case report

Treating symptomatic coronary artery disease in patients with Von Willebrand disease

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There is limited data on the occurrence of coronary artery disease (CAD) in patients with Von Willebrand disease and the literature is even scarce on their management. We at our institute reviewed the medical records of 198 patients with Von Willebrand disease over a period of 15 years, of which 6 were found to have symptomatic CAD. Acute coronary syndrome was noted in 3 patients while the remaining 3 had stable angina. Cardiac catheterization showed that left main coronary artery was the culprit vessel in all of these patients. In terms of management, stents were placed in 3 patients, two of them underwent coronary artery bypass grafting, and the remaining one patient was medically managed. Aspirin, and in some patients clopidogrel, was well tolerated with minimal side effects.

With better quality of treatment and treatment options, patients with congenital bleeding disorders now enjoy increased life expectancy.[1,2] A byproduct of this longevity is increased age-related co-morbidities particularly cardiovascular and cerebrovascular disease.[3–5] Although clear consensus from the American College of Cardiology and American Heart Association is available for the management of coronary artery disease (CAD) in the general population, such evidence-based guidelines are lacking for the bleeding population.[6] All we have are recommendations based on expert opinion.[7] Due to paucity of data on this subject, physicians are faced with increased challenges of managing thrombotic conditions with the use of anti-platelet therapy which can significantly increase the risk of bleeding.

Von Willebrand disease (VWD) is the most common congenital bleeding disorder in which there is either a quantitative or qualitative defect in the Von Willebrand factor.[8] Here, in this case series, we report our center's experience in the management of CAD in this specific patient population.

METHODS

This is a single center, retrospective case study conducted at Henry Ford Hospital in Detroit, Michigan. This study was approved by the institutional review board of the hospital. Initially, 350 patients with the diagnosis of presumed VWD were identified from the hospital's administrative database using the ICD-9 code (286.4), from January 1985 to December 2010. Medical records were reviewed to confirm the diagnosis. Patients with uncertain diagnosis and/or incomplete medical records were excluded from the study. Additionally, patients with acute coronary syndrome within 7–10 days of administration of VWF/FVIII or desmopressin were excluded.

Inclusion criteria

Patients diagnosed with VWD in the setting of a personal history and or family history of bleeding along with laboratory criteria of VWF:RCo<50 IU/dL; VWF:Ag<50 IU/Dl and low to normal levels of FVIII.[9,10]

Outcomes

Primary outcome was the incidence of symptomatic coronary artery disease (CAD) in this patient population.

Definitions

Patients were considered to have acute coronary syndrome (ACS) if there was documentation of myocar-

dial infarction, either STEMI (ST segment elevation), NSTEMI (non-ST segment elevation) or unstable angina. Characteristics of chest pain along with changes on the ECG (pathological Q waves, ST-T segment changes, new onset left bundle branch block) with or without serial elevation in troponin (cTn) were used to define it.[11] Patients with features of angina pectoris along with one or more cardiovascular risk factors were classified as stable angina.[12]

Statistical analysis

Categorical variables were expressed as absolute values and percentages, whereas the continuous variables were expressed as mean ± standard deviation. Statistical analysis was carried out using the PASW v18 (Cary, NC, USA).

RESULTS

Of the 350 patients identified over the 15-year period, 198 patients met the inclusion criteria, of which six (3%) patients had CAD (combination of ACS and stable angina). The mean age at the time of diagnosis was 65.5 ± 10.6 years; four out of the six patients were females. All of them had type-1 VWD. The mean Framingham score was found to be 17.43 ± 4.32. Among the risk factors, hypertension was seen in all six patients, followed by hyperlipidemia in three. Four patients had extensive smoking history, with three of them being active smokers at the time of diagnosis. VWF/FVIII replacement was given both before and after the procedure. The given dose of Humate-P was 50U/kg body weight one hour before the procedure and subsequently the same dose 12 h after the procedure for the first 24–48 h during the hospital stay.

Below is the detailed description of patient characteristics and management of their CAD.

Patient A

A 75-year-old female with a history of hypertension, hyperlipidemia and type-1 VWD (VWF:Ag 45%; VWF:RCo 13%; FVIII:60%). On initial presentation, she was found to have chest pain and cardiac troponin elevation. There was no ST segment elevation on the ECG. Cardiac catheterization showed 80–95% stenosis of proximal and mid left anterior descending artery (LAD). As this was an acute presentation requiring immediate intervention, she received VWF/FVIII replacement after the procedure. The decision was made for her to undergo coronary artery bypass grafting (CABG), following which she was started on aspirin-81 mg. No bleeding episodes were noted during either procedure. She continued to be on aspirin and was followed for a period of five years, with no recurrence of symptoms.

Patient B

A 58-year-old male with a history of hypertension, and type-1 VWD (VWF:Ag 14%; VWF:RCo 3%; FVIII:50%). He was found to have anterior myocardial ischemia on a stress echocardiogram after having complaints of typical chest pain, though without any ECG changes and with a normal troponin. Following this, he underwent cardiac catheterization which showed 80% occlusion of the LAD, in which a bare metal stent was placed. He received VWF/FVIII replacement both before and after the procedure. There were no bleeding episodes during his hospital stay. He was started on aspirin-81 mg and clopidogrel 75 mg. Minor bruising was noted within the next month, at which point clopidogrel was discontinued. He is close to ten months post operative, with no major bleeding episodes.

Patient C

A 74-year-female with a history of hypertension, hyperlipidemia, insulin dependent diabetes mellitus and type-1 VWD (VWF:Ag 15%; VWF:RCo 9%; FVIII:39%) who presented to the emergency department (ED) with complaints of chest pain. There were no ECG changes or troponin elevation. Further work-up including a cardiac catheterization showed 50% stenosis of the LAD; no intervention was undertaken at that time and the decision was made to medically manage her CAD. She received Humate-P before and after the procedure, resulting in no bleeding complications. Keeping her bleeding disorder in mind, no aspirin was given. Five years later, the patient continues to follow with us, with no recurrence of cardiac complaints.

Patient D

A 76-year-old female with a history of hypertension, peripheral vascular disease and type-1 VWD (VWF:Ag 9%; VWF:RCo 13% FVIII:98%). She suffered a massive ischemic stroke involving the left middle cerebral artery with residual right sided hemiparesis. Two years later, nuclear stress test was done for routine preoperative evaluation for an elective total knee replacement surgery, which showed anterior wall ischemia. A decision was made to proceed with cardiac catheterization, which showed 90% occlusion of the mid LAD, following which a drug-eluting stent (DES) was placed. She received factor replacement before and after the procedure