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Potential Synergistic Cardiotoxicity of Nab-Paclitaxel and Prior Anlotinib Therapy in a SMuRF-less Patient: A Case Report

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Case Report

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Abstract

Background

Reports of acute myocardial infarction in patients without standard modifiable cardiovascular risk factors (SMuRF-less) continue to accumulate, and cancer treatment is one of the factors implicated in these events. Whether previous exposure to an anti-angiogenic agent changes the vascular response to a taxane given months later has received little attention.

Case presentation

A 63-year-old man with stage IV lung adenocarcinoma and EGFR and RET alterations, with no standard modifiable cardiovascular risk factor, received nab-paclitaxel 400 mg as a single agent. About 12 h later he developed chest tightness, dyspnoea and loss of consciousness, and spontaneous circulation returned after cardiopulmonary resuscitation. Electrocardiography showed ST-segment elevation in leads II, III and aVF. Coronary angiography showed acute occlusion at the ostium of the right coronary artery, and implantation of a drug-eluting stent restored TIMI 3 flow. His cumulative exposure to anlotinib before this admission was approximately 30 months, ending in August 2025. High-sensitivity cardiac troponin T rose from 816 to 909 pg/mL and D-dimer from 7.015 to 9.84 mg/L. He was discharged on day 16, and echocardiography seven weeks later showed a left ventricular ejection fraction of 63%.

Conclusions

Nab-paclitaxel can be followed within hours by ST-segment elevation myocardial infarction in patients who carry no conventional risk factor, and long-standing preceding anti-angiogenic therapy may lower the threshold for such an event. Chest symptoms developing during or after taxane administration should not be attributed to hypersensitivity before an electrocardiogram has been obtained, and decisions about further anti-cancer treatment in this situation call for cardiology involvement.

Background

Acute myocardial infarction (AMI) in patients without standard modifiable cardiovascular risk factors (SMuRF-less) is being recognised more often and carries a poorer short-term prognosis than infarction occurring in patients with identifiable risk factors [1, 2]. SMuRF-less status does not mean that risk is absent; it means the causative factor has not been found. Malignancy and its treatment belong on that list [3].

Taxanes remain widely used in solid tumours. Myelosuppression, hypersensitivity and peripheral neuropathy are the adverse effects encountered most often, and AMI, although uncommon, is well documented [4]. Nab-paclitaxel was developed to dispense with the Cremophor EL vehicle and thereby reduce hypersensitivity reactions, but reports of AMI have continued with this formulation [5, 6]. Anlotinib, a multitargeted receptor tyrosine kinase inhibitor used in non-small-cell lung cancer, blocks vascular endothelial growth factor signalling and interferes with endothelial repair, and both arterial

thrombotic events and severe hypertension have been attributed to it [7, 8]. What is less clear is whether the vascular effects of an anti-angiogenic agent persist after the drug has been stopped, and whether they modify the response to a taxane given some months later.

We report a man who had taken anlotinib for roughly 30 months and developed ST-segment elevation myocardial infarction (STEMI) with cardiac arrest 12 h after his first nab-paclitaxel infusion, in the absence of any standard modifiable risk factor.

Case Presentation

A 63-year-old man was diagnosed in 2023 with stage IV lung adenocarcinoma with pleural and bone metastases. Molecular testing showed EGFR and RET alterations. He had no history of hypertension, diabetes or dyslipidaemia, had never smoked, and had no family history of premature coronary disease. Blood pressure, fasting glucose and lipid profile were normal at diagnosis.

From March 2023 he received furmonertinib together with anlotinib 12 mg daily. The anlotinib dose was reduced to 8 mg in September 2023 because of poor tolerance. Cumulative exposure to anlotinib came to approximately 30 months. In August 2025, follow-up imaging showed a brain metastasis, the first detected during the course of his disease, and anlotinib was stopped and pralsetinib substituted in the same revision of treatment. He had been taking pralsetinib for about six months at the time of this admission.

On 27 February 2026, at about 17:00, he received his first infusion of nab-paclitaxel 400 mg as a single agent. Nothing untoward happened during the infusion. Some 12 h later, at about 05:00 the following morning, he developed chest tightness, dyspnoea and diaphoresis, followed by loss of consciousness. Cardiopulmonary resuscitation on the ward restored spontaneous circulation. The electrocardiogram showed ST-segment elevation in leads II, III and aVF, and high-sensitivity cardiac troponin T (hs-cTnT) was 816 pg/mL. After aspirin 300 mg and ticagrelor 180 mg he was taken to the catheterisation laboratory for primary percutaneous coronary intervention (PCI).

