

[ CASE REPORT ]

## Thrombocytopenia Caused by a Tea Beverage of *Taxus yunnanensis* (Chinese Yew)

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### Abstract:

A 53-year-old woman presented at our hospital due to nasal bleeding and petechiae with profound thrombocytopenia ( $0.4 \times 10^9/L$ ). Her platelet count returned to the normal range immediately following a platelet transfusion. In this case, tea brewed from *Taxus yunnanensis* was the only suspected agent ingested prior to the onset of thrombocytopenia while all other etiologies for thrombocytopenia were excluded. A re-exposure test to *Taxus yunnanensis* resulted in the recurrence of acute thrombocytopenia. The association of thrombocytopenia with substances other than drugs has so far only been rarely described and to the best of our knowledge, this is the first reported case of thrombocytopenia caused by *Taxus yunnanensis*.

**Key words:** thrombocytopenia, *Taxus yunnanensis*, challenge test

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### Introduction

Thrombocytopenia is a well-recognized adverse effect of many drugs. However, the association of thrombocytopenia with substances other than drugs has so far only been rarely described (1-6), except for reports of thrombocytopenia caused by quinine-containing beverages (7-9). Because patients often do not recognize that they are ingesting substances that may cause thrombocytopenia, it is sometimes difficult to identify these causative substances. However, it is important to investigate these substances to avoid unnecessary medical treatment. We herein report a case of thrombocytopenia in a patient taking a tea brewed from *Taxus yunnanensis* (Chinese yew), which is commercially available as a health beverage.

### Case Report

A 53-year-old woman presented at our hospital in May 2017 due to nasal bleeding and petechiae on her lower legs. She had been diagnosed with rheumatoid arthritis 15 years previously, but had never undergone any treatment. She also reported that she was not taking any other drugs at that

time. She had no history of a bleeding diathesis or any other hematologic abnormality. On examination, she had multiple oral petechiae and hemorrhaging as well as, extensive purpura on her lower legs. There were no other physical findings. The laboratory findings showed profound thrombocytopenia ( $0.4 \times 10^9/L$ ) with anemia and normal white cell count with normal differentiation. Chronic inflammation by arthritis was suspected as the cause of anemia. A chemistry panel and coagulation screen did not show any characteristic abnormalities except for an elevated C-reactive protein (CRP) level due to the rheumatoid arthritis (Table) and there was no evidence of recent viral infection. Testing for platelet-associated immunoglobulin G (PAIgG) showed 299 ng/ $10^7$  platelets (normal range 9-25). Bone-marrow aspiration showed no evidence of hematological disease and normal megakaryocytes, both in number and morphological appearance. She responded to platelet transfusion ( $4.0 \times 10^9/L$  one hour after transfusion) and her platelet count increased to  $5.5 \times 10^9/L$  on the next day without other specific treatment. Her platelet count reached the normal range on the fourth day of hospitalization and she was discharged home (Fig. 1).

Ten days after discharge, she was re-admitted to our hospital due to epistaxis and petechiae, again with a platelet

count of  $0.4 \times 10^9/L$ . Again, her platelet count recovered after platelet transfusion without any other therapy (Fig. 1). Closer examination revealed that she had started consuming tea brewed from *Taxus yunnanensis* (Chinese yew: Hongdoushan™) 10 days before her initial admission, which is commercially available as a health beverage in Japan. She had taken this tea to resolve her symptoms of arthritis. We

obtained her written informed consent and conducted an in-hospital challenge test of intake of this tea. The challenge test was designed to minimize the patient risk by close monitoring of her platelet count. After drinking 2 mL or 20 mL of the tea, her platelet count remained in the normal range for six hours ( $29.5 \times 10^9/L$  and  $25.5 \times 10^9/L$ , respectively). After drinking 200 mL (the usual amount) of the tea, her platelet count rapidly decreased to  $0.3 \times 10^9/L$  three hours after drinking (Fig. 2), and she also developed bleeding symptoms. To avoid life-threatening bleeding, we treated her with platelet transfusions totaling 60 units in two days. Her platelet count recovered within four days and she was discharged. She stopped drinking the tea and the thrombocytopenia did not recur thereafter.

