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Cytomegalovirus-related thrombocytopenia in two immunocompetent siblings following vertical transmission through Breast milk

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Dear Editor,

Thrombocytopenia in infants is uncommon and is most often reported following vaccination or viral infections, including cytomegalovirus (CMV).[1]. CMV infection is typically asymptomatic in immunocompetent hosts; however, it has been reported to cause thrombocytopenia either through the development of anti-platelet antibody-mediated immune thrombocytopenia (CMV-related ITP) or by directly infecting megakaryocytes (CMV-induced thrombocytopenia).[1,2]. Differentiating between these two forms is clinically relevant but can be challenging. CMV infection in infancy may result from vertical transmission from the mother via prenatal, intrapartum, or breast milk routes.[3]. We describe two siblings with CMV-related ITP following vertical transmission of CMV through breast milk.

A 5-month-old female was well until four days before admission when she developed fever and diarrhea. The fever subsided quickly, but she subsequently exhibited generalized petechiae and ecchymosis over her trunk and lower extremities. Laboratory evaluation revealed thrombocytopenia with a platelet count of 11 x 10^9/L, while her white cell counts and hemoglobin levels were within normal ranges. She had a poor response to intravenous immunoglobulin (IVIG) treatment, with her platelet count dropping to 8 x 10^9/L after therapy. However, her platelet count responded well to oral prednisolone. A work-up for immune thrombocytopenia revealed CMV positivity in the urine via shell vial assay, and her platelet counts returned to normal afterward.

Three years later, her younger brother presented to our hospital at one month of age with the abrupt onset of generalized petechiae, but without any preceding infection symptoms. His platelet count was 7 x 10^9/L. After two days of IVIG therapy, his platelet count increased to 58 x 10^9/L, and one week later, it reached 337 x 10^9/L. Laboratory investigations revealed positive results for CMV-IgM and a urine CMV culture. Given consecutive siblings with CMV infection, we checked maternal status. She had no symptoms of CMV infection and the CMV PCR testing was positive on breast milk but negative on blood. He had no hearing impairment and his platelet counts remained normal during follow-up, even though he continued breast-feeding afterward.

The seroprevalence of CMV among childbearing women and children is high in Taiwan.[4,5]. However, the number of children who develop ITP directly after a CMV infection is small, suggesting that additional factors are crucial in the development of anti-platelet antibodies. Most infants with ITP experience only transient thrombocytopenia, indicating that anti-platelet antibodies eventually resolve when the CMV viral antigen is cleared. Based on their response to therapy, our two patients likely had CMV-related ITP rather than CMV-induced thrombocytopenia. The siblings may share the same genetic predisposition to developing transient autoantibodies following exposure to the same antigen. We speculated that they have a genetic predisposition to losing immune tolerance after exposure to the same molecular mimicry of CMV antigens. Our observation provides evidence that immunocompetent infants are still at risk of mother-to-infant CMV transmission. Furthermore, the presentation of specific pathogen-derived peptides (the same CMV strand antigens from the mother's breast milk) can induce anti-platelet antibodies in patients with the same genetic predisposition to loss of immune tolerance.[1,3,4].

CRediT authorship contribution statement

Yuan-Ning Yang: Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Yung-Chieh Lin:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Chao-Neng Cheng:** Writing – review & editing, Writing – original draft, Supervision, Formal analysis, Data curation, Conceptualization.

Patient consent statement

The patient's guardian provided written consent for treatment and publication.

Ethical approval statement

This study has been approved by the Institutional Review Board of National Cheng Kung University Hospital (A-ER-111-141).

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Declaration of competing interest

All authors declare no conflicts of interest.

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