



## Case Report

## Very late stent thrombosis lacking findings of the typical causes on optical coherence tomography in a patient with SARS-CoV-2



Wataru Shinkai (MD), Takehiro Hashikata (MD, PhD), Ryo Kameda (MD, PhD), Nobuhiro Sato (MD, PhD), Yoshiyasu Minami (MD, PhD)\*, Junya Ako (MD, PhD, FJCC)

Department of Cardiovascular Medicine, Kitasato University School of Medicine, Sagami-hara, Japan

## ARTICLE INFO

## Article history:

Received 3 March 2022

Received in revised form 18 April 2022

Accepted 22 April 2022

## Keywords:

Coronavirus disease 2019

Drug-eluting stent

Dual antiplatelet therapy

## ABSTRACT

A 50-year-old male was admitted to our hospital with sudden-onset chest pain. He was a current smoker with severe obesity and diabetes. He had a history of drug-eluting stent (DES) implantation in the left anterior descending artery (LAD) and had continuously taken clopidogrel. Eight days prior to admission, polymerase chain reaction testing confirmed that he was positive for severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2). Emergent coronary angiography revealed total occlusion of previously implanted DES in LAD. Optical coherence tomography (OCT) images demonstrated the presence of large white thrombus within the well-expanded DES with homogenous neointima. There were no findings of malapposed strut, uncovered strut, intimal disruption, or neoatherosclerosis through the stented segment. Subsequent dilation using a drug-coated balloon successfully restored coronary flow in LAD. We experienced a case of very late stent thrombosis without findings of the typical causes on OCT images nor discontinuation of antiplatelet therapy in a patient with SARS-CoV-2. The present case suggests that SARS-CoV-2 infection may induce stent thrombosis irrespective of the presence of known causes and the status of antiplatelet therapy.

**Learning objectives:** The underlying causes of very late stent thrombosis (VLST) include strut malapposition, neoatherosclerosis, uncovered struts and stent underexpansion in addition to inadequate discontinuation of antiplatelet therapy and/or systemic hyper coagulable state. The present case of VLST lacking those factors suggests the enhanced hyper thrombogenicity irrespective of the presence of known causes and the status of antiplatelet therapy in patients with severe acute respiratory syndrome coronavirus type 2.

© 2022 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.

## Introduction

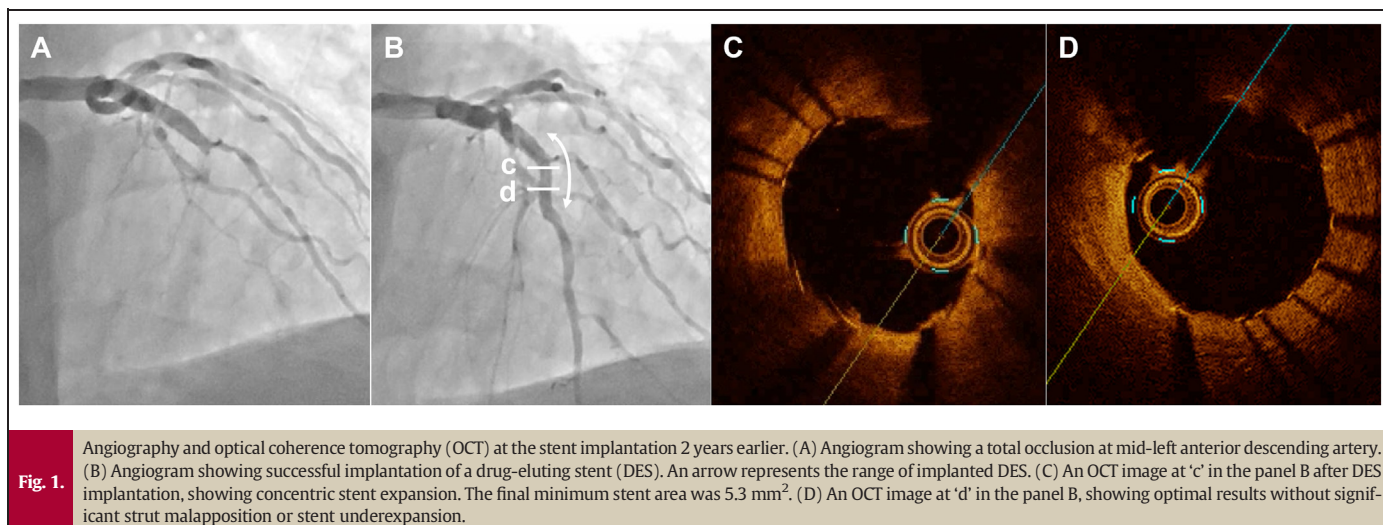
Very late stent thrombosis (VLST) is a fatal adverse event in chronic phase after the implantation of coronary stents. In addition to inadequate discontinuation of antiplatelet therapy and systemic or local hyper coagulable state, several characteristics in stented segments have been reported as the putative cause of VLST, including strut malapposition, neoatherosclerosis, uncovered struts, and stent underexpansion [1]. The severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) infection in combination with those factors has been also reported as an associated factor of the onset of stent thrombosis [2,3]. Because SARS-CoV-2 infection causes dysregulated immune responses and platelet hyperactivation, the patient has an increased

risk of systemic thromboembolism [4]. Herein, we report a case of VLST lacking typical causes of VLST in a patient with SARS-CoV-2, suggesting the central role of infection for the enhancement of hyper thrombogenicity in coronary segment.

