



## Case Report

## A case of Dressler's syndrome successfully treated with colchicine and acetaminophen



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## ABSTRACT

The incidence of Dressler's syndrome after myocardial infarction (MI) has decreased in the reperfusion therapy era. Although guidelines recommend high-dose aspirin for treatment based on evidence from the pre-percutaneous coronary intervention (pre-PCI) era, bleeding and thrombotic concerns occurred upon aspirin administration after coronary stenting. A 69-year-old man with recent MI was admitted to our hospital. The patient presented with chest pain 1 week before admission. Electrocardiography revealed newly detected atrial fibrillation with no ST segment change. Urgent coronary angiography demonstrated a left circumflex artery occlusion. He underwent PCI, and a sirolimus-eluting stent was deployed. Aspirin, prasugrel, and apixaban were administered. However, hospital discharge was delayed because he developed heart failure during hospitalization. Twenty-three days after admission, he developed a fever of  $>39$  °C. Electrocardiography showed anterior ST segment elevation, and echocardiography revealed a 6-mm pericardial effusion. We diagnosed the patient with Dressler's syndrome, and colchicine 0.5 mg/day + acetaminophen 2000 mg/day were administered. His condition clinically improved after treatment and he was discharged 32 days after admission. There was hesitation about administration of high-dose aspirin in a patient who has undergone recent coronary stenting. Combination therapy of colchicine and acetaminophen could be a treatment option for Dressler's syndrome.

**<Learning objective:** Guidelines recommend high-dose aspirin for the treatment of Dressler's syndrome based on evidence from the pre-percutaneous coronary intervention (pre-PCI) era. However, bleeding and thrombotic concerns are present upon high-dose aspirin administration in patients who have undergone PCI. Therefore, a combination therapy of low-dose colchicine and acetaminophen could be a treatment option for patients with Dressler's syndrome who have undergone recent coronary stenting.>

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## Introduction

The incidence of Dressler's syndrome has decreased owing to reperfusion therapy. It can now be experienced only in patients with recent myocardial infarction (MI) who have not undergone primary percutaneous coronary intervention (PCI). Although guidelines recommend high-dose aspirin administration for the

treatment of Dressler's syndrome [1–3], the background evidence for these recommendations was amassed in the pre-PCI era. Although coronary stenting has become a standard therapy against MI, bleeding and thrombotic concerns on high-dose aspirin administration have occurred in the modern era. Herein, we present a case of Dressler's syndrome successfully treated with colchicine and acetaminophen.

## Case report

A 69-year-old man with no prior medical history visited a clinic for persistent chest discomfort. He presented with severe chest