Coronary angiography showed acute total occlusion at the ostium of the right coronary artery (Fig. 1A), with no significant stenosis in the left coronary system (Fig. 1C). Heparin 5000 IU was given, the lesion was predilated, and a 3.0 × 23 mm drug-eluting stent was implanted with high-pressure post-dilatation, restoring TIMI 3 flow (Fig. 1B). ST segments resolved after the procedure. hs-cTnT peaked at 909 pg/mL. D-dimer was 7.015 mg/L on admission (reference < 0.5 mg/L) and rose to 9.84 mg/L afterwards.

He was discharged on day 16 taking aspirin 100 mg daily, ticagrelor 90 mg twice daily and atorvastatin 40 mg at night. Echocardiography seven weeks later showed a left ventricular ejection fraction of 63% with no regional wall motion abnormality. Written informed consent for publication was obtained from the patient, and this report follows the CARE guidelines, with the completed checklist provided as Additional file 1.

Discussion

Coronary events during paclitaxel administration have been explained in several ways. Histamine released in response to the Cremophor EL vehicle can provoke coronary spasm [4, 5]. The drug also injures vascular endothelium, activates platelets and shifts the balance towards thrombosis, and any of these could end in plaque rupture [4, 6]. Our patient was given the albumin-bound formulation, which contains no Cremophor EL, so drug-vehicle spasm is an unsatisfactory explanation for what happened [5, 6].

Twelve hours is a long interval for a drug reaction, and it deserves comment. Reactions driven by the Cremophor EL vehicle, and IgE-mediated events such as Kounis syndrome, characteristically begin during the infusion or within minutes of its end. Published reports are consistent with this: in a review of ten reported cases of paclitaxel-associated myocardial infarction, most events began during the infusion or within minutes of its end, but onset was recorded 6 h after completion of the infusion in one case and 15 h after the start of the infusion in another [9]. An interval of twelve hours therefore sits at the outer edge of what has been reported rather than outside it. Albumin-bound paclitaxel behaves differently: plasma concentrations peak at the end of the infusion and decline with a half-life measured in tens of hours, so twelve hours after the infusion our patient was still under appreciable drug exposure [10]. The timing therefore fits a delayed prothrombotic or endothelial effect better than an immediate hypersensitivity reaction, and the interval is itself an argument against Kounis syndrome here.

Anlotinib blocks VEGF signalling and thereby limits the endothelial repair that normally follows vascular injury [7]. In vitro work describes endothelial cell apoptosis, reduced nitric oxide availability and a shift towards a pro-inflammatory endothelial phenotype [8]. In a real-world series of 62 patients treated with anlotinib, cardiovascular toxicity was common, hypertension predominated, and arterial thrombotic events including fatal myocardial infarction were recorded [11]. The ALTER 0303 trial characterised cardiovascular adverse events across its randomised population [12]. Inhibition of VEGF signalling also raises arterial stiffness and reduces capillary density, and how quickly such changes reverse once treatment stops is not established [3]. Our patient took anlotinib for about 30 months, and the drug was withdrawn six months before this admission. We are not aware of published measurements of how long these effects persist in human coronary arteries after anlotinib withdrawal, and six months may not be enough for the coronary endothelium to return to its previous state.

Putting the two exposures together, they could reasonably be seen as acting in sequence: a prolonged period of impaired endothelial repair leaving a vascular bed more susceptible than usual to an acute trigger, and then the taxane supplying that trigger in the form of spasm, thrombosis, or both. A sequence of this kind is one plausible form that an interaction between the two drugs could take, although it remains an interpretation rather than a demonstrated mechanism, and we put it forward for others to test.

The D-dimer values were higher than the size of the infarct would explain: 7.015 mg/L on admission, roughly 14 times the upper limit of normal (ULN), rising to about 20 times ULN afterwards. Three

processes were probably operating together: the prothrombotic state that accompanies advanced malignancy, endothelial injury from long-standing anlotinib treatment, and acute coagulation activation after the infusion. D-dimer is not specific to any one of them, but the pattern fits the sequence described above.

Chest tightness and dyspnoea during a chemotherapy infusion are usually read as hypersensitivity, and nab-paclitaxel is generally given in outpatient units where cardiac monitoring is not available. Where paclitaxel produces Kounis syndrome the distinction governs treatment entirely, since antihistamines and corticosteroids do nothing for an occluded coronary artery [13]. A patient receiving a taxane who develops chest symptoms should have an electrocardiogram before hypersensitivity is assumed.

