CASE REPORT

First Time Myocardial Infarction in a Rheumatic Patient After Elective Arthroplasty

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Abstract The management of perioperative cardiovascular risk in patients with rheumatoid arthritis (RA) is challenging due to the independent contribution to risk by high grade inflammatory mechanisms and the underestimation of risk by traditional cardiac risk factors alone. RA is associated with accelerated rates of subclinical atherosclerosis and markedly higher rates of both myocardial infarction and sudden cardiac death over non-RA controls. There is an absence of prospectively validated perioperative coronary heart disease (CHD) risk assessment tools for this unique patient population and available guidelines may fail to identify those patients most at risk. We examine a singular case of first time myocardial infarction after uncomplicated elective surgery in an adult RA patient with an unrevealing preoperative cardiac assessment. We also review the current literature for shared pathogenic mechanisms between systemic inflammation and atherosclerosis, discuss clinical and biologic markers such as C-reactive protein (CRP) in RA patients associated with heightened cardiac risk and discuss recommendations based on available evidence for cardiovascular risk management in this at risk cohort.

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Introduction

Clinicians managing patients with rheumatic disease in the perioperative setting face the challenge of assessing for excess cardiovascular risk due to inflammatory factors in spite of the absence of typical, validated risk specific indices. Based on meta-analysis, rheumatoid arthritis (RA) is associated with a 50% increased risk of cardiovascular disease related mortality [3]. Traditional Framingham risk factors alone underestimate cardiovascular risk in rheumatoid arthritis patients [12, 24]. Authors at our institution have previously reported a high prevalence of preclinical atherosclerosis in RA patients independent of traditional risk factors [21]. Coronary heart disease (CHD) in RA often remains unrecognized and is associated with higher rates of sudden cardiac death over non-RA patients [12].

Rheumatoid arthritis patients frequently undergo arthroplasty due to severe pain and functional limitations characteristic of the disease. Similar to traditional cardiac risk scoring, preoperative risk assessment tools may equally fail to predict those RA patients most at risk for adverse events. We describe a singular case of postoperative myocardial infarction after uncomplicated elective arthroplasty in an adult RA patient without known CHD and in whom preoperative stress testing was negative. We also review the current literature for culprit pathogenic mechanisms, potentially useful RA specific clinical and biologic markers associated with heightened cardiac risk and recommendations for perioperative CHD management in RA patients.

Case Report

A 34 year old Caucasian male with juvenile RA presented to his surgeon with complaints of worsening bilateral shoulder pain. CT imaging confirmed bilateral glenohumeral joint

destruction with marked bony deformities. After consultation with his surgeon, the patient agreed to a left total shoulder replacement. His comorbidities included hypertension and diet controlled dyslipidemia with a borderline high density lipoprotein of 40 and an optimal low density lipoprotein level of 81. He had no history of angina, myocardial infarction, heart failure, arrhythmia, diabetes or stroke and he had a high functional capacity. His BMI was 28.1. Prior surgery included a bilateral total hip replacement. Social and family histories were non-contributory. His RA was well controlled on medications including: prednisone, anakinra and leflunomide. Other outpatient medications included: amlodipine, furosemide, spironolactone, colace, losartan, folic acid, methadone and oxycodone. Pre-admission testing was notable for a normal baseline electrocardiogram (Fig. 1), normal chest radiograph, a negative adenosine nuclear stress test, normal electrolytes, serum creatinine of 1.3, white count of 11.8, and a hematocrit of 42. An erythrocyte sedimentation rate done two months prior was 17. Based on ACC/AHA criteria [8] (Table 1), he had no absolute contraindication to surgery.

A regional anesthetic block with sedation was administered and left total shoulder arthroplasty was performed without complications. Two liters of crystalloid were given intraoperatively and estimated blood loss was 200 ml. His mean arterial pressure remained greater than 75 mmHg. Postoperatively, his white count and hematocrit were 15.9 and 28, respectively. Full dose aspirin was given for deep vein thrombosis prophylaxis. During the early morning on postoperative day 2, he became acutely diaphoretic at rest and developed substernal chest pain radiating to his throat and arms bilaterally. Electrocardiogram revealed sinus rhythm with ST segment elevations in leads V2-V5 and aVL with reciprocal ST depressions in inferior leads

(Fig. 2). Therapy for acute coronary syndrome was initiated and he was transferred to the cardiac care unit. Initial cardiac troponin-I was elevated at 0.18 and ultimately peaked at 193 (Table 2). Early bedside echocardiogram revealed no wall motion abnormalities. Cardiac catheterization demonstrated a left dominant circulation with a totally occluded and thrombotic proximal left anterior descending artery and an 80% lesion in the middle left circumflex. His ejection fraction was measured at 40%. A thrombectomy was performed in his left anterior descending artery with subsequent placement of a drug eluting stent. He was scheduled for staged percutaneous intervention for the middle circumflex lesion. His anginal symptoms resolved but his course was complicated by acute kidney injury presumed due to contrast dye induced nephropathy and volume overload. The patient's creatinine peaked at 1.54 (Table 3). He clinically improved with medical management, his creatinine normalized to 1.19 and he was discharged home in stable condition on postoperative day 7. Six weeks later he underwent successful angioplasty and placement of two drug eluting stents to his proximal and distal left circumflex artery.

