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A refractory bicytopenia in a pregnant woman

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1. Indication

A 24-year-old woman was referred to our hospital for an anaemia with thrombocytopenia worsening since 3 months at 36 amenorrhoea weeks of her first pregnancy. She had no significant past medical history. However, a macrocytosis (mean corpuscular volume (MCV), 113 fL) investigated one year earlier remained unexplained. Her body mass index was 18.2 kg/m^2 (1.48 m; 40 kg). The physical examination revealed skin hyperpigmentation ("café-au-lait" spots) of the trunk, left thumb deformity (Fig. 1a) and triangular facial dysmorphia with micrognathia (Fig. 1b).

Despite vitamin B12, folates and iron supplementation, and a therapeutic test with corticosteroids, haemoglobin felt to 65 g/L (MCV 120 fL) and platelets to 17G/L. Laboratory analysis revealed: reticulocytes 50 G/L, haptoglobin 0.64 mg/L (0.54–1.44); haemoglobin electrophoresis: HbA1 92.1% (96–99), HbA2 2.30% (< 3.30), HbF 5.6% (< 2). Bone marrow aspirate and karyotype were unremarkable. A bone marrow biopsy showed a severe hypocellularity (cellularity < 5%) (Fig. 1c). The peripheral blood flow cytometry was negative for paroxysmal nocturnal haemoglobinuria.

Transfusions were needed. Six months after the delivery, the cytopenias resolved, without a bone marrow transplant.

What is the diagnosis?

2. Discussion

The patient's short stature, dysmorphic features, and persistently elevated foetal haemoglobin were consistent with an inherited bone marrow failure syndrome (IBMFs), especially Fanconi Anaemia (FA). The chromosomal breakage test with Mitomycin C attested a defect in DNA repair (43 mitosis on 50 with at least one chromosome break, 17 with ≥3 breaks, 4 radial figures). The FANCD2 mono-ubiquitination test in fibroblasts showed a FA core. Fibroblast DNA screening for FANC gene mutations confirmed heterozygous c.3188G > A/p. (Trp1063*) mutation and heterozygous deletion of the exons 21 and 22 of FANC A genes.

IBMFs are genetic disorders characterized by hematopoietic aplasia, physical abnormalities, and cancer predisposition (acute myeloid leukemia and solid tumors) [1]. FA is the most frequent IBMFs, in which the most commonly reported physical caracteristics are short stature, "café-au-lait" spots, pigmentation disorders, thumb abnormalities, microcephaly, microphthalmia, structural renal anomalies, and hypogonadism [1,2]. In the adulthood, these syndromes may be mistaken for acquired aplastic anaemia, hypoplastic myelodysplastic syndromes, or paroxysmal nocturnal haemoglobinuria which remain the main differential diagnoses. However, an early diagnosis is beneficial since it leads to FA-related malignancies screening. Furthermore, it helps to anticipate the management of high-risk pregnancies by a multidisciplinary collaboration to lead to healthy live births despite pregnancy complications related to the underlying disease [3].

Conflict of interest statement

CHAUDOT Florence: None.
Dr. GERFAUD-VALENTIN Mathieu received honoraria:
- Advisory boards for SOBI.
- Lectures for Novartis and Board.
Pr SEVE Pascal received honoraria:

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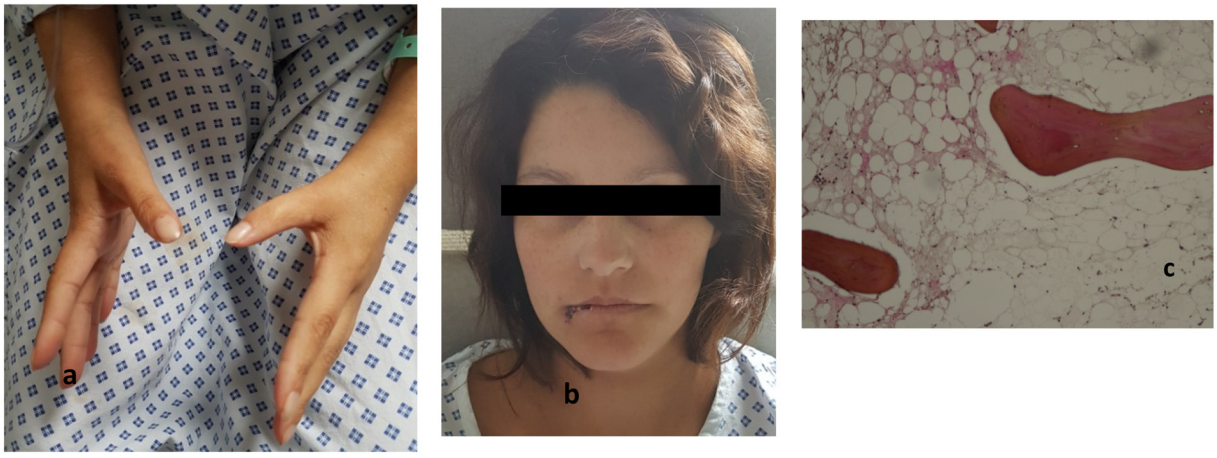

Fig. 1. Dysmorphic features and medullar hypocellularity in a 24-year-old pregnant woman with bicytopenia. a. Left thumb deformity. b. Micrognathia and triangular facial dysmorphia. c. Bone marrow biopsy showing severe bone marrow hypocellularity (< 5%), no megakaryocyte.

- advisory boards for Abbvie and Novartis.
- lectures for LFB, Roche, SOBI, Abbvie, Pfizer.

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