Taxane-associated AMI has been reported across several tumour types. Ten reported cases of paclitaxel-associated infarction were collated in a review published in 2024 [9]; most of those patients had no standard modifiable risk factor, yet in none of them was previous anti-angiogenic therapy recorded. Qian and colleagues described fulminant myocarditis requiring veno-arterial extracorporeal membrane oxygenation (VA-ECMO) after paclitaxel and cisplatin [14], and Muñoz and colleagues reported type I Kounis syndrome with paclitaxel in a young woman with HER2-positive breast cancer [13]. Takotsubo syndrome has been described after combined chemotherapy [15], docetaxel has been implicated in triple-negative breast cancer [16], solvent-based paclitaxel in other settings [17], and anlotinib itself in acute myocardial infarction [18]. To our knowledge, none of those reports concerned a patient without standard modifiable risk factors who had previously received an anti-angiogenic agent.

Recording previous anti-angiogenic exposure before taxane chemotherapy begins would identify patients in whom the margin of safety may be narrower, and continuous electrocardiographic monitoring during the infusion and for the first 24 h afterwards seems reasonable in patients considered to be at increased risk [3]. Beyond that, deciding what to do next for this patient was genuinely difficult. His tumour had progressed through several lines of treatment, so stopping all anti-cancer therapy would permit further progression, whereas resuming it means accepting a risk of recurrence that a single case cannot quantify. He now needs long-term dual antiplatelet therapy, and any agent with prothrombotic or haemorrhagic potential interacts awkwardly with that requirement. The choices are better made together with cardiologists, and in the absence of trial data they rest largely on judgement.

SMuRF-less myocardial infarction is generally ascribed to factors that conventional risk scores miss, among them genetic susceptibility, autoimmune disease and environmental exposure. Previous cancer treatment should be added to that differential diagnosis. How often anti-cancer therapy accounts for events in this group is unknown, and whether prophylactic antiplatelet or statin treatment would protect patients with prior anti-angiogenic exposure is a question that would need prospective study.

This case has several limitations. First, a single case cannot establish causality, and the temporal association between the infusion and the infarction does not prove a causal link. Second, rechallenge with nab-paclitaxel was not performed and would be hard to justify ethically, so any formal causality assessment remains incomplete. Third, we cannot exclude Kounis syndrome as an alternative

mechanism, because tryptase, histamine and specific IgE were not measured at presentation, although the twelve-hour delay argues against an immediate IgE-mediated reaction. Fourth, intracoronary imaging was not performed and no thrombus aspiration was carried out, so we cannot distinguish in-situ thrombosis from plaque rupture, embolism or isolated spasm as the mechanism of the ostial occlusion, and the thrombus burden was not formally assessed. Fifth, D-dimer is non-specific and is influenced by malignancy, infection and infarction itself, so its course provides supportive rather than definitive evidence for the interpretation offered above. Sixth, the patient was taking furmonertinib and pralsetinib at the same time, pralsetinib having been introduced only six months before this event, and multitargeted kinase inhibitors carry cardiovascular risk of their own, leaving unmeasured confounding. A further source of confounding is the episode of severe COVID-19 pneumonia eleven months earlier, which required ventilatory support and interrupted all targeted therapy for about a month. He had recovered, and the interval makes a direct contribution unlikely, but a persistent prothrombotic state after severe infection cannot be excluded and may have contributed to the D-dimer rise. Lastly, follow-up was limited to seven weeks, so long-term outcome and the safety of further anti-cancer treatment remain unknown, and the interpretation proposed here would need confirmation in pharmacovigilance or registry data.

Conclusions

Nab-paclitaxel can be followed within hours by ST-segment elevation myocardial infarction in a patient with no standard modifiable cardiovascular risk factor, and approximately 30 months of preceding anlotinib therapy may have left the coronary circulation more vulnerable to such an event. Whether the two exposures genuinely interact cannot be settled by one case, and we offer the sequence as a hypothesis that others may be able to examine. Until better evidence exists, previous anti-angiogenic treatment should be recorded before taxane chemotherapy starts, monitoring for at least 24 h after the first infusion should be considered, and chest symptoms during treatment should prompt electrocardiography rather than a presumptive diagnosis of hypersensitivity.

