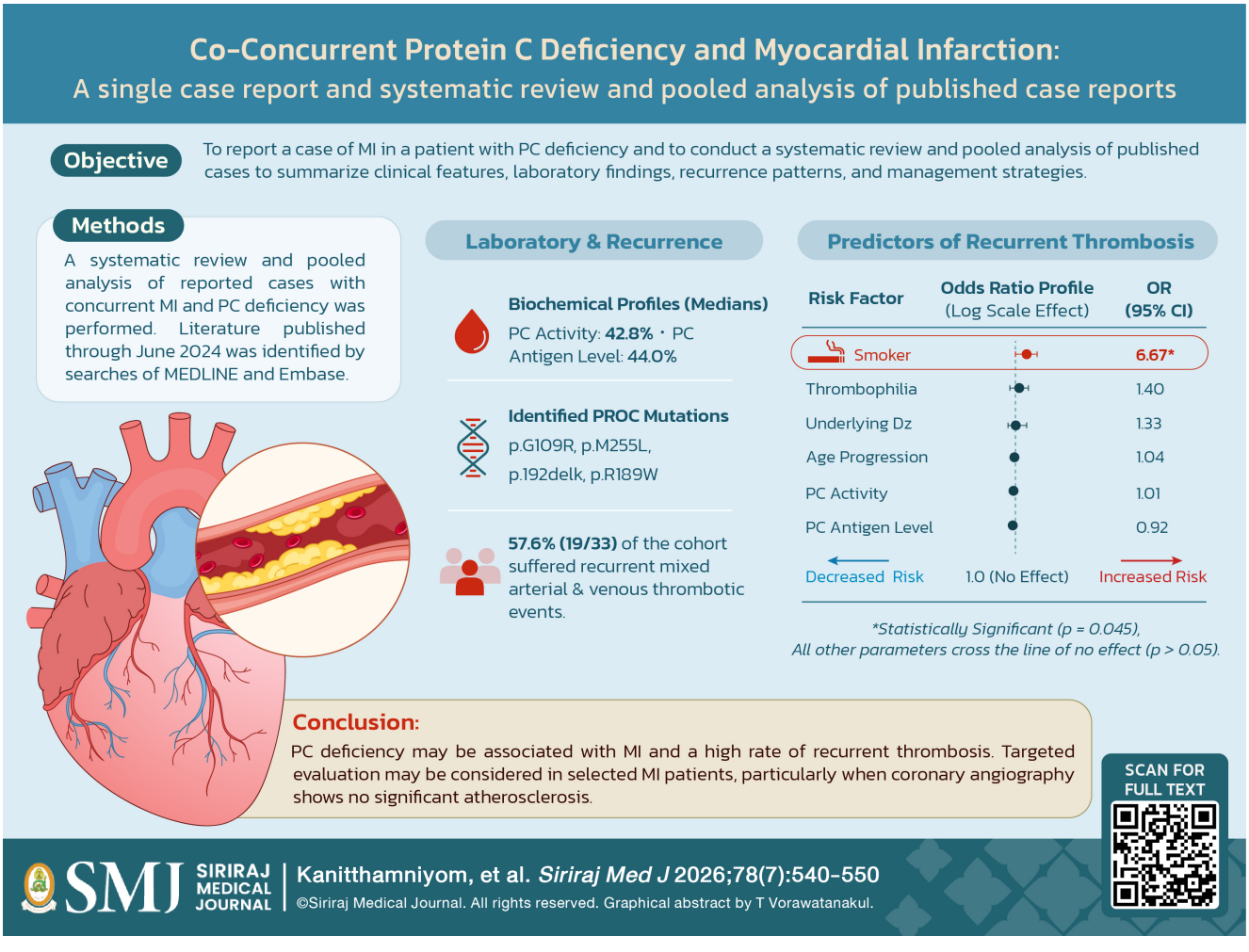
Myocardial Infarction in a Patient with Coexisting Protein C Deficiency: A Single Case Report and Systematic Review and Pooled Analysis of Published Case Reports

Chanakarn Kanitthamniyom, M.D.[1], Tarinee Rungjirajittranon, M.D.[2], Korakoth Towashiraporn, M.D.[3], Thanaphat Lalitrojwong[4], Nattawut Leelakanok, Ph.D.[5], Theera Ruchutrakool, M.D.[2], Yingyong Chinthammitr, M.D.[2], Bundarika Suwanawiboon, M.D.[2], Weerapat Owattanapanich, M.D.[2,*]

[1]Department of Internal Medicine, Texas Tech University Health Science Center, Lubbock, Texas, United States of America, [2]Division of Hematology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [3]Her Majesty Cardiac Center, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [4]Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [5]Division of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Burapha University, Chonburi, Thailand.



