

The unsuspected danger of strawberries: Severe thrombocytopenia during pregnancy

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World Journal of Biology Pharmacy and Health Sciences, 2025, 21(03), 657-660

Publication history: Received on 17 February 2025; revised on 29 March 2025; accepted on 31 March 2025

Article DOI: <https://doi.org/10.30574/wjbphs.2025.21.3.0342>

Abstract

Background : Immune thrombocytopenia (ITP) is a disorder marked by an immune-mediated response affecting platelet's destruction or production. While it is extremely rare, some fruits such as strawberries, can potentially contribute to thrombocytopenia usually due to an allergic reaction. The mechanism likely involves an immunoallergic response, where specific fruit antigens stimulate the production of platelet antibodies and generate low platelet count in the blood. During pregnancy, the immune system undergoes significant adaptations, potentially heightening susceptibility in individuals with underlying immunologic disorders.

Case description : We report novel and particular case of severe ITP in a pregnant woman triggered by strawberry consumption in the context of quiescent adult-onset Still's disease (AOSD). The patient presented with epistaxis, itching and ecchymoses temporally linked to strawberry ingestion. Laboratory findings confirmed severe thrombocytopenia and positive platelet antibodies, supporting an immunoallergic mechanism. Other causes were excluded. Treatment included corticosteroids (CSs), azathioprine (AZA) and dietary avoidance, leading to complete recovery.

Conclusion : This original case is both interesting and enigmatic, raising awareness of the immunoallergic investigations's contribution to diagnostic and therapeutic decisions.

Keywords: Strawberries; Platelet; Allergy; Severe thrombocytopenia; Still's disease; Pregnancy; Corticosteroids; Azathioprine

1. Introduction

Adult-onset Still's disease (AOSD) refers to systemic juvenile idiopathic arthritis emerging after the age of 16 (1). It is an autoinflammatory syndrome characterized by spiking fever, evanescent maculopapular rash, arthritis and leukocytosis (2). The prognosis varies widely, from mild, self-limiting cases to severe outcomes like chronic destructive polyarthritis or life-threatening complications, especially with visceral involvement or reactive hemophagocytic lymphohistiocytosis (3).

Immune thrombocytopenia (ITP) encompasses a diverse range of conditions marked by autoimmune-driven platelet destruction or/and their compromised production. ITP can be primary arising without a clear underlying cause or secondary to various associated conditions (4). Severe thrombocytopenia is defined as a platelet count below 20,000/ μ L, posing a high risk of life-threatening bleeding. While thrombocytopenia in pregnancy is commonly attributed to gestational and autoimmune conditions, this case highlights a rare and previously unreported association

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between strawberry consumption and the onset of severe ITP in a pregnant woman at 20 weeks of amenorrhea, despite her quiescent AOSD.

1.1. Key Points

- This case highlights a rare association between strawberry allergy and severe ITP during pregnancy.
- The diagnosis was supported by the temporal link to strawberry consumption, positive platelet antibodies, and exclusion of other causes.
- Prompt treatment with corticosteroids (CSs) and azathioprine (AZA), along with strawberries avoidance, led to full recovery.
- This observation underscores the importance of considering dietary triggers in thrombocytopenia, especially in pregnant patients with immune-mediated conditions.

2. Case presentation

2.1. Patient History

A 29-year-old pregnant woman at 20 weeks of gestation, with a history of AOSD since the age of 24, was admitted for isolated bilateral epistaxis of moderate severity. During the interview, she reported that the bleeding coincided with the consumption of strawberries and was accompanied by itching. No use of anticoagulants, antiplatelet agents, or other medications was identified. Her medical history included quiescent AOSD, with no prior episodes of thrombocytopenia or allergic reactions to strawberries or other foods.

2.2. Clinical Findings

On admission, the patient appeared pale, hypotensive (100/50 mmHg), with a *Glasgow Coma Scale (GCS)* of 15/15, eupneic (19 breaths/min), tachycardic (101 beats/min), and afebrile (36.9°C). Cutaneous examination revealed recent ecchymoses of varying sizes, predominantly on the lower limbs, with no evidence of skin rash. Abdominal examination showed no hepatomegaly or splenomegaly. Further evaluations for associated bleeding, including oral, ocular, gynecological, and Ears, nose and throat (ENT) examinations, were unremarkable, ruling out lesions, tumors, or other sources of bleeding. Joint examination revealed no signs of arthritis or joint pain.

