Hematochezia in a 36-Hour-Old Well-Appearing Infant

A term male newborn with birthweight of 3,460 g was fed breast milk at one hour after birth, and cow's milk protein-based infant formula at 24 hours. He was found to have visible blood in the stools at 36 hours. Examination revealed stable vital signs, no signs of peritonitis or organomegaly; but multiple large areas of port-wine stain at the left-sided abdominal wall, buttock and pelvic area including left thigh and lower leg. Abdominal radiography and complete blood counts were unremarkable. The physician introduced extensively hydrolyzed formula (EHF), which led to a disappearance of bloody stools in 24 hours. On the fourth day after birth, the infant had fresh blood and mucus in five small-volume bowel movements, although he remained well. Despite an exclusive EHF feeding, bloody stools persisted.

Initial investigations showed leukocytosis with absolute eosinophil count of 1.2×10^9/L, and normal hemoglobin, red blood cell indices, and platelet count. Coagulogram and abdominal radiography were unremarkable. Blood and stool cultures were negative after 48 hours. We decided to perform recto-sigmoidoscopy and found erythematous and slough mucosa with several scattered ulcers. Biopsy showed significant tissue eosinophilia including eosinophilic cryptitis and massive degranulation (**Fig. 1**). Magnetic resonance imaging revealed no gross intrabdominal arteriovenous or lymphatic malformation. After 72 hours of exclusive amino acid formula, bloody stools subsided. At 24 days after birth, breast milk was reintroduced after the mother's strict avoidance of dairy products. Atopic dermatitis on both cheeks was noted. The mother decided to withhold breastfeeding for another two weeks, and then resumed again without bloody stools or rash. He was switched to EHF and regular cow's milk at 15 and 18 months, respectively, which he tolerated well.

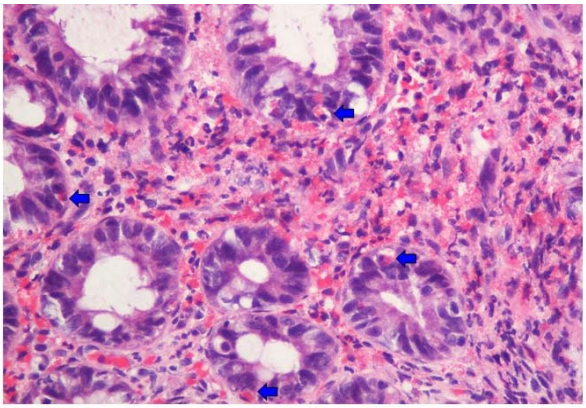

Fig. 1 Rectal biopsy showing prominent eosinophilic infiltrate with significant degranulation of eosinophils in the lamina propria and intraepithelial infiltration (arrows) (HE, 400X).

We made a dignosis of food protein-induced allergic proctocolitis (FPIAP), with the supportive evidence including: *i*) improvement after removal of dairy products in the lactating mother and change of cow's milk-protein infant formula to EHF; *ii*) data from endoscopy and histopathology suggestive of this condition; and, *iii*) tolerance developed at a young age. However, this case did not undergo an initial cow's milk challenge to confirm the diagnosis due to a high level of caregiver concern. Furthermore, we also performed MRI of the abdomen to rule out vascular malformation in the gastrointestinal tract that can also cause significant hema-tochezia, especially in an infant with multiple port-wine stains in the lower extremity. Kumar, et al. [1] reported three cases of full-term newborns that were introduced cow milk within the first hour after birth and presented with bloody stool at the age of 25-28 hours. Friable and edematous colonic mucosa with tissue eosinophilia in the lamina propria were also noted in all cases, which also improved after a switch to EHF [1]. Another series by Kaya, et al. [2], which included 60 patients, revealed that the youngest age of onset of FPIAP was seven days. We believe that cow milk protein in the breast milk of lactating mother may induce symptoms in the newborn during the first week of life. Matangkasombut, et al. [3] demonstrated that beta-lactoglobulin can be detected in breast milk up to seven days after cow milk ingestion. Faber, et al. [4] reported a preterm newborn with a proposed diagnosis of FPIAP that responded well to a switch to amino acid formula. However, we believed that the switch from EHF to amino acid formula in our case may be quite premature, as per the recently established protocols [5]. Studies hypothesized that early development of lower gastrointestinal bleeding derives from in utero food-antigen sensitization, which is likely caused by the passage of IgG across placenta during the third trimester [6].

FPIAP can occur shortly after birth and should be in the differential diagnosis of a newborn presenting with bloody stools. Histopathological finding of tissue eosinophils in the rectosigmoid biopsy may provide useful data. Appropriate dietary avoidance of the triggering antigen with a proper wait-and-see duration is the mainstay management of this condition.

