

diagnosed in the neonatal period [2,3]. PSIV is the torsion of a segment of small intestine without any other abnormalities. Volvulus without malrotation occurs in 19 to 26% of small bowel volvulus, and PSIV affecting ileum during the neonatal period is extremely rare and usually occurs in preterms [4].

The exact cause of PSIV is not clear. Some possible mechanisms include stasis of the bowel content, long, narrow, band-like mesentery, changes in the intraabdominal pressure and hyper-peristalsis, insufficient fixation of the intestines, immoderate initiation of feedings at an early stage of life and abdominal nursing including abdominal wall massage [5,6]. Our patient did not reveal any of these predisposing factors. The differential diagnosis of PSIV includes NEC, spontaneous intestinal perforation, meconium plug syndrome and ileal atresia.

Majority of the previous reports of children with PSIV include preterm neonates and the occurrence of this entity in the neonatal period is extremely rare [5]. Although there are no specific clinical findings revealing PSIV, clinical course of PSIV may involve catastrophic results including massive rectal bleeding causing intractable shock state. We did not observe rectal bleeding in our case but there was clinical evidence of sepsis. In a previous report, of the children with intestinal volvulus, ischemic changes of the affected bowel were seen in 90% of the cases without malrotation as compared to 18% incidence in the cases with malrotation [5]. Colon has the role of a cushion and a fixed cecum results in a tight volvulus while a mobile cecum results in a flexible volvulus. The end result is less severe ischemia and delayed necrosis. It should be kept in mind that extensive intestinal necrosis that may occur in volvulus is one of the three common causes of short

bowel syndrome together with necrotizing enterocolitis and intestinal atresia. A limited segment of ileum was ischemic in our patient. Abdominal cavity was not contaminated and resection of volvulated ischemic intestinal segment with ileo-ileal anastomosis was required in our case.

In conclusion, diagnosis of PSIV is challenging due to the lack of specific clinical and radiologic findings and confirmation of this disease entity is only possible at laparotomy.

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## Colonic Perforation in a Term Newborn with Hereditary Protein C Deficiency

We describe a term infant who experienced recurrent apnea associated with intracranial hemorrhage and later, developed colonic perforation. Plasma protein C activity was below detectable limits and a heterozygous *PROC* mutation was identified. Neonatal colonic perforation is rare, and this case report highlights the importance of considering congenital Protein C deficiency.

Inherited protein C deficiency is a prothrombotic condition caused by homozygous or compound heterozygous defects in the *PROC* gene (2q13-q14). Purpura fulminans, intracranial hemorrhage (ICH), and blindness are the major complications in affected patients. Although heterozygous protein C deficiency is usually of mild severity, it can also cause severe symptoms, especially during the neonatal period.

A 1-day-old female newborn was transferred to our hospital because of recurrent apnea (**Fig. 1**). The baby

was born vaginally at 39 weeks of gestation with a birth weight of 2.7 kg and 1- and 5- minute Apgar scores of 9 and 10, respectively. Her mother had experienced three first-trimester miscarriages prior to the present pregnancy. Her protein C and protein S (PS) levels were relatively low (51% and 70%, compared with reference values of 64-150% and 64-146%, respectively). There was no family history of bleeding or thrombotic disorders.

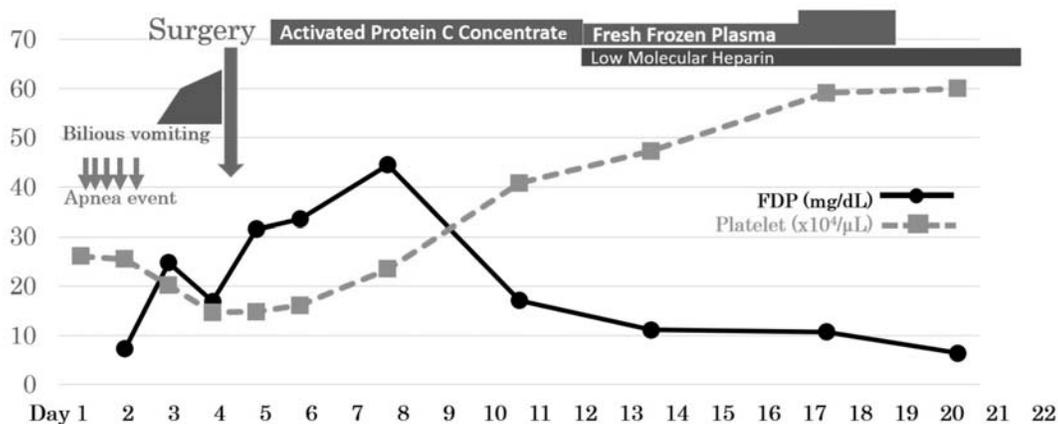
The newborn had normal vital signs and physical examination showed no remarkable findings, including abdominal distension, or skin lesions. Initial evaluations, including a complete blood count with differential, chest-abdominal X-rays and echocardiography, revealed no abnormality. Her apnea events improved over time, and she took her mother's milk every 3 hours. On day 3, she suddenly became lethargic. A brain computed tomography scan showed subarachnoid and posterior fossa subdural hemorrhages. And she experienced repeated bilious vomiting and her abdominal distention progressively worsened. An abdominal X-ray on day 4 showed pneumoperitoneum, suggesting intestinal perforation. Surgical exploration revealed ischemic changes with multiple perforations in the distal transverse colon near the splenic flexure in the anti-mesenteric border. The colon proximal and distal to the area appeared normal, without any features suggestive of necrotizing enterocolitis or Hirschsprung disease. The affected colon was resected, followed by end-to-end anastomosis. A biopsy sample showed normal ganglion cells, with venous congestion and neutrophil infiltration of the mucosa. These findings were compatible with ischemic colitis.