2.3. Paraclinical Findings

Emergency blood tests revealed mild anemia (hemoglobin: 11 g/dL) and severe thrombocytopenia ($<10,000/\text{mm}^3$), confirmed on a citrated tube. Blood smear showed reduced platelet count with anisocytosis but no schizocytes or dacryocytes. Coagulation studies were normal, with no hypofibrinogenemia, prolonged prothrombin time (PT), or elevated D-dimers. C-reactive protein (CRP) was normal (3.6 mg/L), ferritin was also normal (68 ng/mL), and triglycerides were 1 g/L. Serologies for Human immunodeficiency virus (HIV1/2), Cytomegalovirus (CMV) IgM and IgG and Epstein-Barr virus (EBV) IgM and IgG were negative. Liver enzymes and renal function were normal. Platelet antibody testing targeting GPIa-IIa, GPIIb-IIIa, and GPIb-IX was positive for all three. Due to medical ethics and the lack of necessity, neither prick tests nor specific IgE measurements were performed, given their potential risks and limited reliability during pregnancy.

2.4. Diagnostic Approach

The diagnosis of severe ITP secondary to strawberry allergy was established based on the temporal association between strawberry consumption and the onset of symptoms (itching, ecchymoses, bilateral epistaxis), positive platelet antibody testing, and the exclusion of other potential causes such as infections, autoimmune diseases, or medication-induced thrombocytopenia. The absence of other bleeding sources and the rapid response to treatment including trophallergen avoidance and CS therapy further supported this diagnosis.

2.5. Management

After an immediate cessation of strawberry consumption, the patient received 3-day course of methylprednisolone (1 g bolus) followed by oral prednisone (60 mg/day for 1 month, then tapered). AZA (150 mg/day) was initiated as maintenance therapy. Following treatment, the patient showed excellent recovery, with complete resolution of epistaxis and normalization of platelet counts.

3. Discussion

The incidence of food allergies has risen significantly, with approximately 3–4% of adults and 6% of children (5). ITP linked to strawberry allergy involves a complex interplay of immunological mechanisms, primarily driven by immune dysregulation and cross-reactivity. Strawberry allergens, which the immune system mistakenly identifies as harmful, trigger an allergic response characterized by the release of histamine and other inflammatory mediators. This response can lead to symptoms ranging from mild itching and swelling to severe systemic reactions (6). In ITP, the immune system produces autoantibodies that target platelet surface glycoproteins especially GPIIb/IIIa leading to their premature destruction in the spleen and liver (7).

The pathophysiology may involve molecular mimicry (8), where strawberry proteins such as « Fra a » share structural similarities with platelet antigens, causing cross-reactive antibodies to bind to platelets and mark them for destruction by macrophages (9,10). Food allergies are characterized as harmful immune responses to specific foods, categorized into three main types (IgE-mediated, non-IgE-mediated and mixed reactions) (11). Additionally, the Th2-skewed immune response typical of allergies, characterized by elevated IL-4 and IL-10, can exacerbate autoimmune tendencies by reducing regulatory T cell (Treg) activity and promoting autoreactive B cell production of antiplatelet antibodies (12,13). Complement activation during severe allergic reactions further accelerates platelet clearance by opsonizing them for phagocytosis (14). Notably, pregnancy alters the immune system to support fetal development, often promoting a Th2-dominated anti-inflammatory state. This can increase the mother's susceptibility to allergic disorders due to hormonal changes and immune tolerance mechanisms (15). While analogous cases of food-induced thrombocytopenia due to walnuts, cranberry juice and herbal teas were reported (16,17,18), it has not yet documented cases of severe ITP secondary to strawberry allergy revealed during pregnancy, which makes our observation particularly original. Admittedly, various immunological and inflammatory mechanisms inducing thrombocytopenia have been described in the context of food allergies. However, the complex association of various conditions in our patient remains ambiguous. This unique situation raises intriguing questions about the interactions between immune response and strawberries, providing a valuable opportunity to further our understanding of autoimmune diseases and allergic reactions. It is undeniable that AOSD can cause immune-mediated thrombocytopenia through mechanisms like ITP. Whereas, this manifestation occurs when the activity's disease is important. In our case report, the quiescence of AOSD was clinically and biologically confirmed.

The therapeutic management of any food allergy consists first of all in the elimination of the allergen responsible. In severe cases of anaphylaxis, the emergency administration of epinephrine can be life-saving (19). Additionally, adjunctive therapies may involve the use of H1-antihistamines, bronchodilators and CSs (20). In our patient, given the severity of the clinical-biological picture, the immunoallergic mechanism of thrombocytopenia, the underlying terrain of AOSD and pregnancy, we opted for the association of CS therapy and AZA. The results of this combination have been encouraging.

4. Conclusion

Severe ITP secondary to strawberry allergy occurring during pregnancy in the context of inactive AOSD is a unique condition that has never been reported in literature. Our case represents an original illustration requiring appropriate medical attention to manage symptoms and prevent hemorrhagic complications. By shedding light on this unprecedented case, we hope not only to enrich the existing literature but also to pave the way for future research on both clinical and therapeutic implications of this complex association.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Sources of funding

This study was not supported by any institution or company.

Statement of ethical approval

All procedures performed in this study are in accordance with the ethical standards of the institutional and/or national research committee.

Statement of informed consent

Written informed consent was obtained from the patient for publication of this case report.

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