Clinical Pathology Selected Abstracts, 6/13

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Confirmed Ehrlichia ewingii infection likely acquired through platelet transfusion

Ehrlichiosis is a tick-borne disease that may be asymptomatic or result in fatal sepsis. Ehrlichiosis transmitted from transfusion of blood products has not been documented. A case report of a 9-year-old Georgia boy with a history of acute lymphoblastic leukemia is the first report of Ehrlichia ewingii infection transmitted by a platelet transfusion. The authors first describe the patient as presenting to the hospital with complaints of fever, fatigue, malaise, vomiting, diarrhea, and petechial rash. Cultures were performed and broad-spectrum antibiotics started. But despite the antibiotic therapy, the patient's clinical status deteriorated, with worsening neutropenia, thrombocytopenia, and elevated liver enzymes. The hospital laboratory identified morulae in granulocytes on a peripheral smear on day 11 of hospitalization. The patient was started on doxycycline, and the Mayo Clinic and Centers for Disease Control and Prevention confirmed positivity for E. ewingii via real-time polymerase chain reaction testing. The family denied tick exposure or recent outdoor activity. However, the patient had a history of three transfusions of leukoreduced and irradiated platelets in one month. Trace-back investigations were conducted on all three donors. The donors reported feeling well at the time of donation, although one donor gave a history of a tick bite. The donor with tick exposure was positive for Ehrlichia species with an IgG titer of one per 512. Of interest, this was the first confirmed case of this type of Ehrlichia species to be transmitted through a blood transfusion. The authors noted that E. ewingii is a rarely reported species and that this case reinforces that it is possible for infected blood donors to be asymptomatic. Blood screening questions do not address tick exposures, and screening all donated blood products for Ehrlichia by PCR is cost-prohibitive, with no data to support its utility. The authors concluded that suspicion of a transfusion-transmitted disease should include Ehr-lichia in the differential so prompt therapy can be initiated.

Regan J, Matthias J, Green-Murphy A, et al. A confirmed *Ehrlichia ewingii* infection likely acquired through platelet transfusion [published online ahead of print March 19, 2013]. *Clinical Infect Dis.* doi:10.1093/cid/cit177.
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Transfusion strategies for acute upper gastrointestinal bleeding

Restricted transfusion strategies may be indicated in situations where hemorrhage is not too severe. Controlled trials have shown that for critically ill patients, a restrictive transfusion strategy is at least as effective as a liberal strategy. However, these trials excluded patients with gastrointestinal (GI) bleeding. The authors performed a randomized control trial in which they assessed whether a restrictive threshold for patients with acute GI bleeding was safer and more effective than a liberal strategy based on recommended guidelines. They enrolled patients in their trial from June 2003 through December 2009. The patients had upper GI bleeding defined as hematemesis, melena, or both. The patients were randomized to receive either the restrictive transfusion strategy, with a hemoglobin threshold for transfusion of 7 g/dL, or a liberal transfusion strategy, with a hemoglobin threshold for transfusion of 9 g/dL. In both groups, one unit of red blood cells was transfused. The primary outcome measure was the rate of death from any cause within the first 45 days. Secondary outcomes included the rate of further bleeding and the rate of in-hospital complications. The authors noted that 225 of the 461 patients assigned to the restrictive strategy (49 percent) did not receive transfusions as compared with 65 of 460 assigned to the liberal strategy (14 percent). Furthermore, the probability of survival at six weeks was higher in the restrictive strategy group than in the liberal strategy group. The authors concluded that the restrictive strategy significantly improved outcomes in patients with acute upper GI bleeding as compared with the liberal transfusion strategy. The outcomes included risk of further bleeding, rate of complications, need for rescue therapy, and rate of survival.

Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. *N Engl J Med.* 2013;368:11–21.
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Urine proteomics and diagnostic markers of Kawasaki disease

Kawasaki disease, or mucocutaneous lymph node syndrome, presents as a systematic vasculitis in children. Its etiology is unknown. Children with Kawasaki disease (KD) may have prolonged fever, inflammation of the oral mucosa, conjunctivitis, rash, extremity changes, and cervical lymphadenopathy. The incidence in American and European populations is about one in 10,000, but it may be as high as one in 100 in Japan. Kawasaki disease is the most common cause of acquired heart disease in the developed world, and diagnosis may be elusive since KD tends to mimic many other childhood illnesses. No definitive diagnostic test exists for early identification of KD. Investigators at Boston Children's Hospital sought to identify unique markers for KD using high-accuracy mass spectrometry proteomics to analyze clinical urine specimens from patients with the disease. More than 2,000 unique proteins were analyzed. The authors found that the urine proteomes of patients with KD were enriched for cellular injury markers such as filamin and talin, immune regulators such as complement regulator CSMD3, immune pattern recognition receptor muclin, and immune cytokine protease meprin A. Significant elevations of filamin C and meprin A were detected in the serum and urine in two independent cohorts of patients with KD. Meprin A and filamin C also showed superior diagnostic performance in a blinded case-control study of patients with KD. The authors concluded that meprin A and filamin C showed particular promise as diagnostic markers based on receiver operating characteristic analysis. They stated that this discovery may lead to improved diagnosis and classification of children with KD and the development of novel therapeutic agents.

Kentsis A, Shulman A, Ahmed S, et al. Urine proteomics for discovery of improved diagnostic markers of Kawasaki disease. *EMBO Mol Med.* 2012;4:1–11.
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Acute silent cerebral ischemic events in children with sickle cell anemia

Sickle cell anemia is the most common cause of overt stroke in children. Interventions, such as using transcranial Doppler ultrasonography screening to guide chronic transfusion therapy, has helped reduce the incidence of such strokes. However, despite transfusions, silent cerebral infarction (SCI) still occurs and is more common than stroke. SCI is not associated with motor or sensory impairment but results in neurocognitive deficits, which leads to poor school performance and increased risk for subsequent overt stroke. The authors proposed in this study that the recurrent and potentially reversible ischemia that occurs in many organ systems in sickle cell anemia may also occur in the brain. They conducted a study to determine if acute silent cerebral ischemic events (ASCIEs) could be detected in the asymp-
tomatic baseline state and were frequent and possibly transient. The investigators measured and compared the incidence of ASCIEs and progressive SCI in a group of children screened for SCI in the Silent Cerebral Infarct Transfusion trial. They also examined the clinical circumstances just prior to ASCIEs to help understand their causes. The authors studied 966 magnetic resonance imaging (MRI) scans from 732 children who were a mean age of 9.5 (standard deviation, 2.4) years and the majority of whom were male (51 percent) and had homozygous sickle cell anemia (93 percent). This group was further subdivided into ASCIE and SCI MRI groups to calculate incidence rates. The results showed that ASCIEs were detected on 1.3 percent of MRIs in 652 children, for an incidence of 47.3 events per 100 patient-years. Of the two of 10 children who had followup MRIs of the brain after ASCIEs, only one had a silent cerebral infarction in the same location as the ASCIE. Furthermore, the incidence of ASCIEs was statistically significantly higher than the incidence of progressive SCI. The authors concluded that children with sickle cell anemia have ongoing cerebral ischemia far more frequently than previously predicted. Furthermore, consideration of only easily visualized and permanent brain lesions, such as stroke and MRI, will miss the threat of ischemic injury in symptomatic children. The authors recommend further research to better understand the causes of ASCIEs and their treatment options.

Quinn CT, McKinstry RC, Dowling MM, et al. Acute silent cerebral ischemic events in children with sickle cell anemia. *JAMA Neurol.* 2013;70:58–64.
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