First episode of acute hemolysis due to G6PD deficiency in a middle-aged woman and transmission of the enzymatic defect through bone marrow transplant

G6PD deficiency is a common erythrocyte enzymatic disorder characterized by clinical, biochemical and molecular heterogeneity, being point mutations the most frequently detected genetic defect. Because the G6PD gene is located on the X chromosome, the clinical manifestations of the disease are usually confined to hemizygous men. However, female carriers might also have hemolytic anemia in relationship to the pattern of X-chromosome inactivation.

We report on a female patient from the Po valley area who developed favism for the first time at the age of 54. Past medical history revealed a colecistectomy. In 1998, at the age of 50, she underwent bone marrow harvest for her brother affected with CML. At that time, blood counts were normal and no biochemical abnormalities were detected. In June 2002, following fava beans ingestion she developed a clinical picture consistent with acute hemolysis with jaundice, hemoglobinuria, fever and back pain. Hb fell to 6.5 g/dL, total bilirubin level was 10.9 mg/dL (unconjugated 7.38 mg/dL), LDH level was 2969 mU/mL, apotoglobin level was undetectable; WBC count was 13x10^9/L with normal differential count. In the past, she had already ingested fava beans without haemolytic crisis. The patient recovered spontaneously and one month later peripheral blood counts were normal (Hb 13.1 g/dL, RBC 4.0x10^12/L, with moderate reticulocytosis). Erythrocyte G6DP activity was 90 mU/10^12 Erytr. (n.v. 118-144) and 2.71 UI/gHb at the spectrophotometric method (n.v. 6.01±1.1 UI/gHb) at two evaluations performed during the recovery phase. No other causes of acute hemolysis were documented (Coombs test negative, PNH clone absent, glycerol test negative). A molecular typing showed the patient to be heterozygous for G6PD Mediterranean (nt 563 C>T point mutation), that is the most common variant in Italy and in 25-35-year-old healthy women and in 30 to 50% of women older than 60, in neutrophils indeed, that an acquired pattern of skewed X-inactivation is detectable in 15% of 25-35-year-old healthy women and in 50 to 50% of women older than 60, in neutrophils more than in T lymphocytes. It is also possible that acquired skewing, occurring as an age-related stochastic event, worsened a constitutional (genetic) X-inactivation defect, thus promoting disease manifestation. This event has already been reported in other X-linked hematopoietic disorders. At the time of writing, the patient is well with normal blood counts. Nevertheless, tacking into account that a clonal myeloid malignancy has occurred in her brother, clinical follow-up is indicated to check for the emergence of a true clonal hemopoiesis.

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Contributions and Acknowledgments
EO, ML and MV were involved in clinical assessment of patients and drafting the article. GB performed clonality studies. All the Authors contributed to the interpretation of the data and revised the manuscript. The Authors gratefully acknowledge MD Cappellini Maria D., Centro Anemie Congenite, IRCCS Ospedale maggiore Polyclinico, Padiglione Granelli, Dipartimento di Medicina Interna, Università degli Studi di Milano, Italy, for molecular typing of G6PD DNA.

Disclosures: Redundant publication: no substantial overlapping with previous papers
Conflict of interests: none

References