JIRACHART PHROMMAS, PORNTHEP TANPOWPONG,*
CHATMANEE LERTUDOMPHONWANIT
Division of Gastroenterology, Department of Paediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.
**pornthep.tan@mahidol.ac.th*

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Juvenile Dermatomyositis With Macrophage Activation and Severe Encephalopathy

Central Nervous System (CNS) involvement is rarely reported, and is possibly an under-recognized feature in juvenile onset inflammatory myositis. We report a 11-years-old boy with juvenile dermatomyositis (JDM) who was initiated on steroid and methotrexate but developed macrophage activation syndrome (MAS). He recovered from MAS but continued to have persistent severe CNS disease.

An 11-year-old boy presented with 3 weeks history of weakness of both upper and lower limbs, difficulty in swallowing, speaking and mild periorbital swelling with reddish discoloration around the eyes suggestive of heliotrope rash. Investigations showed elevated muscle enzymes, characteristic muscle edema on magnetic resonance imaging (MRI) and electromyography revealed a myopathic pattern in both lower limbs. Myositis specific antibody profile (anti Jo-1, anti TIF1 gamma, anti NXP2, anti MDA5) was sent but values were within normal range. The child was diagnosed with definite JDM as per EULAR/ACR criteria with a total aggregate score of 7.5, and he was initiated on intravenous methylprednisolone at 30 mg/kg/day for 3 days followed by oral prednisolone (2 mg/kg/day) and weekly subcutaneous methotrexate (15 mg/m^2).

Within a week of completing pulse methylprednisolone, he developed shallow respirations due to respiratory muscle weakness, with profuse mucosal bleeding from the oral cavity and progressive drowsiness. He was transferred to the pediatric intensive care unit (PICU); intubated and ventilated. Investigations showed pancytopenia with high serum ferritin (4059 ng/mL) suggestive of MAS. Methotrexate was stopped; pulse doses of methylprednisolone 30 mg/kg/day were restarted and a single dose of 10 g of intravenous immunoglobulin (IVIg) was given. As child did not improve after 3 days of pulse methylpredni-solone; oral cyclosporine (4 mg/kg/day) was added. Over the next 3 days, blood counts improved with lowering of ferritin level (1800 ng/mL). On the day-10 of PICU admission, he started having refractory generalized seizures which were controlled by antiepileptics. MRI brain showed acute ischemic lesions in bilateral parieto-occipital, right posterior temporal and left hippocampal region and features of posterior reversible encephalopathy syndrome (**Fig. 1**). Tracheostomy was done in view of need for prolonged intubation. He recovered from MAS but later developed fever; bronchoalevolar lavage culture grew *Stenotrophomonas maltophilia*, for which appropriate antibiotics were started and cyclosporine was stopped.

Over the subsequent 4 weeks, fever subsided but he remained drowsy with episodic abnormal limb movements. Repeat MRI brain showed extensive brain atrophy with multiple white matter hyperintensities in bilateral frontal regions. Since, he continued to have persistent mucosal bleeds with normal coagulation studies and blood counts, vasculopathy was consi-dered as the possible etiology and the persistent encephalopathy in the absence of any other explanation was ascribed to underlying CNS vasculopathy. MR angiography of cerebral arteries showed no obvious abnormality. CSF examination was not done in view of poor general condition.

Considering CNS vasculopathy, four pulses of cyclophosphamide (750 mg/m^2) were started monthly and two doses of rituximab, (750 mg/m^2) at 15 days interval. With gradual improvement, we started tapering the prednisolone dosage and the tracheostomy tube could be removed after 3 months. After five months of hospitalization, he was discharged and remains stable and ambulatory on tapering doses of prednisolone.

No data is available regarding the incidence of MAS and CNS vasculopathy in JDM. Ramanan, et al. [3] reported two children with JDM who later developed CNS manifestations, and were diagnosed to have a possible cerebral vasculopathy. One child

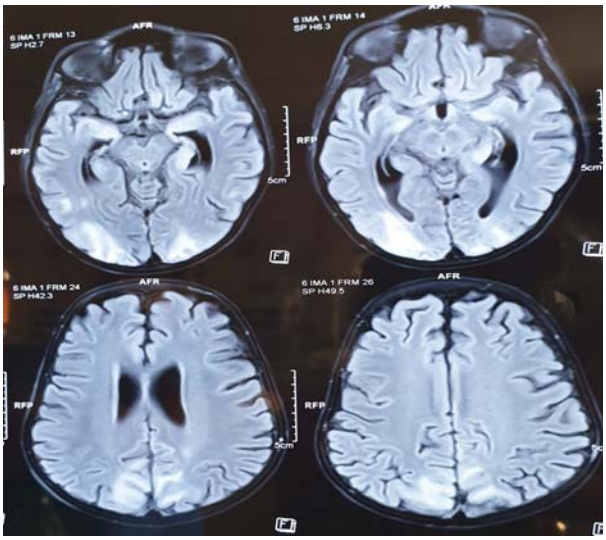

Fig. 1 Axial flair plain MRI brain showing white matter hyperintensities involving bilateral parieto-oocipital and inferiomedial temporal lobes suggestive of ischemia.