Severe Consumptive Coagulopathy in an Extremely-Low-Birth-Weight Infant with Intra-Abdominal Umbilical Vein Varix: A Case Report

Mitsuhiro Haga, MD1 Kanako Itoh, MD, PhD1 Tsuguhiro Horikoshi, MD, PhD2 Fumihiko Namba, MD, PhD1 Kazuhiko Kabe, MD, MMA1

1Department of Pediatrics, Saitama Medical Center, Saitama Medical University, Kawagoe, Saitama, Japan
2Maternal and Fetal Medicine, Center for Maternal, Fetal and Neonatal Medicine, Saitama Medical Center, Saitama Medical University, Kawagoe, Saitama, Japan


Address for correspondence Mitsuhiro Haga, MD, Department of Pediatrics, Saitama Medical Center, Saitama Medical University, 1981 Kamoda, Kawagoe, Saitama, 350-8550, Japan (e-mail: haga_m@saitama-med.ac.jp).

Intra-abdominal umbilical vein varix (IUVV) is a focal dilatation of the intra-abdominal umbilical vein.1 Most research defined IUVV as a focal dilatation over 9 mm or at least 50% larger than the intrahepatic portion.1 IUVV is a rare condition, reported at 0.5 to 2.5 per 1,000 pregnancies.1 Recent studies have shown favorable outcomes of isolated IUVVs in term neonates. Little is known, however, about the prognosis of IUVVs in preterm neonates. We encountered a case of IUVV in an extremely low-birth-weight infant who developed severe consumptive coagulopathy after birth. The patient’s coagulation test normalized as the varix spontaneously obstructed. Although life-threatening hemorrhagic complications were avoided, a cerebellum hemorrhage was found in the brain magnetic resonance imaging at the term-equivalent age. In a literature survey, coagulopathy was reported in 4 out of 15 infants with IUVVs born before 34 weeks of gestation, including our present case. Preterm infants with IUVVs may develop coagulopathy because of the prematurity of their coagulation–fibrinolysis systems. Attention should be given to the coagulation status of preterm neonates with IUVVs.

Abstract

Keywords
► intra-abdominal umbilical vein varix
► consumptive coagulopathy
► extremely-low-birth-weight infants
► intracranial hemorrhages

Case
The mother was a 32-year-old primigravida with a medical history of moyamoya disease. After confirmation of the pregnancy, she was referred to our hospital at 13 weeks of gestation because of her complication. Her pregnancy course had no abnormalities until the second half of second trimester. However, at 23 weeks of gestation, dilatation of the umbilical vein was detected in fetal ultrasonography. The umbilical vein was dilated from the abdomen to the umbilical portion of the portal vein, and the maximum diameter
A male infant was born with a birth weight of 613 g. The Apgar scores were 3 at 1 minute and 8 at 5 minutes. With a diagnosis of respiratory distress syndrome, the infant received tracheal intubation and surfactant replacement therapy. Upon admission to our neonatal intensive care unit, he had petechiae all over the body and apparent bleeding from the venous and arterial insertion sites. The laboratory tests showed severe coagulopathy: prothrombin time >55 seconds activated partial thromboplastin time >180 seconds fibrinogen <20 mg/dL, and D-dimer 26.3 μg/mL. The complete blood count showed a low platelet level (31,000/μL). A large varix of the intra-abdominal umbilical vein was observed with abdominal ultrasonography after birth.

The infant was diagnosed with severe consumptive coagulopathy, and transfusions of fresh frozen plasma (FFP) and platelet concentrate (PC) were administered. The cause of his severe coagulopathy was considered the consumption of coagulation factors through the process of thrombus formation and fibrinolysis within the varix, but anticoagulant therapy was not performed because of his apparent bleeding tendency. His coagulation status gradually normalized as the varix was obstructed with thrombosis. PC and FFP transfusions were discontinued on days 1 and 3 of life, respectively.

The total closure of the varix was confirmed with ultrasonography on day 7, and no thrombosis was found within the portal vein. After the closure of the varix, the patient had no recurrence of coagulopathy. The histopathology of the placenta and umbilicus showed no abnormality. Although he did not suffer from life-threatening hemorrhagic complications, a brain magnetic resonance imaging at term-equivalent age showed a small hemorrhage in the cerebellum. The patient was 18 months old (corrected age, 15 months) when this report was written and had achieved age-appropriate developmental milestones.

**Discussion**

To the best of our knowledge, this report is the first to present a case of IUVV in an ELBWI. Our patient developed severe coagulopathy requiring transfusion of FFP and PC. Fortunately, severe hemorrhagic complications did not occur except for a small cerebellar hemorrhage.