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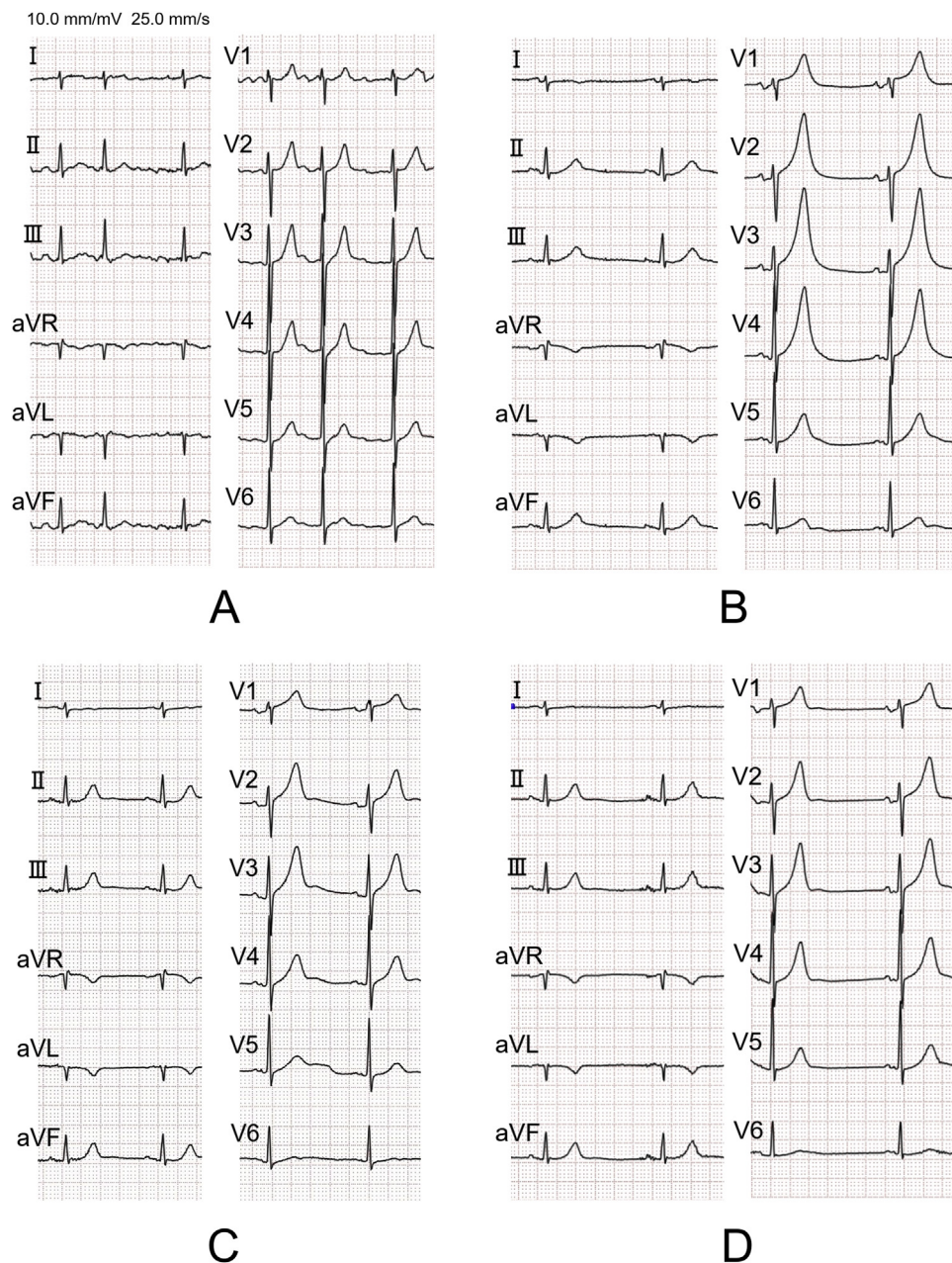
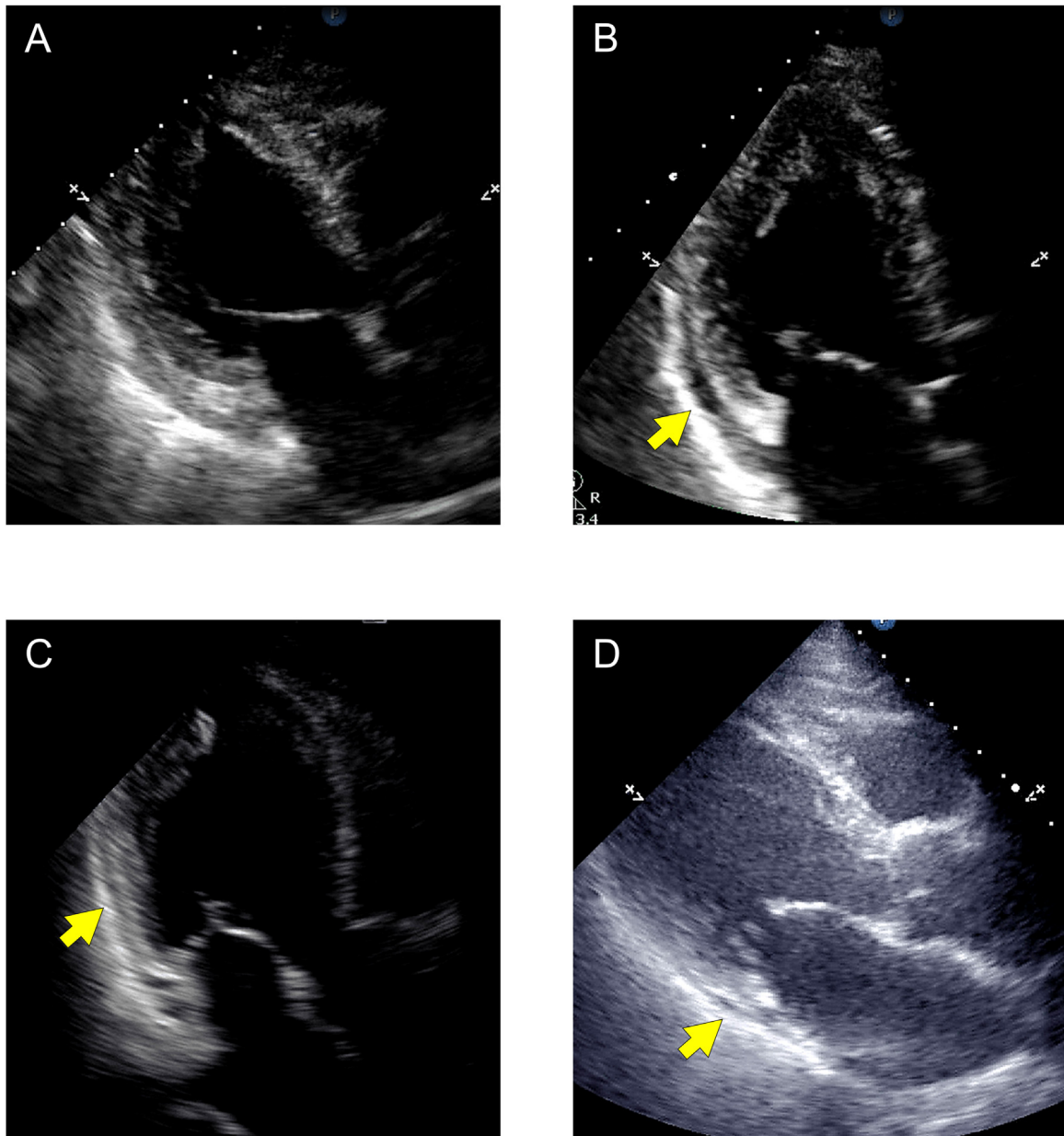


