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Thrombocytopenia in a nutshell

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In January, 2009, a 70 year old man was referred to us because a blood count done after a night of nausea, vomiting, and fever showed a platelet count of $32 \times 10^9/L$. He had no previous history of thrombocytopenia or haemorrhagic diathesis and did not take medications or quinine-containing beverages. 4 days later, the platelet count was normal, and we believed that the low platelet count might be a result of laboratory error. 8 months later, his symptoms recurred and, again, the platelet count ($37 \times 10^9/L$) was low. Other blood values were normal and his platelet count returned to normal in a few days. At this time, our patient recalled eating walnuts before each thrombocytopenic episode, suggesting a possible connection between his complaints and the consumption of walnuts. To test this hypothesis, an in-hospital walnut challenge was undertaken. Our patient's initial platelet count was $233 \times 10^9/L$. He ate 100 g of walnuts at 1700 h and after 4 h developed a fever (temperature $38.7^\circ C$), nausea, and vomiting. No other physical or systemic symptoms, such as rash, angio-oedema, or hypotension, occurred. The nausea and fever resolved during the next 8 h, but he bled from an existing small wound and developed large haematomas at venepuncture sites. His platelet count, measured 15 h after walnut ingestion, was $4 \times 10^9/L$; haemoglobin concentration and white cell count were normal. IgE antibodies specific for tree nuts were not detected. As in previous episodes of thrombocytopenia, the platelet count became normal within 4 days (figure).

The rapid improvement in platelet count after each episode suggested that the thrombocytopenia might have been caused by a platelet-reactive antibody specific for a substance present in walnuts. We studied new blood samples collected when the platelet count was normal. Strong (titre 1 to 32) IgG antibodies were detected in our patient's serum by flow cytometry;¹ they reacted with platelets when a saline extract made from ground English walnuts (*Juglans regia*) was present. Similar activity was not detected in normal control serum samples. His antibody did not react with platelets from a patient with Glanzmann's thrombasthenia lacking the platelet surface $\alpha IIb/\beta IIIa$ integrin. The findings

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RA and CD looked after the patient. RA, HJV, LP, WD, RHA, and CD wrote the report. HJV, BRC, LP, and RHA did the laboratory work. Consent to publish was obtained.

provided strong evidence that our patient's thrombocytopenic episodes were caused by an IgG antibody that reacted with α IIb/ β IIIa integrin when a soluble substance from walnuts was present. He excluded nuts from his diet and at last follow-up in May 2010, he had had no further symptoms.

Many medications are known to cause immune thrombocytopenia, but convincing reports of this complication triggered by foods and beverages are rare. Examples reported were associated with consumption of an African bean,² sesame seeds,³ cranberry juice,⁴ cow's milk, and Jui (a Chinese herbal medicine).⁵ To the best of our knowledge this is the first case in which a patient reported systemic symptoms and in which a platelet-reactive antibody specific for a substance present in the implicated food was identified. With these findings and the positive provocation test, our patient's case met all criteria for establishing a causal association between exposure and thrombocytopenia:⁵ exposure to walnuts resulted in acute thrombocytopenia that rapidly recovered to normal; and no other cause for thrombocytopenia was identified. The provocation test led to profound thrombocytopenia, systemic symptoms, and bleeding, albeit followed by rapid recovery. In retrospect, we should have begun the challenge with a smaller dose of walnuts. Our patient's case shows the clinical importance of product induced thrombocytopenia and its distinction from other more common causes.

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Figure.
Changes in platelet count after exposure to walnuts