The etiology of IUVV is considered as a developing condition rather than a congenital abnormality. Most IUVVs develop in the extrahepatic portion within the abdomen, which is the weakest part of the umbilical vein. In earlier studies, fetal IUVVs were reported to be associated with the increased risk of intrauterine fetal death (IUFD). The causes of IUFD are unclear, but two possible mechanisms are speculated: (1) fetal cardiac failure due to excessive preload or (2) formation of thrombosis within the varix. Recent cohort studies have shown favorable outcomes in term neonates with isolated IUVVs; however, the prognosis of preterm neonates with IUVVs remains unclear.

To review the previous case reports of preterm neonates with IUVVs, we searched the Medline database with the words “umbilical vein varix,” “umbilical vein aneurysm,” “umbilical vein dilatation,” or “umbilical vein ectasia.” This search produced 583 citations from 1985 to 2019. We excluded the literature reporting cases of extra-abdominal UVVs (n = 15), portal vein anomalies (n = 9), vitelline veins (n = 6), umbilical artery aneurysms (n = 5), right umbilical veins (n = 1), and articles not relevant to IUVVs (n = 473). Thus, 74 publications were reporting IUVVs. From the 74 articles, we also excluded cases of non-neonates (n = 7), review articles without new cases (n = 2), a duplicate case (n = 1), and non-English articles (n = 7). Our final literature pool contained 57 articles, from which we reviewed 547
cases. Of the 547 cases, 19 were preterm infants born before 34 weeks of gestation, and detailed clinical data were available in 14 of these cases. Table 1 summarizes gestational age, birth weight, and complications of 15 cases, including the reported 14 cases and our present case. Gestational ages ranged from 27 to 33 weeks, and birth weights were 613 to 2,150 g. Neonatal death was reported in one case due to severe congenital anemia from α-thalassemia. No patients had chromosomal abnormalities, but congenital anomalies were found in three cases (one case with an atrial septal defect and two cases with gastroschisis). Coagulopathy was reported in four cases (27%), and two cases had intracranial hemorrhage. There were no apparent differences in gestational age and birth weight between the premature infants with coagulopathy and the ones without coagulopathy. No cases of coagulopathy or hemorrhagic complications were reported in neonates born after 34 weeks of gestation (n = 528).

This study does not demonstrate the actual incidence rates of coagulopathy in preterm and term infants with IUVVs. However, because the reports of IUVV cases with coagulopathy are limited to the neonates born before 34 weeks of gestation, preterm infants with IUVVs are considered more susceptible to developing coagulopathy. Coagulopathy associated with IUVVs is thought to be induced by the consumption of coagulation factors during thrombus formation and fibrinolysis within the varices. Preterm neonates have significantly lower coagulation factors and coagulation inhibitor activities than term neonates, and the presence of IUVV in a neonate with a premature coagulation-fibrinolysis system may be associated with the development of coagulopathy.

We have reported on our first case of IUVV in an ELBW infant who developed severe coagulopathy after birth. Other case reports of coagulopathy existed in preterm neonates with IUVVs. We should anticipate that preterm infants with IUVVs have a risk of developing coagulopathy.

Informed Consent
Informed consent was obtained from the patient’s parents for the publication of this case report and any accompanying images.

Disclosure
The authors declare that they have no known competing financial interests or personal relationships that could influence the work reported in this paper.

Conflict of Interest
None declared.

Acknowledgments
The authors would like to show our appreciation to the nursing staff at Saitama Medical Center, Saitama Medical University, for their assistance in collecting the clinical data. We are also grateful to Dr. Hirotaka Ishido for his generous support for this study. We would also like to thank Dr. Ayumi Oshima, Dr. Shuntaro Oka, and Dr. Ayumi Sasaki for their valuable advice on this report. We also would like to thank Enago (www.enago.jp) for the English language review.

References

Table 1 Reported cases of IUVV before 34 weeks of gestational age with or without complication of coagulopathy

<table>
<thead>
<tr>
<th>Cases without coagulopathy (n = 11)</th>
<th>Cases with coagulopathy (including the present case) (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td><strong>GA (wk)</strong></td>
</tr>
<tr>
<td>Mahony et al⁴</td>
<td>33</td>
</tr>
<tr>
<td>Batton et al⁵</td>
<td>32</td>
</tr>
<tr>
<td>Rahemtullah et al⁶</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>30</td>
</tr>
<tr>
<td>Viora et al⁷</td>
<td>32</td>
</tr>
<tr>
<td>Fung et al⁸</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>33</td>
</tr>
<tr>
<td>Kuwata and Matsubara¹²</td>
<td>32</td>
</tr>
<tr>
<td>Rosenblatt et al¹³</td>
<td>29</td>
</tr>
<tr>
<td>Ikeda et al¹⁴</td>
<td>32</td>
</tr>
</tbody>
</table>

Abbreviations: BW, birth weight; GA, gestational age; IUVV, intra-abdominal umbilical vein varix.