## Case report

A 50-year-old male was admitted to our hospital with sudden-onset chest pain and dyspnea. He was a current smoker with severe obesity (body mass index: 39.2 kg/m<sup>2</sup>) and diabetes. He had a history of successful drug-eluting stent (DES; Ultimaster™ 2.75/24 mm; Terumo, Tokyo, Japan) implantation for a chronic total occlusion lesion at the middle part of left anterior descending artery (LAD) without suboptimal findings on optical coherence tomography (OCT) 2 years earlier (Fig. 1). Eight days prior to admission, polymerase chain reaction testing confirmed that he was positive for SARS-CoV-2 although he was

\* Corresponding author at: Department of Cardiovascular Medicine, Kitasato University School of Medicine, 1-15-1 Kitasato, Minami-ku, Sagami-hara, 252-0373, Japan.  
E-mail address: [nrg12391@yahoo.co.jp](mailto:nrg12391@yahoo.co.jp) (Y. Minami).



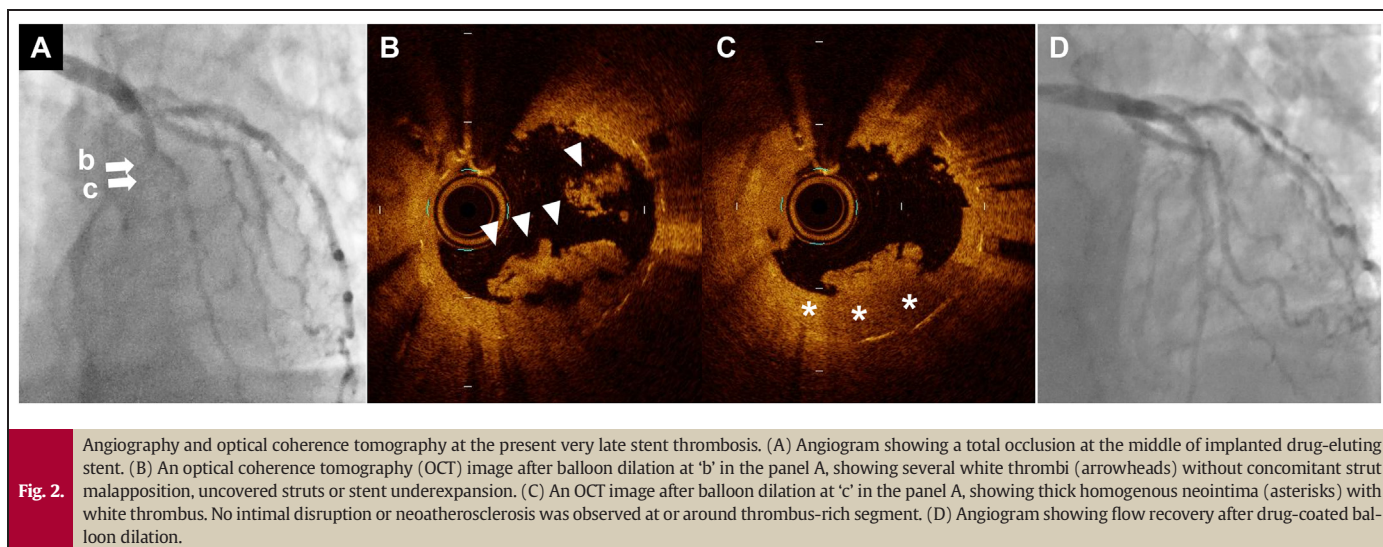
asymptomatic. Laboratory findings showed increased levels of white blood cells ( $15.2 \times 10^3$  cells/ $\mu$ L), lactate dehydrogenase (507 U/L), fibrin degradation products (5.20  $\mu$ g/mL), D-dimer (1.86  $\mu$ g/mL), and C-reactive protein (1.24 mg/dL). Lymphocytopenia ( $0.7 \times 10^3$  cells/ $\mu$ L) was also observed. Electrocardiography revealed ST-segment elevation in lead V1–4. Emergent coronary angiography revealed total occlusion of previously implanted DES in LAD (Fig. 2A) (Video I). OCT images after pre dilation demonstrated the presence of large white thrombus within the well-expanded DES with homogenous neointima (Fig. 2B, C). There were no findings of malapposed strut, uncovered strut, intimal disruption, or neoatherosclerosis through the DES (Video II). Subsequent dilation using a drug-coated balloon successfully restored coronary flow in LAD (Fig. 2D) (Video III). We added aspirin 100 mg to his daily clopidogrel 75 mg. After cardiac rehabilitation and treatment for concomitant heart failure, he was discharged on postoperative day 21.

