

Severe thrombocytopenia after uterine pregnancy embryo residue with latent infection: A case report

Hong Xie^{1**}; Wanqiu Huang^{2*}; Jian Huang^{2#}

¹Department of gynecology, Shenzhen People's Hospital, 2nd Clinical Medical College of Jinan University, Shenzhen, 518120, Guangdong Province, China.

²Key Laboratory of Systems Biomedicine (Ministry of Education), Shanghai Centre for Systems Biomedicine, Shanghai Jiao Tong University, Shanghai, 200240, China.

*These authors have contributed equally to this work and share first authorship.

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***Corresponding Author:** Hong Xie & Jian Huang
Shenzhen People's Hospital, Department of gynecology, Shenzhen, Guangdong, China.
Shanghai Centre for Systems Biomedicine, Shanghai Jiao Tong University, Shanghai, China.
Tel: 08613922802221 & 08613917640385;
Email: 1720388991@qq.com & jianghuang@sjtu.edu.cn

Abstract

A 30-year-old woman came to the hospital with irregular vaginal bleeding that had lasted for two months after a medical abortion. An ultrasound revealed uneven echoes in her uterine cavity. Subsequently, a hysteroscopy was performed, revealing the presence of Retained Products of Conception (RPOC) in the lower uterine segment. The doctor performed hysteroscopic resection of the remaining uterine tissue. However, the patient developed a high fever and severe thrombocytopenia four hours after the surgery. After receiving intensive anti-infection treatment, the patient recovered and was discharged. Through the diagnosis and treatment of this case, we have identified several key points: Firstly, prolonged presence of RPOC may lead to latent infection. Secondly, hysteroscopic fluid dilation can facilitate the entry of bacteria into the bloodstream, potentially causing sepsis. Lastly, the sharp decrease in platelet count serves as an early defensive response by the body, indicating the seriousness of the condition and the need for urgent measures. These experiences hold significant value in enhancing the diagnosis and treatment of RPOC.

Keywords: Retained Products of Conception (RPOC); Hysteroscopic resection; Latent infection; Intensive anti-infection treatment; Platelet count; Severe thrombocytopenia.

Introduction

Retained Products of Conception (RPOC) refers to the continued retention of embryonic or placental tissue in the uterus after abortion or childbirth. RPOC may result in complications such as vaginal bleeding and infection. Pathological examination showed that villous tissue was the basis for diagnosis of RPOC. The overall incidence of RPOC is about 1%-6% [1]. With hysteroscopy, the position and size of RPOC can be directly observed and accurately located, and the residual tissue in the uterine cavity can be completely removed. This technique can minimize damage and bleeding, and the postoperative recovery time is short. Prolonged RPOC can lead to intrauterine infections, which in turn can cause symptoms such as lower abdominal pain and vaginal drainage. After standard anti-infective treatment, the course of RPOC is generally 5-7 days,

and the course of disease in a few patients is extended to about 14 days. In the course of treatment, the vast majority of patients are generally in good condition, with normal vital signs and rare crises [2]. However, recently, we received a patient with uterine embryo residue and infection. The patient developed severe thrombocytopenia after hysteroscopic surgery. After intensive anti-infection treatment, the patient recovered and was discharged.

Case report

A 30-year-old female went to the gynecological clinic of our hospital due to "irregular vaginal bleeding for two months after medical abortion" (2023-10-25). After inquiry, the doctor learned that 2 months ago, when she was 7+ weeks pregnant, she went to a hospital near her home to receive medical abor-

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tion. After the miscarriage, she had irregular vaginal bleeding, sometimes more and sometimes less. But there was no fever or abdominal pain. The doctor examined her at the outpatient clinic and found nothing abnormal. The lab results showed that the blood beta-HCG was 37.24 IU/L. The ultrasound examination revealed a 30×18 mm heterogeneous echo in the middle and lower segment of the intrauterine cavity. The posterior wall of the echo showed abundant blood flow signals with a range of 26×13 mm (Figure 1A-1D). The outpatient doctor preliminarily diagnosed her with RPOC. She was recommended to be hospitalized for hysteroscopy.