**Table. Laboratory Findings on Initial Admission.**

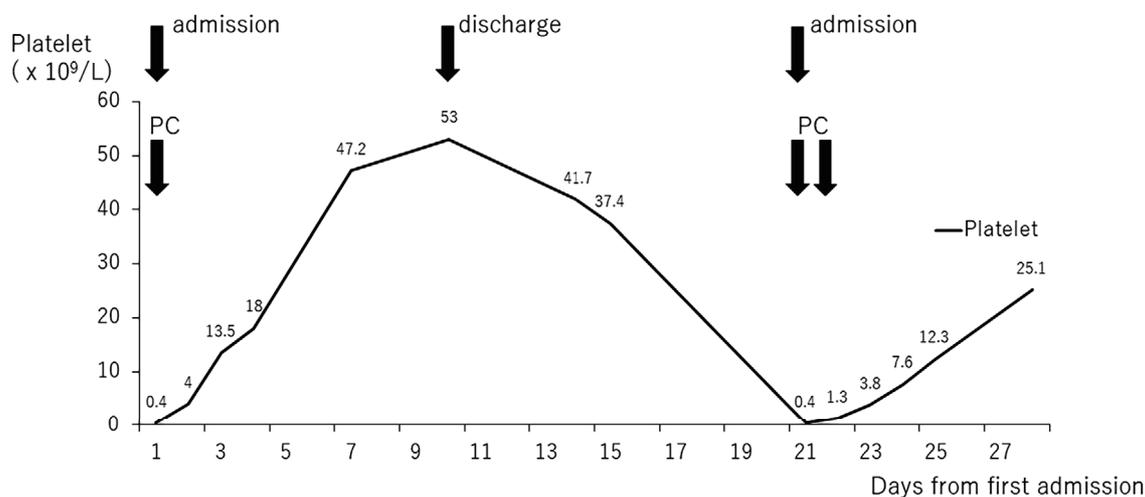
WBC	4,900 / $\mu$ L	AST	23 U/L
Neutro	69 %	ALT	9 U/L
Eosino	0 %	ALP	170 U/L
Baso	1 %	LDH	282 U/L
Mono	4 %	$\gamma$ -GTP	9 U/L
Lympho	25 %	T.Bil	0.7 mg/dL
RBC	$337 \times 10^9/L$	TP	8.7 g/dL
Hb	7.1 g/dL	Alb	3.0 g/dL
Plt	$0.4 \times 10^9/L$	BUN	12.9 mg/dL
		Cr	0.34 mg/dL
PT	12.0 sec	UA	3.3 mg/dL
APTT	29.5 sec	Na	134 mEq/L
Fbg	429 mg/dL	K	3.8 mEq/L
FDP	11.1 $\mu$ g/mL	Cl	100 mEq/L
D-dimer	6.68 $\mu$ g/mL	BS	141 mg/dL
		CRP	7.68 mg/dL
		VitB12	276 pg/mL
		Folic acid	5.4 ng/mL
		PAIgG	299 ng/ $10^7$ cell

WBC: white blood cell, Neutro: neutrophil, Eosino: eosinophil, Baso: basophil, Mono: monocyte, Lympho: lymphocyte, RBC: red blood cell, Hb: hemoglobin, Plt: platelet, PT: prothrombin time, APTT: Activated Partial Clotting Time, Fbg: fibrinogen, FDP: fibrinogen/fibrin degradation products, AST: aspartate aminotransferase, ALT: alanine transaminase, ALP: alkaline phosphatase, LDH: lactate dehydrogenase,  $\gamma$ -GTP:  $\gamma$ -glutamyl transpeptidase, T-bil: total bilirubin, TP: total protein, Alb: albumin, BUN: blood urea nitrogen, Cr: creatinine, UA: uric acid, Na: sodium, K: potassium, Cl: chloride, BS: blood sugar, CRP: C-reactive protein, PAIgG: platelet-associated IgG

