Background: A 2 month old boy presented to our institution after a 1 month hospitalization in Japan. He was admitted there, several weeks after his unremarkable term birth to an AB Rh positive woman, with lethargy, failure to thrive, bloody mucoid stools with eosinophilia, and an elevated serum white count. He was found to be anemic and thrombocytopenic and required multiple transfusions. Additionally, he had a diffuse, scaling, erythematous rash over his inner thighs and abdomen (Figure 1a).

Methods: Records received with the patient included English and Japanese-language reports, and the suspected diagnosis at the outside institution was not known. Initial workup was suspicious for an allergic / necrotizing enterocolitis. The patient had an elevated LDH and potassium, and concern was raised for leukemia with possible tumor lysis syndrome. Standard panels of flow cytometric studies performed at our institution showed no increase in blasts, and a nonspecific finding of increased CD4:CD8 T-cell ratio (Figure 2). The baby’s antibody screen performed at our institution was positive and anti-E was identified. In addition, AHG testing was positive using polyspecific (anti-IgG; -C3d), anti-IgG and anti-complement (anti-C3b; -C3d) reagents. His RBC antigen phenotype was positive for E, e, and C antigens.

Concern for hemolytic disease of the newborn due to maternal anti-E was raised as was the possibility of passive transfer of anti-E from administered blood products. However, records review confirmed the maternal antibody screen was negative, and confirmed he had been transfused with antibody-negative units. Further workup revealed no infection or hematologic proliferation. Biopsy of his rash showed spongiotic dermatitis (Figure 1b). His clinical course deteriorated, and he developed hepatomegaly and jaundice. A concern for Wiskott-Aldrich syndrome was raised, and workup showed normal immunoglobulin levels, but with elevated IgE (15270 kU/l; RR: 0.2-9). Anti-platelet antibodies were identified. Three days after admission, testing was sent for genetic alterations of FOXP3, while simultaneously a Japanese-speaking physician at our institution was located and asked to interpret a figure of FOXP3, while simultaneously a Japanese-speaking physician at our institution was located and asked to interpret a figure of FOXP3, while simultaneously a Japanese-speaking physician at our institution was located and asked to interpret a figure of FOXP3, while simultaneously a Japanese-speaking physician at our institution was located and asked to interpret a figure of FOXP3, while simultaneously a Japanese-speaking physician at our institution was located and asked to interpret a figure of FOXP3. While rare, the presentation of a neonatal patient with a positive antibody screen and DAT with a negative maternal workup is cause to consider possible autoimmune diseases, including IPEX. The FOXP3 protein is a transcription factor which directly binds to the forkhead DNA binding domain protein, a "master regulator" of tTreg development and function. FOXP3 plays a critical role in the maintenance of regulatory T cells (tTregs) by inhibiting the expression of effector T-cell genes, including cytokines essential for immune responses. Mutations in this gene, located at Xp11.23, result in IPEX syndrome, a rare and severe disorder characterized by polyclonal lymphopenia, enteropathy, X-linked thrombocytopenia, and autoimmunity. IPEX is an autosomal recessive disorder caused by mutations in the FOXP3 gene, which encodes a transcription factor that is essential for the maintenance of regulatory T cells. Mutations in FOXP3 lead to loss of function, resulting in the dysregulation of immune responses and the development of autoimmune diseases. The clinical presentation of IPEX syndrome is highly variable, and can range from mild to severe, with varying degrees of severity in different cases. Common features of IPEX syndrome include autoimmune enteropathy, liver abnormalities, and immune dysregulation. The diagnosis of IPEX syndrome is typically made based on clinical presentation and laboratory findings, and can be confirmed by genetic testing. Treatment options for IPEX syndrome are limited and depend on the severity of the disease and the specific manifestations. The mainstay of treatment is the use of immunosuppressive agents to reduce the severity of inflammation and prevent complications. However, the long-term prognosis of IPEX syndrome remains poor, and the development of novel therapies is urgently needed to improve outcomes for patients with this disorder. While rare, the presentation of a neonatal patient with a positive antibody screen and DAT with a negative maternal workup is cause to consider possible autoimmune diseases, including IPEX. The neonate was transferred to an outside institution as a stem cell transplantation candidate and the subsequent clinical outcome is unknown.