Fig. 1. Electrocardiography on admission (A), day 23 (B), and 3 (C) and 6 (D) months after discharge.

pain 1 week before admission; he was subsequently referred to our hospital for suspected acute coronary syndrome. On physical examination, the patient was afebrile with an irregular pulse of 108 beats/min and a blood pressure of 98/69 mmHg. The oxygen saturation was 98% on room air. No heart murmurs or edema were noted. Electrocardiography revealed newly detected atrial fibrillation with no ST segment change (Fig. 1A). Moreover, echocardiography showed inferior-lateral wall asynergy, with mild mitral valve regurgitation and no pericardial effusion (Fig. 2A). Left ventricular contraction was preserved, with an ejection fraction of 50%. Laboratory tests showed an elevation of myocardial and liver enzymes and signs of heart failure as follows: white blood cell count, 11,000 cells/ $\mu$ L (neutrophils, 69%; eosinophils, 0.5%); C-reactive protein, 14.3 mg/dL; creatinine kinase (CK), 197 U/L; CK-muscle/brain, 7 U/L; troponin I, 4.4 ng/mL; B-type natriuretic peptide, 357 pg/mL; aspartate transaminase, 81 U/L; alanine

aminotransferase, 77 U/L; and total bilirubin level, 2.1 mg/dL. Chest radiography revealed mild left pleural effusion with no congestion. Urgent coronary angiography demonstrated a middle left circumflex artery occlusion (Online Fig. S1). The patient underwent PCI, and a sirolimus-eluting stent was successfully deployed. The levels of myocardial enzymes were monitored by laboratory tests every 4 h after admission, although no CK elevation was noted. Considering the clinical course and results from the examinations, we diagnosed the patient with recent MI, which developed 1 week before admission. We administered aspirin 100 mg/day, prasugrel 3.75 mg/day, and apixaban 10 mg/day as antithrombotic therapy. Hospital discharge was delayed because of worsening heart failure. Considering the high bleeding risk, we reduced antiplatelet drugs to clopidogrel 75 mg/day (single antiplatelet therapy) on post-admission day 14. On post-admission day 23, the patient developed a fever of 39.6 °C and experienced a left lateral chest