*Corresponding author: Weerapat Owattanapanich
E-mail: weerapat.owa@mahidol.ac.th
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ORCID ID: http://orcid.org/0000-0002-1262-2005
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ABSTRACT

Objective: To report a case of MI in a patient with PC deficiency and to conduct a systematic review and pooled analysis of published cases to summarize clinical features, laboratory findings, recurrence patterns, and management strategies.

Materials and Methods: A systematic review and pooled analysis of reported cases with concurrent MI and PC deficiency was performed. Literature published through June 2024 was identified by searches of MEDLINE and Embase.

Results: Thirty-three patients, including the present case, were analyzed. Median age at presentation was 37 years (IQR 26.5–44). Traditional atherosclerotic risk factors were reported in 6 patients (18.2%). Recurrent arterial and/or venous thrombosis occurred in 19 patients (57.6%). Median PC activity and antigen levels were 42.8% (IQR 32.3–50.5%) and 44.0% (IQR 39.7–52.2%), respectively. Four distinct PROC mutations were described. Coronary angiography most often showed thrombotic occlusion without clear atherosclerotic disease. Combination anticoagulant and antiplatelet therapy was the most common treatment approach. Active smoking was associated with recurrent thrombosis (odds ratio 6.667, 95% CI 1.047–42.431; p=0.045).

Conclusions: PC deficiency may be associated with MI and a high rate of recurrent thrombosis. Targeted evaluation may be considered in selected MI patients, particularly when coronary angiography shows no significant atherosclerosis.

Keywords: Myocardial infarction; patient; coexisting protein C deficiency; single case report; systematic review (Siriraj Med J 2026;78(7):540-550)

INTRODUCTION

Protein C (PC) is an endogenous anticoagulant protein that works together with protein S (PS) to downregulate coagulation by inactivating clotting factors V and VIII.[1] Deficiency of PC has been consistently linked to an increased risk of venous thromboembolism (VTE), as demonstrated across multiple clinical studies.[1-4] In a prospective cohort, Mahmoodi et al. estimated the annual incidence of VTE among individuals with hereditary deficiencies of natural anticoagulants to be about 1%, corresponding to an approximately fourfold higher risk than that observed in the general population.[5]

In contrast to venous thrombosis, the association between PC deficiency and arterial thrombotic events remains less clearly defined.[6] A recent systematic review and meta-analysis reported that PC-deficient individuals had roughly double the risk of ischemic stroke compared with controls.[6] However, information regarding recurrence patterns and implications for treatment decisions in arterial events is still limited. Evidence relating specifically to myocardial infarction (MI) is even more sparse. Prior investigations of inherited thrombophilia in arterial disease have largely focused on factor V Leiden and prothrombin gene variants, with heterogeneous and sometimes conflicting findings.[7-10] Given these uncertainties, some experts propose that thrombophilia evaluation may be considered in selected younger patients (younger than 50–55 years) with arterial thrombosis after other causes have been carefully excluded.[11] Conversely, the British Society for Haematology notes insufficient supporting evidence and does not recommend routine inherited thrombophilia testing in patients with arterial thrombosis.[12]

Because hereditary anticoagulant deficiencies, including PC deficiency, are uncommon, robust observational data examining their relationship with arterial thrombosis—particularly MI—are lacking. To address this knowledge gap, the present study had two primary objectives: first, to describe a patient with PC deficiency who developed cerebral venous sinus thrombosis followed by MI at our center; and second, to perform a systematic review and pooled analysis of published cases of MI occurring in the setting of PC deficiency, with emphasis on clinical features, laboratory characteristics, treatment approaches, and factors associated with recurrent thrombosis.

