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## Early intervention prevented intrauterine fetus death due to placental abruption in woman with JAK2V617F mutation-positive essential thrombocythemia

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## CLINICAL VIGNETTE

**Early intervention prevented intrauterine fetus death due to placental abruption in woman with *JAK2V617F* mutation-positive essential thrombocythemia**

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## INTRODUCTION

Essential thrombocythemia (ET) is a rare, clonal myeloproliferative neoplasm (MPN) characterized by the activation of the JAK-STAT signaling pathway due to the acquisition of somatic mutations in Janus tyrosine kinase (*JAK2*), calreticulin (*CALR*), thrombopoietin (*MPL*), or other genes. Abnormal JAK-STAT pathway signaling results in bone marrow hyperplasia and thrombocytosis in the peripheral blood. Overproduction of inflammatory cytokines by the bone marrow and microenvironment cells causes the “cytokine storm” and chronic inflammatory state. Other consequences of *JAK2* gene mutation positive MPN include increased venous and arterial thrombotic risk [1]. The above-mentioned factors negatively affect the pregnancy outcomes (*i.e.* miscarriages, fetus intrauterine growth retardation, deep vein thrombosis) with live birth and spontaneous abortion rates of 50% to 70% and 25% to 50%, respectively [2].

## CLINICAL VIGNETTE

## **Case report**

A 39-year-old female diagnosed in 2020 with *JAK2V617F* gene mutation [NM\_004972.3:c.1849G>T, variant allele frequency (VAF) — 5.75%] positive ET (maximal platelet count 519G/L), with a history of miscarriage in the first trimester (8<sup>th</sup> week) in 2022. The thrombosis risk assessment according to the revised international prognostic score (r-IPSET) showed low risk [3]. The second pregnancy was diagnosed in the early stage in 2022. Therefore, low-molecular-weight heparin (Clexane 40 mg) and acetylsalicylic acid (150 mg BID) as thrombosis prophylaxis were introduced [4]. Pregnancy outcome was regularly monitored in Hematology and Gynecology & Obstetrics outpatient departments. At 29+4 weeks of pregnancy, the patient started to complain of pain in the lower part of the abdomen. At that time her BP was 175/110 mmHg. Therefore, methyldopa (Dopegyt 250 mg) was administered. Because of clinical suspicion of preterm delivery, she was transferred to a Gynecology and Obstetrics Hospital. The first obstetric examination revealed a formed and dilated to 1 cm cervix. Moreover, the fetal ultrasound didn't show any abnormalities. During a three-hour strict obstetric observation, the patient was given methyldopa, diazepam, dexamethasone for lung maturation, and magnesium sulfate for neuroprotection. At this stage, the patient's blood pressure was 150/100 mmHg. Complete blood count results were: Hgb 7.7 mmol/L, Hct 35.5%, WBC 17.7 G/L, PLT 314 G/L. Global coagulation assays: APTT, INR, PT, and fibrinogen values were normal. However, the D-dimer level was elevated – 16675 ng/mL. Serum lactate dehydrogenase activity (LDH) was slightly elevated (264 U/L). When sinusoidal cardiotocographic recording appeared, the patient started bleeding from the vagina (Fig. 1) [5]. For this reason, immediate baby delivery via cesarean section was carried out. During procedure the complete placental abruption was found. Despite that, no major bleeding was noted during surgery.

## **Newborn's history**

After delivery, the Apgar score was 5, 6, 6, body weight was 1340 g. The newborn's blood gas analysis was pH 7.06 (BE -11.3) in the umbilical artery and pH 7.08 (BE -11.2) in the umbilical vein. In the labor room, the baby was ventilated with NeoPuff because of being premature and having breathing disorders. Routine laboratory tests revealed no significant abnormalities. During hospitalization, significant improvement in the baby's status was noted. The patient was discharged from the neonatological ward over 40 days after delivery.

## **CONCLUSION**

Pregnancy in *JAK2V617F* positive ET patients bears risk of unfavorable outcome. Therefore, pregnancy should only be planned if the platelet count is reduced (preferably with the help of interferon  $\alpha$ ) and appropriate thrombosis prophylaxis according to r-IPSET thrombosis score is introduced. The mentioned strategy, in line with regular clinical status monitoring, limits the risk of unfavorable pregnancy outcome and fetal loss. In the presented case a successful pregnancy outcome was only possible because increased vigilance was maintained, and early surgery intervention was performed.

#### Article information and declarations

#### **Ethics statement**

Written informed consent for publication was obtained from the patient.

#### **Author contributions**

Artur Handziuk: writing — original draft preparation, investigation; data curation; formal analysis; Dominika Galli: acquisition of the clinical data; Aleksandra Pralat: acquisition of the clinical data; Zuzanna Kandula: preparation of genetic material and molecular analysis; Krzysztof Lewandowski: writing — original draft preparation, investigation; data curation; formal analysis; Wieslaw Markwitz: supervision, writing — review and editing

All authors have read and agreed to the published version of the manuscript.

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#### **Conflict of interest**

The authors declare no conflict of interest.

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**Figure 1.** Cardiotocography. abnormal, sinusoidal pattern of recording (arrow) noted immediately after patient admission to Gynecology & Obstetrics Department. Its appearance is mostly observed in the case of severe fetal anemia, fetal-maternal hemorrhage, twin-to twin transfusion syndrome, and ruptured vasa previa

