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Concurrent Protein C Deficiency and Myocardial Infarction: A Case Report and Systematic Review and Meta-analysis

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202480047

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 August 2024 and was last updated on 08 August 2024.

INTRODUCTION

Review question / Objective The study reports a case of MI in a patient with PC deficiency and performs a systematic review and meta-analysis to characterize MI presentations, PC deficiency details, risk of recurrence, and treatments in affected patients.

Rationale Protein C (PC) is a critical natural anticoagulant that functions in conjunction with protein S (PS) to inhibit factors V and VIII. In individuals with PC deficiency, multiple studies have demonstrated a significant association with venous thromboembolism (VTE). Data from Mahmoodi et al. indicated an annual VTE incidence of approximately 1%, with a fourfold increased risk relative to the general population.

On the other hand, the association of arterial thrombosis in patients with protein C deficiency is not well characterized. A recent systematic review and meta-analysis reported a twofold higher rate of ischemic stroke in patients with PC deficiency compared to controls. Although the results indicated some signal of association, there remains a paucity of data regarding the rate of recurrence and its influence on treatment decision-making. Data on myocardial infarction (MI) in this context are even less available. Most studies have focused on patients with factor V Leiden and prothrombin gene mutations, and the results have been conflicting. Based on the currently available data, experts suggest considering thrombophilia testing in selected patients under 50-55 years of age with arterial thrombosis after an extensive work-up has ruled out other causes. However, the British Society for Hematology emphasizes the lack of evidence linking heritable thrombophilia to arterial thrombosis. Therefore, routine testing is not recommended in this condition.

Because of the rarity of heritable deficiencies, including PC deficiency, there are currently no well-designed observational studies that assess potential associations between PC deficiency and arterial thrombosis, especially MI. As a consequence, we present a case report of a man with PC deficiency who presented with cerebral venous sinus thrombosis (CVST) followed by MI at

our center. Additionally, we conducted a systematic review and meta-analysis of cases involving PC deficiency and MI and identified risk factors associated with recurrent thrombosis.

Condition being studied Patients with PC deficiency and myocardial infarction.

METHODS

Search strategy We searched electronic databases (EMBASE, Ovid MEDLINE) with no language restrictions, from database inception to June 2024, to identify case reports or case series of patients with PC deficiency and myocardial infarction. We used the search terms "Protein C" and "Myocardial infarction." . This systematic review is reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Participant or population Adult patients (≥18 years), with a history of confirmed PC deficiency who presented with myocardial infarction.

Intervention Three investigators (CK, TL, and WO) selected the relevant articles, and extracted data independently. In cases of disagreement or questions regarding the eligibility of an article, a fourth investigator (TR) intervened to make the final decision. The three investigators (CK, WO, and TR) reviewed the baseline characteristics and outcomes of all included studies. To ensure accuracy, the extracted data were cross-checked among the reviewers.

Comparator No comparator.

Study designs to be included Systematic Review and Meta-analysis.

Eligibility criteria Articles were included if they: 1) recruited adult patients (≥18 years), 2) recruited patients with a history of confirmed PC deficiency, 3) recruited patients with MI, 4) were classified as case reports or case series (had no control arm), and 5) provided sufficient details in patient presentations. The exclusion criterion was insufficient information on PC assessments.

Information sources EMBASE, Ovid MEDLINE.

Main outcome(s) We present a case report of a man with PC deficiency who presented with cerebral venous sinus thrombosis (CVST) followed by MI at our center. Additionally, we conducted a systematic review and meta-analysis of cases involving PC deficiency and MI Information on PC deficiency.

Additional outcome(s) Identify risk factors associated with recurrent thrombosis.

Data management Using electronic searches in the EMBASE and Ovid MEDLINE databases, 15,210 potentially relevant articles were collected until June 2024. One-hundred two hundred and forty-seven duplicated articles were excluded. Three investigators (CK, TL, and WO) reviewed the titles and abstracts of the remaining 13,963 articles. Of those, 13,871 articles were excluded if they met at least one of the following three criteria: 1) Absence report outcome of interest, 2) the articles were reviews, commentaries, or editorials, or 3) reports irrelevant to participants we were interested. A total of 92 full-length articles were identified. Of those, 60 articles were excluded due to a lack of interesting outcomes and/or absence of PC information. The remaining 32 case reports and our case were included in the present systematic review. We subsequently reviewed their demographic characteristics, baseline laboratory data, clinical thrombosis, CAG findings, and treatments.

Quality assessment / Risk of bias analysis The risk of bias in the included studies was assessed by two authors (CK and TR) using the Joanna Briggs Institute (JBI) critical appraisal tool for case reports. Any discrepancies were resolved by discussion with a third author (WO).

Strategy of data synthesis Three investigators (CK, TL, and WO) selected the relevant articles, and extracted data independently. In cases of disagreement or questions regarding the eligibility of an article, a fourth investigator (TR) intervened to make the final decision. The three investigators (CK, WO, and TR) reviewed the baseline characteristics and outcomes of all included studies. To ensure accuracy, the extracted data were cross-checked among the reviewers.

Subgroup analysis No subgroup analysis.

Sensitivity analysis No sensitivity analysis.

Language restriction No.

Country(ies) involved 1. Thai/ Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand 2. Thai/ Texas Tech University Health Science Center, Lubbock, Texas, USA.

Keywords Protein C; Myocardial infarction.

Contributions of each author

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