MATERIALS AND METHODS

Data retrieval for the index case

Clinical information for the patient described in this report was obtained from the institutional electronic medical record system at our center. According to local policy, single case reports are not required to undergo institutional review board evaluation; therefore, formal ethics approval was not requested. Written informed consent for use and publication of clinical data was obtained from the patient. The case description was prepared in accordance with the CAse REport (CARE) reporting guideline.[13] (Supplementary Data 1).

Search strategy for the systematic review and pooled analysis of published case reports

A systematic literature search was performed in the MEDLINE and Embase databases from database inception through June 2024. No language restrictions were applied. The objective was to identify case reports and case series describing patients with both protein C deficiency and myocardial infarction. The core search terms included "Protein C" and "Myocardial infarction". Detailed database-specific search strategies are provided in Supplementary Data 2. The review process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations.[14] (Supplementary Data 3). The study protocol was prospectively registered in the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY202480047).

Eligibility criteria and data extraction

Publications were considered eligible if they met all of the following criteria: (1) involved adult patients aged 18 years or older; (2) documented confirmed protein C deficiency; (3) reported myocardial infarction as a clinical outcome; (4) were designed as case reports or case series without a control group; and (5) contained sufficient clinical detail for data extraction. Studies that did not fulfill these criteria were excluded.

Article screening and data extraction were performed independently by three investigators (CK, TL, and WO). Any uncertainties regarding study eligibility were resolved by consultation with TR1. Baseline characteristics and outcome variables from included reports were independently reviewed by CK, WO, and TR1. Extracted datasets were subsequently cross-verified among these reviewers to improve accuracy and consistency.

Quality assessment

Methodological quality and risk of bias of the included reports were evaluated independently by two reviewers (CK and TR1) using the Joanna Briggs Institute critical appraisal checklist for case reports.[15] (Table 1). Differences in assessment were resolved through discussion with WO.

To evaluate the certainty of exposure and diagnostic accuracy across the pooled cases, we performed a quality assessment using the JBI checklist. We identified that 14 patients, including the current case, were not receiving anticoagulation therapy at the time of testing, strengthening the reliability of the protein C (PC) deficiency diagnosis. Conversely, in six cases, PC levels and functional assays were measured while patients were on warfarin or heparin, which may mask or confound the results. Only two reports (Wypasek et al. and Yaarubi et al.) explicitly confirmed the deficiency through repeat testing. In the remaining cases, the specific timing and conditions of the PC assays were not reported. Regarding outcome ascertainment, the diagnosis of myocardial infarction (MI) was robustly confirmed in all 33 cases through clinical presentation, electrocardiographic changes, cardiac enzyme kinetics, and coronary angiography. Finally, we identified several potential confounders, including smoking, concurrent thrombophilias, family history, and underlying comorbidities, which may contribute to atherosclerotic risk alongside PC deficiency.

Statistical methods

The pooled analysis comprised 33 patients: 29 derived from individual case reports, 3 from a single case series, and 1 from the present case. For statistical analysis, individual patients from published reports were combined and analyzed as a single observational cohort, following the approach described by Sampayo-Cordero et al.[16]

Associations between selected variables (age, smoking status, family history, protein C mutation status, and protein C activity level) and the presence of concurrent thrombosis were evaluated using binomial logistic regression with SPSS Statistics software (SPSS Inc., Chicago, IL, USA). Sensitivity analyses for heterogeneity, as proposed in the reference methodology, were not conducted because no prior meta-analysis addressing this specific outcome was available for comparison.

Categorical variables are presented as counts and percentages. Continuous variables with non-normal distribution are summarized as median and interquartile range (IQR). A two-sided p-value <0.05 was considered to indicate statistical significance.

RESULTS

The single case report given in the present study

A 47-year-old Thai man presented to the emergency department of our tertiary referral center in March 2016 with a seizure. He had no known comorbid conditions and reported no regular medication use, substance abuse, smoking, or alcohol intake. Computed tomography venography demonstrated extensive cerebral venous sinus thrombosis involving multiple sites, including cortical veins in the right frontoparietal and left parietal regions, the superior sagittal and confluence sinuses, the right transverse and sigmoid sinuses, the right internal jugular vein, and part of the left transverse sinus.

Given a family history of venous thrombosis in a sibling and the absence of other provoking factors, an

TABLE 1. Characteristics of the patients included in this systematic review.