Further examination on day 3 showed plasma protein

C activity below detectable limits (<10%), whereas plasma protein S activity was within normal limits for her age (35%). The patient was started on 600 U/kg/day activated PC (aPC) concentrate (Anact C, Teijin/Chemo-Sero-Therapeutic Research Institute, Tokyo, Japan), for a total of 6 days. She was subsequently switched to fresh frozen plasma with low molecular heparin. Her post-operative course was uneventful and oral feeding was initiated on day 7. Ophthalmological examination on day 9 revealed no bleeding. Anti-coagulation therapy was continued until day 21, when serum concentrations of fibrin degradation products normalized. Follow-up brain magnetic resonance imaging on day 25 showed no evidence of ventriculomegaly, ischemic changes or vascular malformations. Her growth and development were appropriate at follow-up at 3 months. The clinical and diagnostic profile of the patients is depicted in **Fig. 1**.

After obtaining informed consent from her parents, genomic DNA was extracted from the newborn's peripheral blood leukocytes. The coding region of *PROC* (exons 1-9) was amplified by polymerase chain reaction (PCR), followed by direct sequencing of the PCR products. A heterozygous missense mutation was observed in exon 9 (c.1015G>A, p.Val339Met). This mutation was previously reported in Japanese families with PC deficiency [1]. These two vascular events *viz.* intracranial hemorrhage and focal colonic ischemia, were attributed to a decreased level of plasma protein C activity. After starting aPC replacement, followed by anticoagulant therapy, the patient did not develop any other complications.

The initial manifestations of severe protein C deficiency include intracranial thrombosis and



**Fig. 1.** Clinical course of the neonate with hereditary Protein C deficiency.

hemorrhage and/or purpura fulminans, occurring during the first two weeks of life. An increased risk of thrombosis in the fine blood vessels within the germinal matrix is probably associated with a risk of neonatal intracranial hemorrhage. In our patient, intracranial hemorrhage along with the recurrent miscarriage history of her mother strongly suggested the possibility of a thrombotic disorder.

Neonatal colonic perforation is extremely rare. A state of increased coagulability may be a significant factor in the pathogenesis of colonic ischemia [2]. Ischemic perforation in the colon has been reported in an adult patient with antiphospholipid syndrome [3]. Perioperative management of the patient was challenging because of the competing risks of bleeding and recurrent thrombosis. Administration of aPC concentrate seems appropriate for both the treatment and prophylaxis of thrombosis, without increasing the risk of bleeding [4].

It is challenging to screen for inherited protein C deficiency in neonates because their levels are lower than reference levels in adults. It may be useful to compare protein C and protein S levels, a low protein C and protein S ratio may be more diagnostic than low levels alone [5].

In conclusion, this case highlights the importance of recognizing congenital protein C deficiency in early neonates who experience intracranial hemorrhage or colonic perforation.

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## IgG4-related Disease at Rectovesical Pouch Mimicking Inflammatory Myofibroblastic Tumor

Fever of unknown origin frequently remains a diagnostic challenge. Immunological diseases account for about 20- 30% cases of these fevers. We report the case of a boy who presented with high fever for 2 months and was finally diagnosed as a case of IgG4-related disease at the rectovesical pouch.

**Keywords:** *Inflammation, Pyrexia of unknown origin, Positron emission tomography.*

**I**gG4-related disease is an immune-mediated chronic inflammatory condition characterized by tissue infiltration with lymphocytes and IgG4-secreting plasma cells with various degrees of fibrosis [1]. It is

a relapsing–remitting disease associated with a tendency to mass forming, tissue destructive lesions in multiple sites with systemic symptoms like fever and allergies.

A 9-year-old boy presented to us with intermittent fever for 2 months (102<sup>0</sup>-103<sup>0</sup>F, usually 2 peaks/day). Other than mild pallor, systemic examination was normal. Investigations showed hemoglobin of 8.2 g/dL, total leukocyte count 12.4x10<sup>9</sup>/L (Neutrophil 80%, Lymphocyte 10%) with persistently high C-reactive protein (270, 301 and 276 mg/L on three separate occasions done at an interval of 5 days) and elevated platelet count (820x10<sup>9</sup>/L). Serum ferritin was 657 ng/mL (Normal 7-84 ng/mL). Urea, creatinine, serum electrolytes, liver function test, Lactate dehydrogenase, uric acid, procalcitonin, and urine microscopic examination were normal; cultures showed no growth. Scrub typhus, tuberculin skin test, sputum for acid fast bacilli (AFB) and Cartridge based nucleic acid amplification test (CBNAAT), brucella IgM,