Abbreviations

AMI
acute myocardial infarction
hs-cTnT
high-sensitivity cardiac troponin T
LVEF
left ventricular ejection fraction
PCI
percutaneous coronary intervention
SMuRF-less
without standard modifiable cardiovascular risk factors
STEMI
ST-segment elevation myocardial infarction

TIMI
Thrombolysis in Myocardial Infarction
ULN
upper limit of normal
VA-ECMO
veno-arterial extracorporeal membrane oxygenation
VEGF
vascular endothelial growth factor

Declarations

Ethics approval and consent to participate

This is a single case report with retrospective data collection. The requirement for institutional ethics committee approval was waived by the Ethics Committee of The 969th Hospital of the Joint Logistics Support Force of the Chinese People's Liberation Army according to local institutional guidelines for case reports.

Consent for publication

Written informed consent for publication of this case report and any accompanying images was obtained from the patient. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

All data supporting the conclusions of this article are included within the article (and its additional file).

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TL and HT wrote the manuscript. WZ, YZ, YY, PH, and BS collected clinical data and interpreted the results. HT conceived the study and supervised the project. All authors read and approved the final manuscript.

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Authors' information

Not applicable.

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Figures

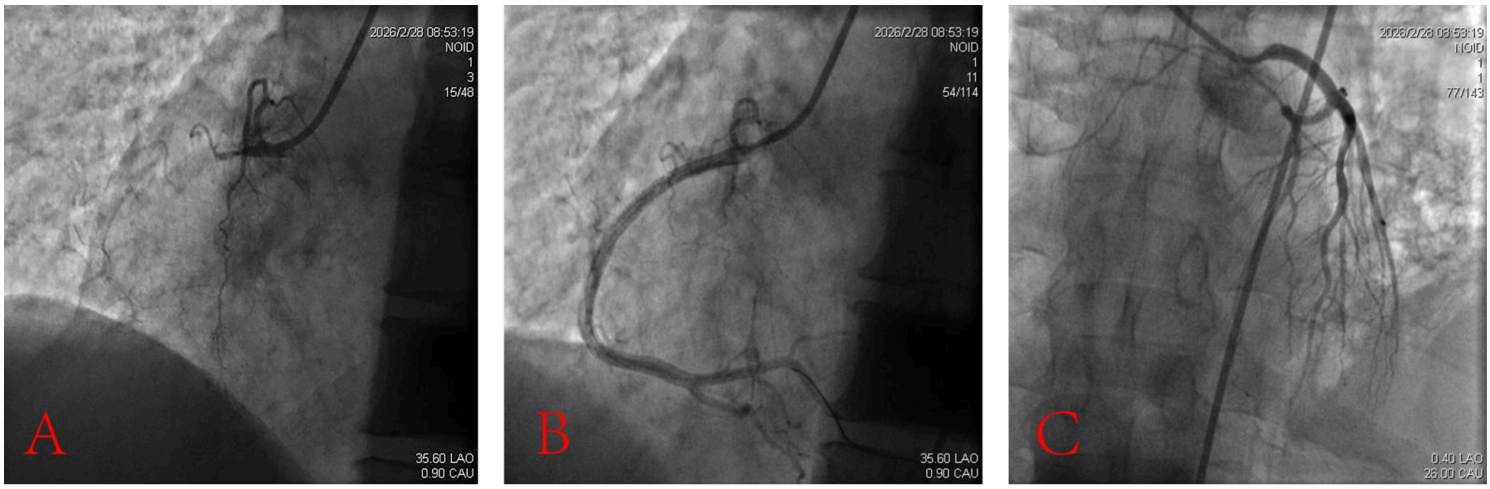


Figure 1

Coronary angiography findings. (A) Acute total occlusion of the right coronary artery ostium (arrow). (B) Restored TIMI 3 flow after drug-eluting stent implantation. (C) Left coronary system showing no

significant stenosis.