First author (Year of publication)	Age/ gender	Concurrent thrombosis	Comorbidity	Current smoker	Concomitant thrombophilia	Protein C mutation	Protein C activity (%)	Protein C level (%, IU/dL)	Family	OAC	Antiplatelet	QA
Coller (1987)[17]	23/M	Yes (DVT/PE)	No	Yes	No	N/A	33%	20%	Yes	Warfarin	Dipyridamole	8/8
Hacker (1991)[18]	28/M	No	Asthma	Yes	No	N/A	51%	N/A	Yes	Warfarin	ASA	8/8
Kario (1992)[19]	29/M	No	No	Yes	N/A	N/A	51%	N/A	Yes	Warfarin	ASA	8/8
Bux-Gewehr (1999)[20]	35/F	Yes (DVT/PE)	No	No	No	N/A	57%	N/A	Yes	Phenprocoumon	No	7/8
Ninomiya (2001)[21]	76/M	Yes (DVT)	N/A	N/A	No	N/A	48%	41%	N/A	Warfarin	ASA & dipyridamole	7/8
Ninomiya (2001)[21]	64/M	Yes (MI)	N/A	N/A	No	N/A	15%	49%	N/A	Warfarin	ASA & dipyridamole	6/8
Ninomiya (2001)[21]	60/F	No	N/A	N/A	No	N/A	26%	60%	N/A	Warfarin	ASA	6/8
Sadiq (2001)[22]	22/F	No	Asthma	Yes	No	N/A	33%	N/A	No	Warfarin	No	7/8

Abbreviations: ASA, aspirin; AT, antithrombin; BID, twice daily; CVST, cerebral venous sinus thrombosis; DLD, dyslipidemia; DM, diabetes mellitus; DVT, deep vein thrombosis; F, female; FV Leiden; factor V Leiden; HT, hypertension; IJV, internal jugular vein; IU/dL, international units per deciliter; M, male; mg, milligram; MI, myocardial infarction; MTHFR, methylenetetrahydrofolate reductase; N/A, not available; OAC, oral anticoagulant; PAD, peripheral artery disease; PAI-1, plasminogen activatable inhibitor-1; PE, pulmonary embolism; PROC gene – Protein C, Inactivator Of Coagulation Factors Va and VIIIa gene; PS, protein S; QA, quality assessment (evaluated using the Joanna Briggs Institute checklist); QD, once daily; SVC, subclavian vein; SVT, superficial vein thrombosis

inherited thrombophilia evaluation was performed. Protein C activity was reduced to 40% (reference range 70–140%), whereas free protein S and antithrombin levels were within normal limits. Testing for antiphospholipid syndrome was negative, including lupus anticoagulant and antiphospholipid antibodies. Next-generation sequencing identified a pathogenic homozygous PROC variant, c.565C>T (p.R189W) at exon 7, with a variant allele frequency of 99.62%.

Long-term anticoagulation with a vitamin K antagonist (warfarin) was initiated with ongoing risk–benefit counseling. The patient later discontinued warfarin on his own. One week after treatment interruption, he returned with acute chest pain and was diagnosed with inferoposterolateral ST-elevation myocardial infarction based on electrocardiographic ST elevation in leads II, III, aVF, and V4–V6. Coronary angiography demonstrated complete thrombotic occlusion of the left anterior descending and left circumflex arteries without evidence of underlying atherosclerotic disease. Thrombus aspiration and balloon angioplasty were performed without stent placement. Clopidogrel was started but discontinued after two weeks because of concern regarding thrombophilia-related thrombosis. Warfarin was resumed with a plan for indefinite therapy due to recurrent thrombotic events.

Systematic review and pooled analysis of published case reports

Study selection

The database search identified 15,210 records from MEDLINE and Embase through June 2024. After removal of 1,247 duplicates, 13,963 titles and abstracts were screened by three reviewers. A total of 13,871 records were excluded because they did not report the outcome of interest, were reviews/editorials/commentaries, or involved non-eligible populations. Ninety-two full-text articles underwent detailed assessment. Sixty were excluded because of insufficient protein C–related data or lack of relevant outcomes. Thirty-two published case reports, together with the present case, were included in the final analysis (N=33).[17-46] The selection process is illustrated in Fig 1. Extracted variables included demographic features, laboratory findings, thrombotic manifestations, coronary angiographic patterns, and treatment strategies (Tables 1 and 2).

