Severe Gastrointestinal Bleeding during Pregnancy in a Case of Blue Rubber Bleb Nevus Syndrome

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ABSTRACT

Blue rubber bleb nevus syndrome (BRBNS) is a rare disorder characterized by distinctive cutaneous and gastrointestinal venous malformations that usually cause massive or occult gastrointestinal hemorrhage and iron deficiency anemia secondary to the bleeding episodes. Only two reports of BRBNS in pregnant women can be found, according to the MEDLINE search. Both cases did not describe severe complications during pregnancy. This is the first case report of BRBNS with severe intestinal hemorrhage in a pregnant woman. The woman had been symptom-free for 5 years before the pregnancy and remained symptom-free for 2 years after delivery. This suggests that pregnancy induced the hemangiomas of the gastrointestinal tract to bleed. Celiotomy was needed to deal with massive gastrointestinal bleeding. We propose that women with BRBNS should be checked for systemic hemangiomas before pregnancy. However, it is difficult to check the small intestine thoroughly for hemangioma. Therefore, adequate attention needs to be paid to possible gastrointestinal bleeding when caring for patients with this condition. Our experience suggests that when dealing with pregnant women with BRBNS, it is essential to bear in mind the possibility that pregnancy may trigger the symptoms of hemangioma to become manifest, possibly causing life-threatening massive bleeding from the digestive tract.

KEYWORDS: Blue rubber bleb nevus syndrome, hemangioma, thrombus, pregnancy, intestinal hemorrhage

Objectives: On completion of the article, the reader should be able to (1) summarize the important points in assessing a woman with blue rubber bleb nevus syndrome who can conceive, and (2) protect the woman from severe gastrointestinal bleeding during pregnancy.

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CASE REPORT
We encountered a patient with blue rubber bleb nevus syndrome (BRBNS): a 25-year-old woman, gravida 0, para 0. The woman had systemic congenital hemangioma. A giant hemangioma was found in the right femoral region. She had developed Kasabach-Merritt syndrome and undergone radiation therapy when she was 1 year old. During childhood, she underwent several sessions of surgery to remove small hemangiomas occurring on the surface of her body. At age 11, she lost suddenly consciousness. At that time, minor bleeding was detected by magnetic resonance imaging (MRI) in the right parietal lobe of her brain; she recovered in response to conservative treatment. The bleeding was attributed to a ruptured hemangioma; the MRI revealed a sign suggestive of hemangioma in that region. At age 19, she developed gastrointestinal bleeding. At that time, multiple hemangiomas were detected endoscopically in the large intestine, and she underwent clipping. Her condition had remained stable over the last 5 years.

When she was found to be pregnant at our hospital, at 6 weeks of gestation (wG), a 10 × 7 cm hemangioma was palpable below the skin in the right femoral region. Many small hemangiomas, a few millimeters in diameter, were visible on various sites across her body surface, such as the right axilla (Fig. 1A), buttock (Fig. 1B), planta, and face. In the hematologic workup, the fibrin/fibrinogen degradation products (FDP) -E fraction of 1800 mg/L was abnormally high; the normal upper limit is 120 mg/L. The hemoglobin of 12.5 g/dL, the platelet counts, and the other clotting system parameters were within the normal range. Because the elevation of FDP might result from a chronic production of very small thrombi in the many hemangiomas, her general condition did not reveal anemia or acute disseminated intravascular coagulation (DIC). At 11 wG, melena began during evacuation. Colon fiberscopy revealed approximately 20 hemangiomas throughout the entire colon at that time. Because her hemoglobin level decreased from 11.7 to 8.8 g/dL in 5 days, she was examined by gastric fiberscopy and colon fiberscopy at 12 wG and was found to have four hemangiomas in her stomach and approximately 20 hemangiomas in her colon. A total of 50 clips and four indwelling snareurs were then applied to the hemangiomas to stop the bleeding. The arrows in Fig. 2A and 2B indicate multiple hemangiomas affecting the large intestine. Fig. 2C shows clipped hemangiomas and Fig. 2D shows snared hemangiomas.