Laboratory examination (2023-10-26): On the day of admission, the patient's white blood cell count was $7.42 \times 10^9/L$, neutrophil absolute value was $4.19 \times 10^9/L$, neutrophil percentage was 56.50%, red blood cell count was $4.62 \times 10^{12}/L$, hemoglobin concentration was 131g/L, and platelet count was $143 \times 10^9/L$. All hematologic markers were normal. Hysteroscopy showed that 4×4 cm of pregnancy embryo remained in the lower uterine segment of the patient, and the base of the residue was mainly located in the posterior wall and left lateral wall of the lower uterine segment (Figure 1E-1H). After hysteroscopic withdrawal, the patient had about 50ml of vaginal bleeding. After injecting oxytocin 10U into the patient's cervix and intravenous infusion of oxytocin 10U, vaginal bleeding decreased and the patient had no discomfort. Based on the results of laboratory examination, ultrasound examination, and hysteroscopy, the patient met the diagnostic criteria for RPOC, and the patient was recommended to undergo hysteroscopic resection of uterine residual tissue. The patient gave informed consent during the whole process.

A-D: Ultrasound examination results; E-H: hysteroscopy results; I-L: Results of histopathological examination.

On 2023-10-27, the doctor successfully performed excision of residual uterine tissue for the patient. The residual tissue that was removed had a distinctly foul odor. The patient was given an intravenous infusion of Cefuroxime Sodium 1 hour before surgery to prevent infection, and received conventional anti-infection therapy after surgery. The operation went smoothly. The patient told the nurse that she had chills four hours after the operation. After examination, the doctor found no vaginal bleeding, body temperature 39.2°C, blood pressure 95/60 mmHg, heart rate 112 beats/min, clear breathing sound in both lungs, no hearing of dry and wet rales, soft abdomen, and no abdominal tenderness or rebound pain. The doctor draws the patient's blood and obtains the patient's cervical secretions, then sends the sample to the laboratory for bacterial culture examination. The laboratory examination found that the patient's blood potassium was 2.62 mmol/L. White blood cell count was $4.48 \times 10^9/L$, hemoglobin concentration was 109g/L, neutrophil percentage was 93.10%, neutrophil absolute value was $4.17 \times 10^9/L$, and platelet count was $52 \times 10^9/L$. The results of inflammatory factor examination showed fast C-reactive protein 35.1 mg/L, serum amyloid A 111.64 mg/L, procalcitonin 6.393 ng/ml and interleukin-6 2990 pg/mL. The doctor highly suspected that the patient had sepsis. The doctor immediately performed an intravenous drip of ertapenem and metronidazole. Symptomatic treatments such as potassium supplementation and antipyrexia were also given. One hour after medication, the patient's fever retreated, no vagi-