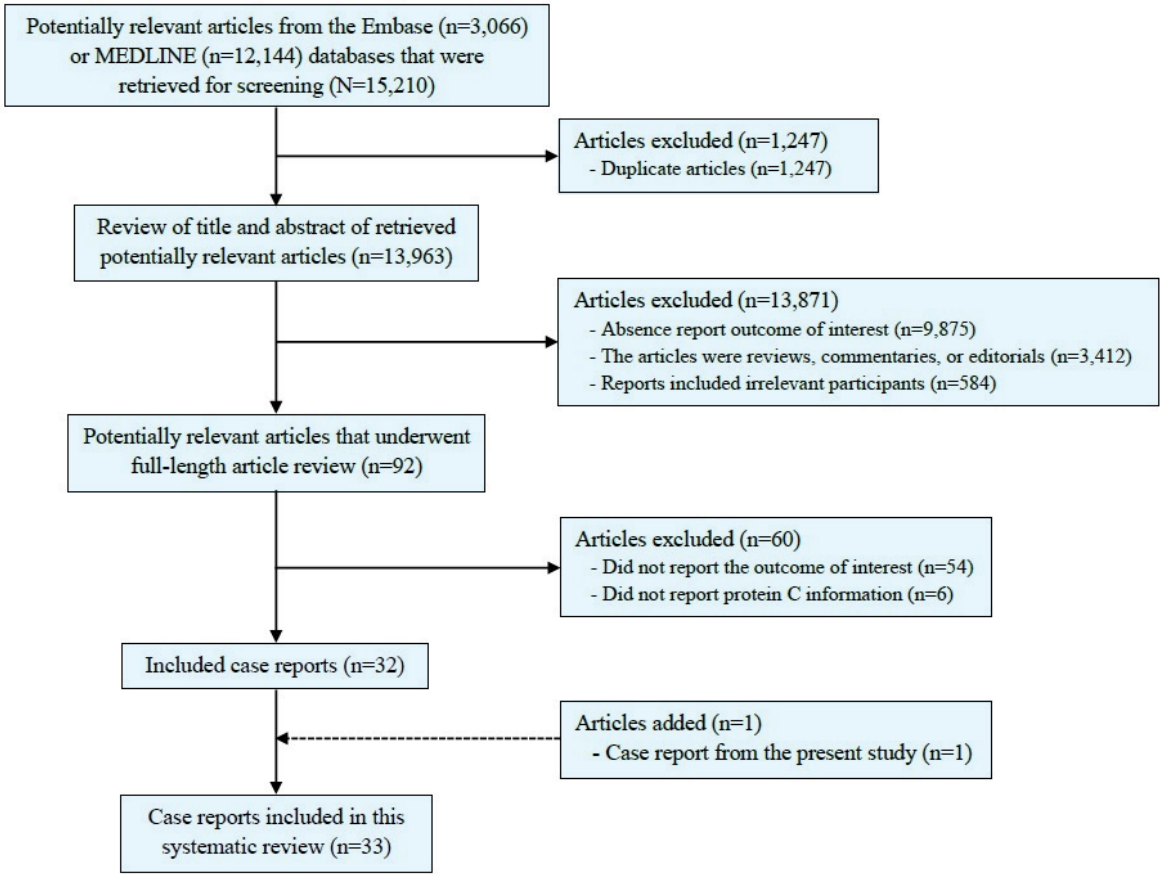


Fig 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart describing the literature review procedure.

TABLE 2. Coronary angiography findings of the patients included in this systematic review.