**Fig. 2.** Echocardiography on admission (A), day 23 (B), and 3 (C) and 6 (D) months after discharge. The yellow arrowhead indicates the pericardial effusion.

pain. Pericardial friction rub was audible on auscultation with the forward leaning position. Widespread ST segment elevation and PR segment depression were demonstrated in the electrocardiogram (Fig. 1B). No signs of infection or acute coronary syndrome were detected after performing laboratory tests, urinary test, computed tomography, echocardiography, and coronary angiography. The eosinophil count increased to 5.1% (291 cells/ $\mu$ L) in the laboratory test, and echocardiography revealed a newly detected pericardial effusion of 6 mm (Fig. 2B). We diagnosed the patient as having Dressler's syndrome and administered colchicine and acetaminophen at 0.5 and 2000 mg/day, respectively. His physical signs and laboratory data improved within several days, and he was discharged on post-admission day 32 (Online Fig. S2).

Three months later, his widespread ST segment elevation had returned to normal (Fig. 1C), and his pericardial effusion had improved (Fig. 2C). Colchicine 0.5 mg/day was continued without

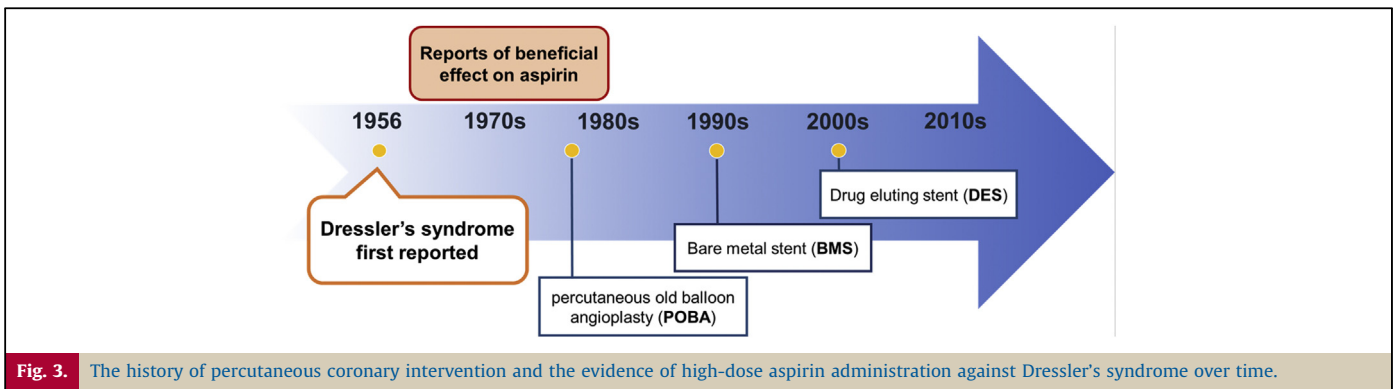
any side effects for 6 months, with no recurrence in symptoms noted or examinations repeated (Figs. 1D, 2D).

### Discussion

We report a patient with Dressler's syndrome successfully treated with colchicine and acetaminophen. Dressler's syndrome, which is a secondary form of pericarditis that is typically demonstrated weeks to months after MI, is presumed to be mediated by an autoimmune mechanism [2]. The incidence of this syndrome has remarkably decreased in the reperfusion therapy era and is reported as only 0.1% in patients with acute MI [4].

High-dose aspirin administration (2000–4000 mg/day) is recommended as class I therapy in guidelines [1–3], and administration of other non-steroidal anti-inflammatory drugs should be avoided because they may impair scar formation [5] or





diminish coronary blood flow [6]. Corticosteroids are suggested as a second option because of the risk of favoring the chronic evolution of the disease and promoting drug dependence [1]. However, the background evidence for these recommendations was amassed in the pre-PCI era, and there is no established treatment after primary PCI has become a standard therapy. Fig. 3 shows the history of PCI and the evidence of high-dose aspirin administration against Dressler's syndrome over time. Dressler's syndrome was first reported in 1956. The beneficial effects of aspirin were reported around the 1970s, which was before coronary stenting became a standard therapy in the 1990s. Evidence is lacking after primary PCI has become a standard therapy in MI patients due to the decreased morbidity.