On the basis of her disease history and the latest episode of gastrointestinal bleeding, the patient was diagnosed as having BRBNS. Because she had not received a detailed examination of her hemangioma immediately before she became pregnant, she underwent cranial MRI, chest x-ray, and abdominal ultrasonography to examine hemangiomas on her whole body except the small intestine. The cranial MRI revealed a sign of hemangioma in the right precentral gyrus (Fig. 3), but it had not changed markedly from the one detected 10 years before. The chest x-ray disclosed several nodular shadows of calcification, seemingly representing traces of past bleeding. It was not possible to make a detailed examination of her lungs because CT scans had to be avoided during pregnancy. Hepatic ultrasonography revealed no hemangiomas larger in size than a few millimeters. Thus, no giant hemangiomas were seen at any other site with the exception of the femoral region. It was not possible to check for hemangiomas of the small intestine because the endoscope did not reach this area.

The melena disappeared following endoscopic hemostasis. Her hemoglobin level recovered to 10.3 g/dL in response to iron preparations. She was discharged from the hospital at 16 wG. At 19 wG, she suddenly developed palpitation and melena. At that time, the hemoglobin level had decreased to 5.6 g/dL. She was immediately hospitalized. During her hospital stay, intense melena was seen, and the hemoglobin level decreased further to 3.9 g/dL. She then received a
transfusion of concentrated erythrocytes, 1000 mL in total. Gastric fiberscopy and colon fiberscopy, which were performed on an urgent basis, revealed no marked locus of bleeding in the stomach or large intestine, suggesting that the small intestine might be the source of bleeding. Because the gastrointestinal bleeding persisted, she underwent an emergency celiotomy.

The opened peritoneal cavity was checked with the help of an endoscope. While the small intestine was being moved by hand, bleeding within the lower segment of the ileum was detected, and a total of 13 hemangiomas were found in the ileum. Most of these hemangiomas were cut with an automated suturing device, followed by suturing of the serous membrane and the muscular layer. The ileum was incised at one point of the ileocecal region, and the hemangiomas in this region were resected under direct vision. Fig. 4A indicates the large amount of bleeding in the ileal cavity (arrow). Fig. 4B shows the resection of hemangiomas and subsequent suturing using an automated suturing device. Figs. 5A (×100) and 5B (×400) show microscopic findings of resected tissues, in which erosion of the surface of the hemangioma and exposure of blood vessels on the surface of the ileal mucosa were visible, suggesting that bleeding had occurred at these sites. The pathologic findings revealed subcutaneous, cavernous, blood-filled or empty spaces lined with normal endothelial cells, conditions that were consistent with hemangiomas. After surgery, her uterus contracted. To suppress uterine contractions, she received a drip infusion of ritodrine hydrochloride. Because there was a possibility that very hard feces injured hemangiomas within the digestive tract, the patient was treated orally with magnesium hydrochloride to soften her feces. Bleeding subsided, and her hemoglobin level recovered to 11.3 g/dL in response to iron preparations. She was discharged at 29 wG.

During the subsequent course of her pregnancy, gastrointestinal bleeding never recurred, and intrauterine fetal growth was normal. A cesarean section was selected

Figure 2  Findings by gastrointestinal fiberscopy at 12 weeks of gestation (wG). (A and B) Multiple hemangiomas affecting the large intestine; (C) clipped hemangiomas; (D) snared hemangiomas.

Figure 3  Cranial magnetic resonance image (MRI) at 19 weeks of gestation (wG). Cranial MRI revealed a sign of hemangioma in the right precentral gyrus.
at 38 wG because her hip joints had limits in flexion and abduction due to the influence of hemangioma and radiation therapy. During surgery, no hemangioma was macroscopically visible on the surface of the small or large intestine or around the uterus. The woman delivered a boy weighing 3346 g without any abnormality. He has no evidence of this syndrome. On the day following surgery, the maternal FDP levels increased from 1500 (preoperative level) to 13,100 mg/L, and platelet counts decreased slightly from 16.0 to 11.0 × 10^10/L, suggesting increased activation of the clotting system. Four days after surgery, her FDP returned to the preoperative level and DIC had not developed. The subsequent course was uneventful for both the mother and the infant, allowing them to be discharged 11 days after surgery.