First author (Year of publication)	Coronary angiography findings
Coller (1987)[17]	Occluded left anterior descending coronary artery without evidence of coronary artery atherosclerosis
Hacker (1991)[18]	Thrombus in the left main coronary artery, large normal right coronary artery, and normal left circumflex coronary
Kario (1992)[19]	Slight stenosis of the left anterior descending coronary artery (25% diameter reduction)
Byux-Gewehr (1999)[20]	Occlusion of the left anterior descending coronary artery but no evidence of arteriosclerosis
Ninomiya (2001)[21]	Repeated thrombo-occlusion of coronary artery bypass grafts (5 recurrences)
Ninomiya (2001)[21]	Repeated occlusion of the left anterior descending coronary artery
Ninomiya (2001)[21]	Repeated complete thrombo-occlusion of the graft
Sadiq (2001)[22]	Total occlusion of the left proximal anterior descending artery by a thrombus, and 70-80% occlusion at the origin of the first diagonal branch by a thrombus
Cakir (2002)[23]	Occlusion of the proximal left anterior descending artery
Peterman (2003)[24]	Total occlusion of the distal left anterior descending coronary artery without collaterals
Tiong (2003)[25]	Acute thrombotic occlusion at the junction of the distal right coronary artery and the posterior descending artery with a normal left coronary system
Cakir (2007)[26]	Occlusion of the left anterior descending coronary artery
Ahmed (2009)[27]	Ectatic epicardial coronary arteries with no flow-limiting stenosis
Yokoyama (2009)[28]	Thrombus localized at the right coronary cusp and occluded right coronary artery
Eshtehardi (2011)[29]	Total thrombotic occlusion of the left anterior descending coronary artery at the bifurcation of the first diagonal branch with no evidence of atherosclerosis
D'Angelo (2011)[30]	Thrombus in proximal left anterior descending artery with no atherosclerotic

Patient characteristics

Baseline characteristics of the 33 included patients are summarized in Table 1. Most were male (25/33, 75.8%). The median age at MI presentation was 37 years (IQR 26.5–44). Traditional atherosclerotic risk factors, such as diabetes mellitus, hypertension, or dyslipidemia, were reported in 6 patients (18.2%). Recurrent thrombotic events at arterial and/or venous sites other than the index MI were documented in 19 patients (57.6%), including 11 with venous events, 7 with arterial events, and 1 with both. In a cohort of 11 patients with concurrent venous thromboembolism (VTE) and myocardial infarction (MI), 5 patients (46%) developed VTE prior to their MI, mostly presenting with deep vein thrombosis (DVT) and/or pulmonary embolism (PE). The remaining 6 patients (54%) experienced MI before the onset of VTE. Fourteen patients were described as current smokers.

PC deficiency-specific information

Median protein C activity across reported cases was 42.8% (IQR 32.3–50.5%), and the median antigen level was 44% (IQR 39.7–52.2%). Genetic data were incompletely reported; only nine cases specified mutation status, comprising eight heterozygous variants and one homozygous variant (the present case). Four reports included detailed *PROC* gene analyses identifying the following variants: c.325G>A (p.G109R), c.764T>A (p.M255L), c.577_579delAAG (p.192delK), and c.565C>T (p.R189W).

These variants are known to reduce protein C function and are consistent with a thrombophilic phenotype. Coexisting inherited thrombophilia was described in nine patients, including protein S deficiency (n=6), methylenetetrahydrofolate reductase mutation (n=1), factor V Leiden (n=1), and combined abnormalities involving antithrombin, plasminogen activator inhibitor-1, and MTHFR (n=1). A family history of protein C deficiency was noted in ten cases.

Coronary angiography (CAG) findings

In most reports, coronary angiography demonstrated thrombotic occlusion, most frequently involving the left anterior descending artery, without clear angiographic evidence of atherosclerotic plaque. Less common findings included recurrent graft thrombosis and thrombosis at atypical arterial locations, such as the aorta and the coronary sinus of Valsalva.

Management

Antithrombotic treatment approaches varied. Combination therapy with an antiplatelet agent plus an oral anticoagulant was reported in 15 patients (45.5%). Anticoagulant monotherapy was used in 9 patients (27.3%), including warfarin (n=6), rivaroxaban (n=2), and phenprocoumon (n=1). Antiplatelet therapy alone was described in 6 patients (18.2%), consisting of dual antiplatelet therapy with aspirin and clopidogrel (n=3), aspirin alone (n=2), or clopidogrel alone (n=1).

Association between variables and recurrent thrombosis

Among evaluated variables—age, smoking status, family history, protein C mutation status, and protein C activity—current smoking was the only factor significantly associated with recurrent thrombosis. Active smokers had more than a sixfold higher odd of recurrent thrombotic events compared with non-smokers (odds ratio 6.667, 95% confidence interval 1.047–42.431; p=0.045) (Table 3).