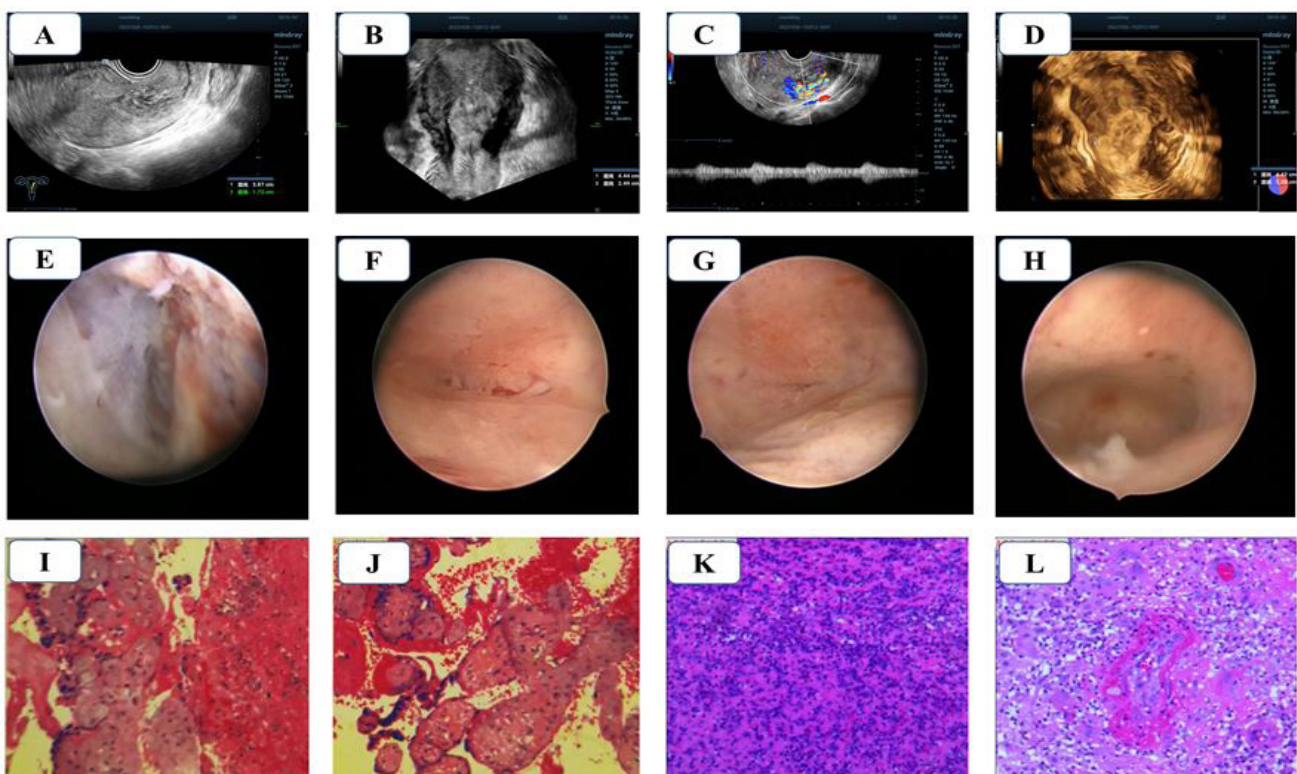


Figure 1: Examination results of the patient before and after admission.

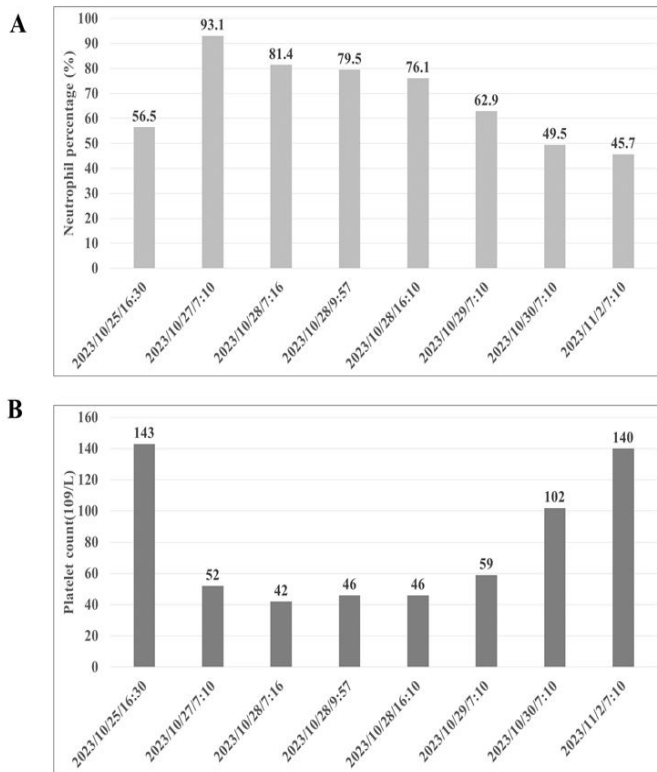


Figure 2: Summary of neutrophil percentage and platelet count of the patient before and after admission.

nal bleeding, no abdominal pain and other symptoms, the skin and mucous membranes of the whole body without bleeding points. Her vital signs were normal. 2023-10-28 (the first day after surgery), according to the patient's symptoms, the doctor continued to treat the patient with antibiotics, and no abnormal symptoms occurred during treatment. Her body temperature was 36.8°C, no vaginal bleeding, no abdominal pain and other symptoms, and no bleeding points on the skin and mucosa of the whole body. Vital signs were normal. Laboratory examination: white blood cell count $7.21 \times 10^9/L$, hemoglobin concentration 102 g/L, platelet count $42.00 \times 10^9/L$, neutrophil percentage 81.40%, neutrophil absolute value $5.87 \times 10^9/L$; Fast C-reactive protein 73.25 mg/L, serum amyloid A 326.48 mg/L, procalcitonin 8.664 ng/ml, interleukin-6 13.63 pg/ml; Potassium ion 3.55 mmol/L, sodium ion 136.85 mmol/L, chloride ion 112.02 mmol/L, calcium 2.03 mmol/L, phosphorus 0.73 mmol/L, magnesium 0.66 mmol/L; Alanine aminotransferase 24.00 U/L, aspartate aminotransferase 27.77 U/L, total protein 53.1g/L, albumin 30.72 g/L, total bilirubin 15.4 umol/L, indirect bilirubin 11.90 umol/L, urea nitrogen 1.80 mmol/L, creatinine 62.0 umol/L. 2023-10-29 (the second day after surgery), according to the patient's symptoms, the patient continued to receive antibiotic treatment, and no abnormal phenomenon occurred during treatment. Laboratory examination: white blood cell count $4.79 \times 10^9/L$, hemoglobin concentration 109 g/L, platelet count $59 \times 10^9/L$, neutrophil percentage 62.90%; Sodium ion 136.75 mmol/L; Fast C-reactive protein 41.73 mg/L, procalcitonin 4.28 ng/ml; The results of coagulation function test were normal. 2023-10-30 (the third day after surgery) continued antibiotic treatment according to the patient's symptoms, and no abnormal phenomenon occurred during treatment. Laboratory tests:

white blood cell count $5.01 \times 10^9/L$, hemoglobin concentration 118 g/L, neutrophil percentage 49.50% (Figure 2A), neutrophil absolute value $2.48 \times 10^9/L$, platelet count $102 \times 10^9/L$ (Figure 2B), procalcitonin 2.495 ng/ml, fast C-reactive protein 21.64 mg/L. On the following two days, the patient continued to receive antibiotic treatment, and no abnormal phenomenon occurred during treatment.

Figure 2: Summary of neutrophil percentage and platelet count of the patient before and after admission.

In 2023-11-2 (the sixth day after surgery), the pathological examination of the residual tissue showed that the uterine tissue of the patient had decidua and placental villi tissue (Figure 1I-1J), which was consistent with the diagnosis of pregnancy embryo residue. The bacterial culture results of the patient's blood and cervical secretions were negative. After 7 days of anti-infective treatment, the patient's vital signs were normal. According to the principles of anti-infective treatment in the Criteria for Diagnosis and Treatment of Sepsis (2023) [3], patients with sepsis whose source of infection has been controlled can be treated with antibiotics for a short course, usually 7-10 days. For patients with immune deficiency, difficult to control the source of infection, fungal infection, and slow improvement of clinical symptoms, the course of antibacterial drugs can be longer than 10 days. Considering that the patient's multiple examination results have returned to normal and clinical symptoms have disappeared, the doctor suggested that the patient stop using antibiotics and leave the hospital to home.

Discussion

At 7+ weeks of gestation, the patient underwent a medical abortion with informed consent. After the abortion, the patient had irregular vaginal bleeding, which lasted for about two months and was not paid attention to. After suspecting their menstrual disorders, went to the hospital for medical treatment. Before admission, the patient had no fever, no vaginal discharge, no odor of vaginal discharge, no abdominal pain, and no abnormalities were found in blood routine examination. After consultation, the doctor found that she may be the residue of pregnancy embryo, and recommended her hospitalization. When the patient is in the outpatient clinic, the attending physician fails to detect or suspects that the patient has gestational embryo residue and may already have an underlying infection.

After admission, routine hysteroscopic surgery was performed to remove the residual tissue. This is despite the routine use of intravenous antibiotics 1 hour before surgery to prevent infection. However, the patient suddenly developed a high fever (39 °C) 4 hours postoperatively. Residual tissue removed from the patient's uterine cavity during surgery has a foul odor, indicating a serious infection in the uterine cavity (Figure 1K and 1L). Preoperative ultrasound examination indicated that there was abundant blood flow between the residual tissue in the uterine cavity and the muscle layer of the posterior wall of the uterus, possibly arteriovenous fistula (Figure 1C). The increase of dilation pressure during hysteroscopic surgery would

also lead to rapid entry of bacteria into the blood. Therefore, the postoperative fever of the patient may be due to sepsis caused by the entry of bacteria into the blood at the residue. The negative bacterial culture results of blood and cervical secretions may be due to the effect of preoperative prophylactic antibiotics on the results of postoperative blood culture and cervical swab culture, resulting in the failure to culture pathogenic bacteria.

Gestational embryo residue (RPOC) is a common complication of abortion and postpartum. In China, routine hysteroscopic surgery to remove RPOC does not cause serious infection (such as sepsis). Intravenous antibiotics before surgery can also prevent infection after surgery. Even if a mild infection occurs, severe thrombocytopenia will not occur in the short term. The patient's platelet count before surgery was $143 \times 10^9/L$, and the platelet count was only $52 \times 10^9/L$ on the day after surgery. The platelet count was $42 \times 10^9/L$ the next day after surgery. However, the patient did not have severe symptoms such as septic shock and coagulation dysfunction DIC. In order to rule out laboratory testing errors, the platelet count was repeated, and peripheral blood smear examination also confirmed the correct platelet count. According to the consensus of Chinese experts in the diagnosis and treatment of adult patients with severe thrombocytopenia, it is severe thrombocytopenia, suggesting that the patient's condition may be critical [4].