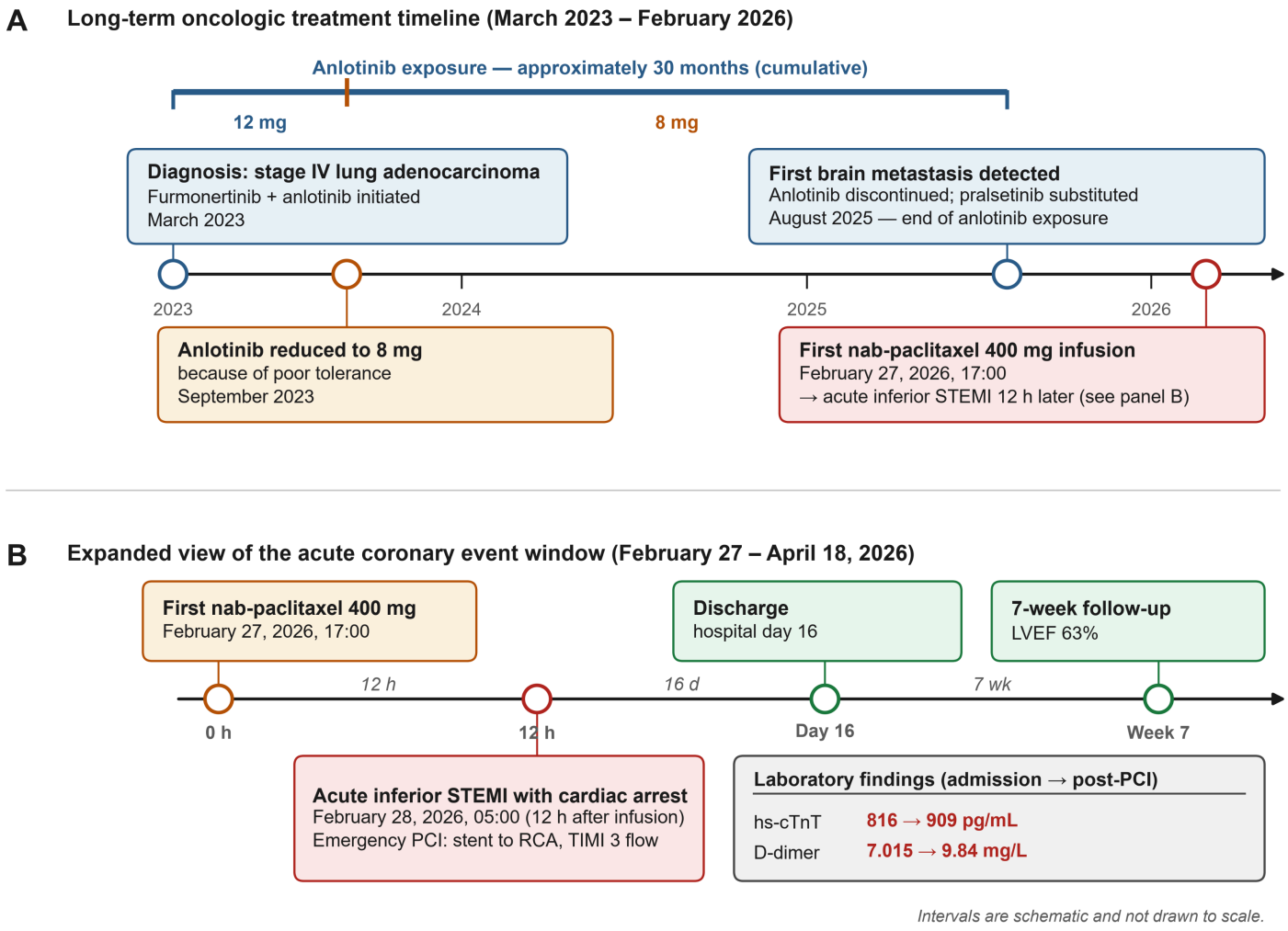


Figure 2

Clinical timeline. (A) Long-term oncologic treatment timeline from the diagnosis of stage IV lung adenocarcinoma in March 2023 to the acute coronary event in February 2026. Furmonertinib plus anlotinib was initiated at diagnosis; the anlotinib dose was reduced to 8 mg in September 2023 because of poor tolerance. After detection of the first brain metastasis in August 2025, anlotinib was discontinued and replaced by pralsetinib, marking the end of approximately 30 months of cumulative anlotinib exposure. (B) Expanded view of the acute coronary event window. The first infusion of nab-paclitaxel 400 mg was administered at 17:00 on February 27, 2026. Twelve hours later (05:00, February 28, 2026), the patient developed acute inferior ST-segment elevation myocardial infarction (STEMI) with cardiac arrest and underwent emergency percutaneous coronary intervention with stent implantation to the right coronary artery (RCA), achieving TIMI 3 flow. hs-cTnT rose from 816 pg/mL on admission to 909 pg/mL after the procedure, and D-dimer from 7.015 mg/L to 9.84 mg/L. The patient was discharged on hospital day 16, and a 7-week follow-up echocardiogram showed a left ventricular ejection fraction (LVEF) of 63%. Intervals in panel B are schematic and not drawn to scale.