DISCUSSION

This combined case report and systematic review with pooled analysis of published case reports highlights a group of patients with protein C (PC) deficiency who developed myocardial infarction (MI), a presentation less commonly described than venous thromboembolism. The median age at MI onset in the collected cases was 37 years, which is substantially lower than the reported average age of MI in the general population (approximately 68.6±12.6 years).[47] A proportion of patients also had conventional cardiovascular risk factors, including smoking, diabetes, dyslipidemia, and hypertension. These coexisting factors may contribute to arterial thrombosis when superimposed on an inherited prothrombotic background, suggesting a possible contributory interaction rather than a single direct cause.

With respect to genetic findings, several PROC variants identified in this review have previously been described in association with venous thrombosis but not arterial events. The G109R substitution and the in-

TABLE 3. Analysis for factors significantly associated with recurrent thrombosis.

Factors	Odds ratio	95%CI	p-value
Age	1.038	00980-1.098	0.202
Family history	0.429	0.073-2.500	0.346
Male gender	0.059	0.082-3.0142	0.467
Protein C activity	1.007	0.941-1.076	0.845
Protein C level	0.917	0.822-1.023	0.122
Current smoker	6.667	1.047-42.431	0.045
Thrombophilia	1.400	0.290-6.769	0.676
Underlying disease	1.333	0.2696-0.606	0.725

A p-value<0.05 indicates statistical significance
Abbreviation: 95%CI, 95% confidence interval

frame deletion c.577–579delAAG (p.192delK) have been reported in patients with venous thrombotic disease.[48,49] The c.565C>T (p.R189W) variant at exon 7, which was also detected in our index case, has been described in prior reports from our center and appears relatively frequent in the Thai population.[50] Another variant, c.764T>A (p.M255L), has been documented only once previously in a patient with both MI and superficial vein thrombosis.[37] Taken together, these observations broaden the clinical spectrum associated with PROC mutations and indicate that arterial manifestations, including MI, may occur in selected cases.

Current recommendations do not strongly support routine testing for natural anticoagulant deficiencies in patients with arterial thrombosis.[11,12] Nevertheless, selective testing may be appropriate in younger individuals or in cases lacking an alternative explanation after comprehensive evaluation.[11,12] Also, the timing and clinical context of testing are critical for accurately diagnosing protein C deficiency. Specifically, testing during acute thrombotic events or active anticoagulation therapy can interfere with assays, leading to misinterpretation.[60] The entity of myocardial infarction with normal coronary arteries (MINCA) describes patients with coronary thrombosis in the absence of angiographic atherosclerosis.[51] Several prothrombotic disorders, including antiphospholipid syndrome and myeloproliferative neoplasms, have been reported in this setting.[52,53] A related concept, myocardial infarction with non-obstructive coronary arteries (MINOCA), refers to MI with less than 50% coronary stenosis despite evidence of atherosclerosis.[54] A pooled analysis estimated that approximately 14% of MINOCA patients have an underlying thrombophilic disorder.[55] In our review, most cases demonstrated thrombotic occlusion without clear atherosclerotic lesions on coronary angiography, consistent with a MINOCA-like pattern.[56] In such scenarios, evaluation for thrombophilia, including PC deficiency, may be considered when no other cause is identified.

Optimal management of MI occurring in the context of PC deficiency remains uncertain because evidence-based treatment guidance is lacking. In the cases reviewed, combination therapy with an oral anticoagulant and antiplatelet agent was the most frequently used approach, often with warfarin as the anticoagulant. However, the appropriate intensity and duration of antithrombotic therapy in this population are not well defined and require further study.

While smoking appeared to be associated with recurrent thrombosis (OR 6.667), the extremely wide 95% confidence interval (1.047–42.431) and the biased nature of self-selected case reports render this finding exploratory. Additionally, the small sample size restricts our ability to perform subgroup analyses to differentiate arterial from venous recurrence. These results do not provide a definitive measure of risk for the broader population but instead serve as a basis for future hypothesis-driven research.