In clinical practice, platelet count $< 100 \times 10^9/L$ is usually defined as thrombocytopenia, and platelet count $< 50 \times 10^9/L$ is defined as severe thrombocytopenia. The causes of thrombocytopenia can be divided into primary and acquired. Primary thrombocytopenia is mainly caused by blood diseases. The etiology of acquired thrombocytopenia involves infection, trauma, immune disorders, nutritional disorders and many other diseases. Sepsis is the most common cause of thrombocytopenia in severe patients, which can lead to systemic inflammatory response syndrome, or even severe septic shock or multiple organ dysfunction, with a fatality rate of more than 15% [5]. The probability of thrombocytopenia in sepsis patients can be as high as more than 50% [6]. The platelet count results of this patient suggest that she may develop sepsis, and may develop complications such as multiple organ failure, with a high fatality rate. As a result of timely and intensive anti-infective treatment, the patient's vital signs were normal and did not show any signs of danger. The platelet count on day 1 was $52 \times 10^9/L$; The platelet count on day two was $42 \times 10^9/L$; Without platelet infusion, the platelet count increased to $78 \times 10^9/L$ on the third day and $102 \times 10^9/L$ on the fourth day, which was basically close to normal. After 7 days of anti-infective treatment, various inflammatory indexes returned to normal, the patient stopped taking antibiotics, recovered and was discharged from hospital. Platelets are small, non-nucleated blood cells that circulate in the blood with a concentration of $150-400 \times 10^9/L$ and are mainly responsible for hemostasis and thrombosis [7,8]. Platelets are also major sensors of invasion agents, such as bacteria, viruses, and fun-

gi, and play an important role in inflammation, innate immunity [9,10], and sepsis [11,12]. Sepsis refers to life-threatening organ dysfunction caused by an dysregulated host response to infection by pathogenic microorganisms such as bacteria and fungi. The clinical symptoms of sepsis are nonspecific and complex, which can rapidly progress to septic shock, multiple organ dysfunction, and even death [13]. Bacteria are the most common pathogens causing sepsis, while *Staphylococcus aureus*, *Streptococcus* and *Escherichia coli* are the most common sources of infection. *Escherichia coli* is a common component of the outer membrane of Gram-negative bacteria by releasing the bacterial endotoxin lipopolysaccharide (LPS), which belongs to pathogen-associated molecular patterns (PAMPs) and can induce sepsis. Many studies have shown that LPS is a true platelet agonist or primer for platelet activation, which is involved in the formation of intravascular thrombosis [14-15]. In the early stage of infection, in order to protect itself, the body forms micro-thrombus to limit the infection site. Platelets are an important factor in the formation of thrombus, and micro-thrombus enables better control of infection. In the later stage of infection, thrombus may prevent antibiotics, white blood cells and macrophages from entering the site of primary infection, thus causing multiple organ dysfunction or death in the human body [16].

Abortion with legal and informed consent is acceptable in China. But a routine ultrasound should be performed after a miscarriage to prove there is no intrauterine residue. Women who experience persistent vaginal bleeding for 2 weeks or more after a miscarriage should go to the hospital immediately to confirm whether there is an intrauterine residue. If the residue remains in the uterine cavity for a long time, the attending doctor should consider the possibility of latent infection so that early and correct treatment can be given. The rapid entry of bacteria into the bloodstream due to increased dilation pressure during hysteroscopic surgery may lead to sepsis. Therefore, anti-infection treatment before surgery is very important and necessary treatment measures. The infection index and the number of platelets must be monitored continuously during the hospitalization to prevent accidents. The apparent foul odor of the remnant tissue removed from the patient indicates that the patient has developed a localized infection while at home. Although sepsis has not developed, the potential risk is very serious. After admission, the infection was triggered by the operation, causing sepsis. The patient developed a fever about 4 hours later, and the number of platelets dropped sharply, suggesting that the disease might progress rapidly. The patient's vital signs were stable, indicating that the infection was still in the early stage; after timely strengthening anti-infection treatment, the disease was effectively controlled, the number of platelets returned to normal, the level of inflammatory factors returned to normal, so the patient did not have serious consequences.

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