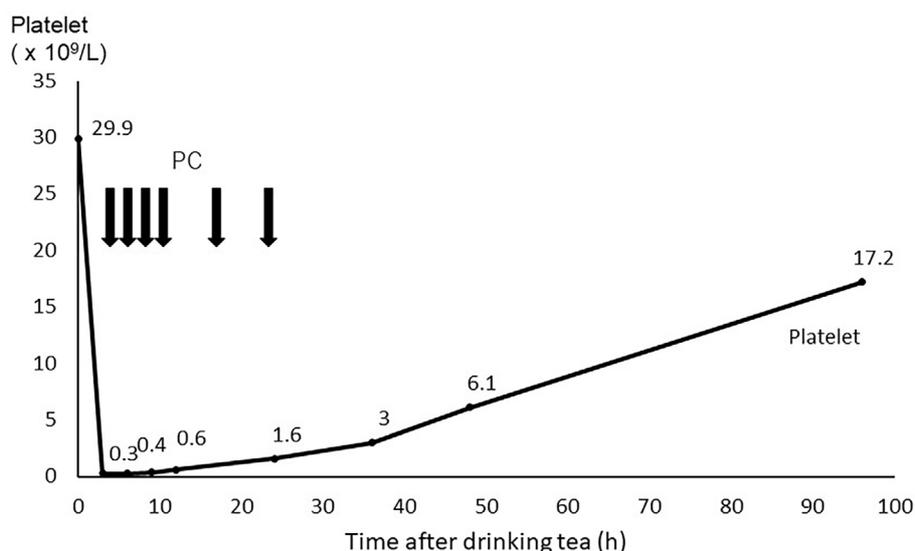
## Discussion

In comparison with drug-induced thrombocytopenia, reports of thrombocytopenia associated with substances other than drugs, including alternative medicines and health beverages, are limited (1-6), except for reports of thrombocytopenia associated with quinine-containing beverages (7-9). When clinicians ask about the medicines that patients are taking, patients often do not explicitly describe substance other than drugs; therefore, it is often difficult to identify the cause of thrombocytopenia in such cases. However, it is important to investigate these causative substances to avoid unnecessary medical treatment.

Laboratory methods for confirming drug-induced thrombocytopenia have not yet been established (10). However, the direct challenge of a patient with a drug suspected of causing thrombocytopenia can be hazardous. Despite this, when the substance suspected of causing thrombocytopenia is critical for the patient's welfare and life, such a challenge may be attempted (11). When a challenge test is performed, sufficient explanation and written consent from the patient are necessary and adequate plans should be prepared for un-



**Figure 1.** The clinical course of thrombocytopenia from the first admission. PC: platelet concentration



**Figure 2.** Thrombocytopenia after drinking the tea brewed from *Taxus yunnanensis*. PC: platelet concentration

expected complications.

Royer et al. (12) proposed the criteria to determine the level of evidence for a causal association with thrombocytopenia as follows: 1) ingestion of a candidate substance preceded thrombocytopenia and the platelet count recovered to the normal range if the patient had an established disorder with chronic mild thrombocytopenia; 2) the candidate substance was the only suspected agent ingested prior to the onset of thrombocytopenia; 3) other etiologies for thrombocytopenia were excluded; and 4) re-exposure to the substance resulted in recurrent acute thrombocytopenia. In this case, the tea brewed from *Taxus yunnanensis* was the only suspected agent ingested prior to the onset of thrombocytopenia, other etiologies for thrombocytopenia were excluded and re-exposure to *Taxus yunnanensis* resulted in recurrent acute thrombocytopenia.

*Taxus yunnanensis* (Chinese yew) is a large, ornamental evergreen shrub that is widespread in China. The tea brewed from the bark of this plant is called red bean cedar tea or yew tree tea and is distributed as a health beverage. *Taxus* (yew) trees contain alkaloids called taxanes that have anti-cancer activity and are the basis of the semisynthetic anti-cancer drugs paclitaxel and docetaxel (13, 14). Along with other *Taxus* species, *Taxus yunnanensis* may also contain taxanes, which can cause predictable dose-dependent thrombocytopenia. However, the clinical course of this case clearly differed from bone marrow suppression and it is strongly suspected that the cause of thrombocytopenia was an immunological mechanism. To the best of our knowledge, this is the first reported case of thrombocytopenia caused by *Taxus yunnanensis*. Two previous reports (3, 4) described patients with thrombocytopenia caused by *Jui* Chinese herbal tea which contains substances extracted from *Taxus cuspidata* (Japanese yew). In the first case (3), a 50-year-old woman developed thrombocytopenia with mucocutaneous bleeding associated with *Jui* herbal tea consumed

several days before her annual health examination. A challenge with *Jui* caused thrombocytopenia within one day. In the second case (4), a 54-year-old man had three episodes of thrombocytopenia with platelet counts of zero and mucocutaneous bleeding. An association with *Jui* was noted. A challenge with *Jui* caused his platelet count to rapidly decrease to zero in six hours, which recovered to pre-challenge levels on day 6.

In conclusion, in this case, we considered *Taxus yunnanensis* to be the causative substance of thrombocytopenia. The substances extracted from *Taxus* (yew) should be added to the list of those that cause thrombocytopenia.

#### Author's disclosure of potential Conflicts of Interest (COI).

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