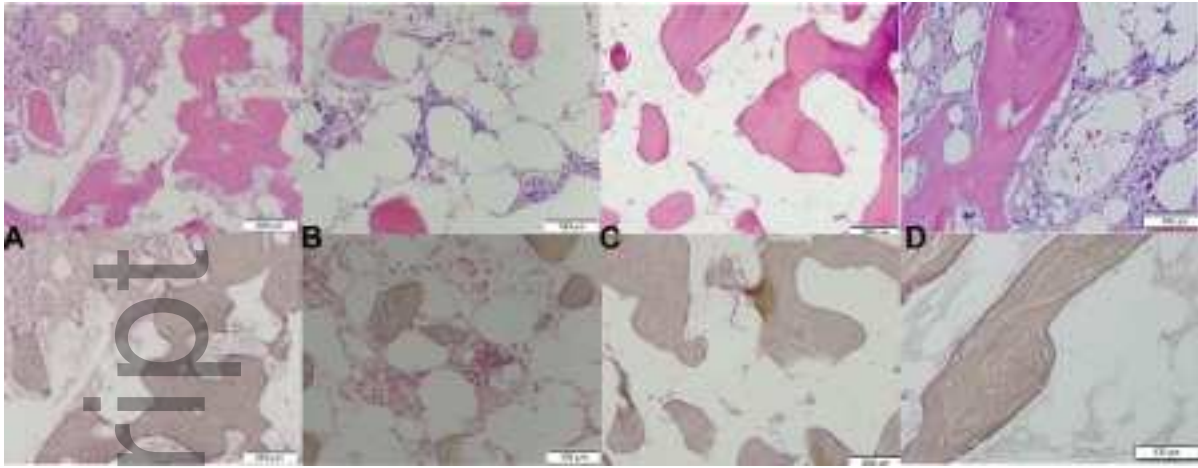
Figure legends

Figure 1. Histopathological findings from sequential bone marrow biopsies (panels A-D) of a patient with primary myelofibrosis that ultimately developed fatty replacement of his marrow. (H&E, top panels; Reticulin, bottom panels).

Figure 2. Quantitative fat MRI shows replacement of bone marrow with fat. Top row) Representative transaxial image of the pelvis shows water only (left) and fat only (only acquisitions from a quantitative fat imaging sequence. Yellow arrows show iliac crests. Bottom row) Images display the percent fat in each voxel with a gray scale display (right) or pseudocolor display that depicts 100% fat and 0% fat as red and dark blue,

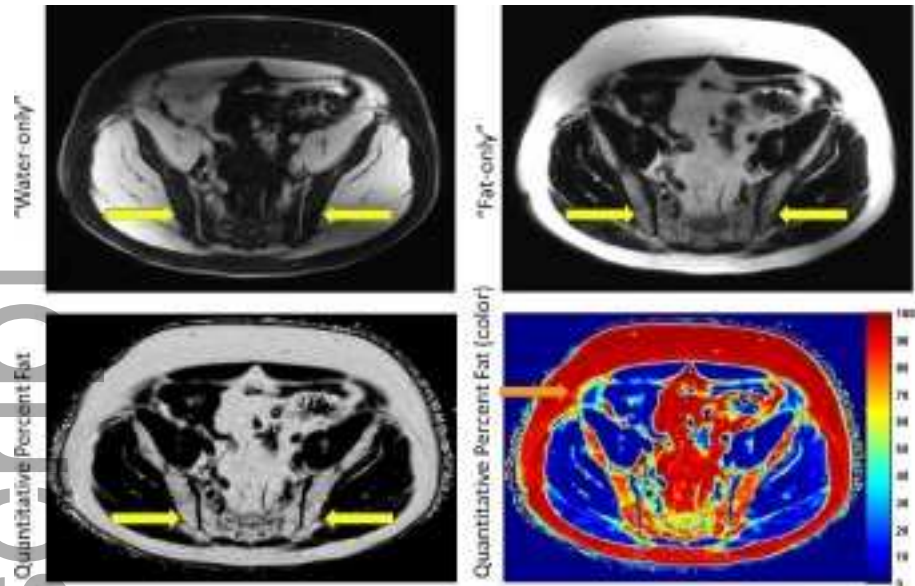
respectively (left). Percent fat in bone marrow approximates values measured in subcutaneous fat (orange arrow).

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