There are thrombotic and bleeding concerns in the administration of high-dose aspirin in patients who underwent recent coronary stenting or those who take other antithrombotic drugs. High-dose aspirin may have a different antithrombotic effect compared with the low dose, a complex mechanism known as the aspirin dilemma. Aspirin inhibits two major mechanisms to obtain antithrombotic effects: platelet thromboxane-A<sub>2</sub> production and cyclooxygenase enzyme in the vascular endothelium [7]. The antithrombotic effect differs according to the aspirin dose. While lower doses inhibit the endothelial cyclooxygenase activity mildly, higher doses can achieve the inhibition more completely and rapidly, which may weaken the antithrombotic effect [7]. Aspirin dilemma is a mechanism that occurs with high-dose aspirin and might have thrombotic concerns compared with the low dose. Therefore, we decided to continue clopidogrel and apixaban as antithrombotic therapy instead of prescribing high-dose aspirin. As atrial fibrillation was not observed after successful reperfusion therapy, there was an option to stop anticoagulants (i.e. apixaban). However, since the patient had developed heart failure during hospitalization, his CHA<sub>2</sub>DS<sub>2</sub>-VASc score was 3 points (age ≥65 years, heart failure, and vascular disease). Considering the result from the Canadian Registry of Atrial Fibrillation study that approximately half of all newly detected atrial fibrillations would recur [8], we chose to continue anticoagulants in this patient.

Colchicine is an anti-inflammatory medication that targets the white blood cells and causes microtubule depolymerization, which in turn causes motility, phagocytosis, and degranulation. It also inhibits interleukin-1 beta and interleukin-18 by interfering with the NLRP3 inflammasome protein complex, which is increasingly recognized to have a role in acute coronary syndrome. In addition to the fact that colchicine is an inexpensive drug with only a few reports of serious side effects, it may reduce adverse cardiovascular events [9] or recurrent pericarditis [1]. Under these circumstances, we suggest that colchicine administration could be a treatment option for Dressler's syndrome.

Although the pathogenesis of early post-infarction pericarditis (typically a few days after acute MI) is believed to be different from

that of Dressler's syndrome, combination therapy of high-dose aspirin and colchicine is recommended for treatment. Colchicine is already reported as a useful agent for acute pericarditis to improve remission rates in the acute phase and reduce recurrence rates in the chronic phase [10]. From these reports, combination therapy of colchicine and acetaminophen can be one of the treatment options for acute pericarditis in patients with an indeterminate response to high-dose aspirin administration.

In the present case, there was hesitation about high-dose aspirin administration because the patient had undergone recent coronary stenting, and clopidogrel + apixaban were already prescribed. We successfully treated the patient with low-dose colchicine and acetaminophen without any side effects. Considering the risk of aspirin dilemma and the reported beneficial effect against recent MI, combination therapy of colchicine and acetaminophen could be a treatment option for patients with Dressler's syndrome who underwent recent coronary stenting. The pharmacological mechanism of aspirin dilemma remains unclear and further research is necessary. As a limitation of this case report, the use of colchicine for Dressler's syndrome is not covered by insurance in Japan, and careful informed consent is necessary upon prescription. Furthermore, although guidelines recommend continuing colchicine for 3–6 months [3], it remains unclear when to stop the therapy. In our case, we stopped prescribing colchicine after 6 months from discharge.

In conclusion, we experienced a case of Dressler's syndrome that developed during hospitalization. There was hesitation about the administration of high-dose aspirin in a patient who has undergone recent coronary stenting due to thrombotic and bleeding concerns. Combination therapy of colchicine and acetaminophen could be a treatment option for patients with Dressler's syndrome who underwent recent coronary stenting.

#### Conflict of interest

The authors declare that there is no conflict of interest.

#### Acknowledgment

None.

#### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at <https://doi.org/10.1016/j.jccase.2020.10.019>.

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