**DISCUSSION**

BRBNS is a rare disorder characterized by distinctive cutaneous and gastrointestinal venous malformations that usually cause massive or occult gastrointestinal hemorrhage and iron deficiency anemia secondary to the bleeding episodes. The first case was reported by Gascoyen in 1860, however, the name was not applied until almost a century later, and in 1958 Bean described the syndrome. BRBNS patients present typical skin lesions, with some lesions having a rubber-like nipple appearance; the number of skin and gastrointestinal lesions and the severity of anemia are correlated. Mostly BRBNS occurs sporadically, but it can be inherited as an autosomal dominant trait. Recent analysis identified a locus on chromosome 9 responsible for venous malformations.

Skin hemangiomas assume various forms, including the large cavernous type, blue rubbery type, and blue spot-like type. Gastrointestinal hemangiomas occur most frequently in the small intestine, followed by the large intestine and then the stomach. Other organs where hemangiomas can develop include the liver, lungs, brain, spleen, gall bladder, kidneys, adrenals, skeletal muscles, thyroids, and bones. Thus, hemangiomas may appear throughout the body. Laboratory data are characterized by chronic anemia and consumption coagulopathy. The major treatment for hemangiomas is surgical resection in the case of bleeding. In situations where surgery is not possible, administration of iron...
other than anemia. The woman in the first report was followed an uneventful course of pregnancy and showed no major abnormalities. Domini et al. reported that management with electrocautery or laser photocoagulation were usually not effective, although some reports recommend them.

The influence of pregnancy on the prognosis of BRBNS is unknown because only few reports exist. Only two reports of BRBNS in pregnant women can be found, according to the MEDLINE search. Neither case described severe complications during pregnancy. Both reported cases followed an uneventful course of pregnancy and showed no major abnormalities other than anemia. The woman in the first report was 34 years old and was diagnosed at age 3. Multiple hemangiomas were noted in the skin of the neck, left hand, vulva, and both feet. During her pregnancy anemia was detected, but no occult blood was found in her stool. The hematological examination revealed a hemoglobin level of 9.6 g/dL, a platelet count of 11.3 × 10^10/L, and FDP of 658 mg/L. These data suggested an increased consumption of platelets and coagulation factors and activation of the fibrinolytic system. At 38 wG, an elective cesarean section was performed because of the risk of ruptures of hemangiomas located at the vulva and other unidentified sites. The second report described a 34-year-old woman, diagnosed 11 years previously. There were no episodes of abnormalities in the hemoglobin level and platelet counts during pregnancy. She was known to have a hemangioma on the right labium majus. The possibility of uncontrollable bleeding from vaginal or vulval hemangiomas was considered a contra-indication to a vaginal delivery, and an elective cesarean section was performed at 38 wG. In both of the prior reports, there were no clinical signs of preeclampsia or thrombosis.

The patient described in this article developed severe gastrointestinal bleeding during pregnancy. In this case of BRBNS-complicated pregnancy, the woman had been symptom-free for the 5 years before this pregnancy and remained symptom-free for 2 years after this delivery. This suggests that pregnancy caused the hemangiomas of the gastrointestinal tract to bleed. We needed endoscopic hemostasis at 12 wG to stop the gastrointestinal bleeding and celiotomy at 19 wG to deal with massive small intestinal bleeding. After resolution of the hemangiomas of the small intestine, gastrointestinal bleeding never recurred and intrauterine fetal growth was normal.

We suggest that women with BRBNS should be checked for systemic hemangioma using MRI and gastrointestinal endoscopy before pregnancy. Evaluations of anemia and the clotting system are needed. Furthermore, genetic counseling is recommended. However, it is difficult to check the small intestine thoroughly for hemangioma. Therefore, adequate attention needs to be paid to possible gastrointestinal bleeding when dealing with patients with this condition. Our experience suggests that when dealing with pregnant women with BRBNS, it is essential to bear in mind the possibility that pregnancy triggers the symptoms of hemangioma, possibly causing life-threatening massive bleeding from the digestive tract.

REFERENCES