Limitations

This study has several limitations that should be acknowledged. First, because protein C deficiency is uncommon, the number of eligible cases was limited, which reduces statistical power and the precision of estimates. Second, published case reports often lack complete clinical and laboratory details, and unreported coexisting risk factors or thrombophilic conditions may have been present. Third, the absence of a control group prevents firm conclusions regarding the magnitude of association between PC deficiency and MI. Furthermore, the reliance on case reports and small case series introduces significant publication bias, as unusual or severe clinical presentations are more likely to be reported. Consequently, applying regression models to non-consecutive, self-selected cases is subject to severe statistical limitations; such data lack a defined population denominator and are not representative of the general patient population. Despite these constraints, the compiled data provide clinically useful descriptive information regarding this rare presentation.

CONCLUSIONS

In summary, the present analysis indicates a possible association between protein C deficiency and myocardial infarction, supported by the observed frequency of recurrent thrombotic events and the predominance of non-atherosclerotic coronary findings. Screening for PC deficiency may be considered in a select subgroup of MI patients—specifically young individuals presenting with no significant atherosclerosis. In this population, testing should be pursued only after coronary angiography confirms the absence of obstructive coronary artery disease and other common thrombophilia etiologies (e.g., antiphospholipid syndrome) have been excluded.

Data Availability Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request from the Editor-in-Chief of Siriraj Medical Journal.

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DECLARATIONS

Grants and Funding Information

This was an unfunded study.

Conflict of Interest

The authors declare that they have no competing interests.

Registration Number of Clinical Trial

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Author Contributions

CK, KT, WO, and TR1 designed the study. CK, WO, and TR1 collected the data for the single case reported in this study. CK, TR1, TL, and WO collected the case report data for the systematic review. WO performed the statistical analyses. CK and TR1 drafted the manuscript, TR1 prepared the final version, and WO made critical revisions to the manuscript. CK and TR1 are co-first authors, and WO is the corresponding author. TR2, BS, and YC critically reviewed the manuscript for important intellectual content. All authors have read and approved the final version of the manuscript to be submitted for journal publication.

Use of Artificial Intelligence

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Ethics Approval and Consent to Participate

In Thailand, a case report does not require institutional review board approval; however, the protocol for the systematic review and pooled analysis of published case reports was approved by the Siriraj Institutional Review Board (SIRB) of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. Written informed consent to participate was obtained from the patient profiled in the single case report part of this study.

Consent for Publication

Written informed consent was obtained from the patient profiled in the single case report part of this study permitting us to submit details specific to his case for journal publication. A copy of that signed consent form is available upon reasonable request from the Editor-in-Chief of Siriraj Medical Journal.

INPLASY registration number: INPLASY202480047

List of Abbreviations

95%CI, 95% confidence interval; ASA, aspirin; AT, antithrombin; BID, twice daily; BS, Bundarika Suwanawiboon; CAG, coronary angiography; CARE, CAse REport; CK, Chanakarn Kanitthamniyom; CVST, cerebral venous sinus thrombosis; DLD, dyslipidemia; DM, diabetes mellitus; DVT, deep vein thrombosis; F, female; FV Leiden; factor V Leiden; HT, hypertension; IJV, internal jugular vein; IL, Illinois; Inc., incorporated; INPLASY, International Platform of Registered Systematic Review and Meta-Analysis Protocols; IQR, interquartile range; IU/dL, international units per deciliter; JBI, Joanna Briggs Institute; KT, Korakoth Towashiraporn; M, male; mg, milligram; MI, myocardial infarction; MINCA, Myocardial Infarction with Normal Coronary Arteries; MINOCA, Myocardial Infarction with Non-Obstructive Coronary Arteries; MTHFR, methylenetetrahydrofolate reductase; N/A, not available; NL, Nattawut Leelakanok; OAC, oral anticoagulant; OR, odds ratio; PAD, peripheral artery disease; PAI-1, plasminogen activatable inhibitor-1; PC, protein C; PE, pulmonary embolism; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROC gene – Protein C, Inactivator Of Coagulation Factors Va and VIIIa gene; PS, protein S; QA, quality assessment; QD, once daily; SPSS, Statistical Package for the Social Sciences; SVC, subclavian vein; SVT, superficial vein thrombosis; TL, Thanaphat Lalitrojwong; TR1, Tarinee Rungjirajittranon; TR2, Theera Ruchutrakool; USA, United States of America; VTE, venous thromboembolism; WO, Weerapat Owattanapanich; YC, Yingyong Chinthammitr

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