## Discussion

We have witnessed a case of VLST without findings of typical causes on OCT images or inappropriate discontinuation of antiplatelet therapy in a patient with SARS-CoV-2. Because of the high spatial resolution, the use of OCT enables identification of putative causes of VLST in daily practice. Taniwaki et al. reported that the underlying putative cause could be identified in 98% of VLST cases by using OCT and that the most frequent findings were strut malapposition, neoatherosclerosis,

uncovered struts, and stent underexpansion [1]. In fact, recent reports of stent thrombosis in patients with coronavirus disease 2019 (COVID-19) showed that those findings could be identified by OCT [2,3]. On the other hand, none of those findings were observed by OCT in the present case. In addition, we further confirmed that the initial DES had been successfully implanted without suboptimal findings on OCT. These facts suggest that the systemic hyper thrombogenic state and any invisible change affecting focal thrombogenicity at the stented site were playing the role for the development of thrombus in the present patient.

The enhanced prothrombotic state in patients with COVID-19 has been reported and explained by the dysregulated immune responses and platelet hyperactivation [4]. Some reported cases of stent thrombosis in COVID-19 patients with appropriate antiplatelet drugs may support the existence of their hyper thrombogenicity in coronary lesions [3,5]. The higher thrombus burden in COVID-19 patients with ST-segment elevation myocardial infarction shown in a recent study also supports their enhanced thrombogenicity in coronary lesions [6]. The focal enhancement of thrombogenicity may be partly caused by the change in microenvironment of endothelium via activated inflammatory response, including endothelial cell erosion and deterioration of endothelial glycocalyx [7]. The white thrombus-dominancy without other visible morphological abnormalities on OCT images in the present case might be a proof of focal endothelial damage in neointimal tissue and subsequent platelet aggregation [8]. Another characteristic of the



present case is the lack of symptoms of COVID-19 before the onset of VLST. This may suggest that the dysregulated immune responses, platelet hyperactivation, and endothelial dysfunction resulting in coronary thrombosis already initiate even if a patient with SARS-CoV-2 is asymptomatic. The concomitant severe obesity, current smoking, and diabetes may further activate and modulate systemic thrombogenicity in the present case. Although we added aspirin to his daily clopidogrel in the present case, the prescription of prasugrel instead of clopidogrel might be a safer option given the presence of potential drug interaction with agents for the treatment of COVID-19 and the potential of limited anti-platelet efficacy caused by gene polymorphism of P2Y12 receptors [9]. Further strategies are urgently required to prevent fatal adverse event in patients with prior coronary stent implantation in this COVID-19 pandemic era.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jccase.2022.04.011>.

#### Declaration of competing interest

None.

#### Acknowledgment

None.

#### References

- [1] Taniwaki M, Radu MD, Zaugg S, Amabile N, Garcia-Garcia HM, Yamaji K, et al. Mechanisms of very late drug-eluting stent thrombosis assessed by optical coherence tomography. *Circulation* 2016;133:650–60.
- [2] Antuña P, Rivero F, Val DD, Cuesta J, Alfonso F. Late coronary stent thrombosis in a patient with coronavirus disease 2019. *JAMA Cardiol* 2020;5:1195–8.
- [3] Prieto-Lobato A, Ramos-Martínez R, Vallejo-Calcerrada N, Corbí-Pascual M, Córdoba-Soriano JG. A case series of stent thrombosis during the COVID-19 pandemic. *JACC Case Rep* 2020;2:1291–6.
- [4] Higashikuni Y, Liu W, Obana T, Sata M. Pathogenic basis of thromboinflammation and endothelial injury in COVID-19: current findings and therapeutic implications. *Int J Mol Sci* 2021;22:12081.
- [5] Elkholly KO, Khizar A, Khan A, Hakobyan N, Sahni S. Subacute stent thrombosis in a patient with COVID-19 despite adherence to antiplatelets. *Cureus* 2021;13:e13194.
- [6] Choudry FA, Hamshere SM, Rathod KS, Akhtar MM, Archbold RA, Guttman OP, et al. High thrombus burden in patients with COVID-19 presenting with ST-segment elevation myocardial infarction. *J Am Coll Cardiol* 2020;76:1168–76.
- [7] Yamaoka-Tojo M. Vascular endothelial glycocalyx damage in COVID-19. *Int J Mol Sci* 2020;21:9712.
- [8] Jia H, Abtahian F, Aguirre AD, Lee S, Chia S, Lowe H, et al. In vivo diagnosis of plaque erosion and calcified nodule in patients with acute coronary syndrome by intravascular optical coherence tomography. *J Am Coll Cardiol* 2013;62:1748–58.
- [9] Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, et al. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up: JACC state-of-the-art review. *J Am Coll Cardiol* 2020;75:2950–73.