Discussion

This case describes a singular, serious cardiac event occurring after uncomplicated elective arthroplasty in a young RA patient without known cardiac disease. The overall one year incidence of postoperative myocardial infarction for orthopedic patients at our institution is low near 0.6% [25]. However, studies have demonstrated the risk of first time myocardial infarction in RA patients over non-RA patient controls is nearly doubled [7, 23]. Anecdotal evidence suggests the perioperative incidence of ischemic cardiac events

Fig. 1. Normal preoperative electrocardiogram.

Table 1 Summary of excerpts from ACC/AHA Perioperative Cardiac Risk Assessment guidelines

Predictors of cardiac risk	Major (may delay or cancel surgery): A. unstable coronary syndromes B. decompensate heart failure C. significant arrhythmias D. severe valvular disease Intermediate/revised cardiac risk indices: E. history of ischemic heart disease F. history of compensated/prior heart failure G. history of stroke H. history of diabetes I. renal insufficiency Minor: i.e. advanced age, abnormal ekg, rhythm other than sinus, uncontrolled hypertension
Functional capacity	i.e. metabolic equivalents
Surgery specific risk	High risk: valvular surgery Intermediate risk: i.e. orthopedic, head and neck, carotid endarterectomy, intrathoracic, intraperitoneal, and prostate surgeries Low risk: endoscopic and superficial procedures, cataract, breast and ambulatory surgeries
Non-invasive cardiac testing (when clinically indicated)	i.e. exercise versus pharmacologic stress testing; assessment of left ventricular function via echocardiogram or angiography

*Fleisher LA, Beckman JA, Brown KA, et al., 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *J Am Coll Cardiol* 2009; 54(22): e23–e44.

is heightened in RA patients with longstanding disease and previous authors have described the necessity for careful cardiac monitoring in such patients [9]. The prevalence of

cardiovascular disease in RA patients is comparable to that found in patients with the coronary risk equivalent diabetic mellitus [26]. Autopsy studies have found an increased frequency of vulnerable plaques in RA patients versus matched non-RA controls suggesting large unstable plaque rupture may account for the findings of a negative stress test and a total coronary artery occlusion in this case [2]. Contemporary cardiac screening modalities are better at detecting fixed obstructive coronary lesions rather than rupture prone thin cap fibroatheromas with lipid rich cores responsible for at least 50% of cases of acute coronary thrombotic events [22] and likely even more in RA patients. Recent advances in non-invasive cardiac imaging, however, are being developed to improve vulnerable plaque detection [5, 15].

Atherosclerosis is an inflammatory disease [22]. Shared mechanisms by which systemic inflammation is linked to atherosclerosis include: induction of endothelial dysfunction, coagulation cascade activation and alteration of lipid metabolism [22]. Pro-inflammatory cytokines such as tumor necrosis factor alpha and interleukin-6, the acute phase reactant C-reactive protein (CRP), immune complexes and serum amyloid A-rich high density lipoprotein have all been implicated in accelerating atherogenesis [14]. A particularly strong association exists between the inflammatory marker CRP and coronary disease; given that statin induced lowering of CRP is associated with a 44% decrease in the rate of cardiovascular events even in patients with normal serum lipids [20]. Marked elevations of CRP have been found postoperatively in patients undergoing complex orthopedic procedures [11]. Interestingly, although CRP levels were not measured, the acute rise of other inflammatory markers such as interleukin-6 and tumor necrosis factor alpha following complex surgical procedures has been positively correlated to a systemic

Fig. 2. Abnormal electrocardiogram during acute myocardial infarction.

Table 2 Select cardiac injury biomarker data from the patient's labs

	POD 2 Initial draw	^a 8 and 10h later	POD 3
Troponin-I	0.18	^a 193	65
CK-MB	6.3	569	130

^a Troponin-I and CK-MB values were obtained at 8 and 10h post initial biomarker lab draw, respectively.

inflammatory response and resulting acute lung injury [27]. However, the contribution of this post-operative inflammatory response to acute ischemic risk is less well defined.

Assessing CHD risk in RA patients is frequently complicated by a lack of traditional risk factors. Paradoxically, RA is also associated with reduced levels of both total cholesterol and low density lipoprotein often with concomitant reduced levels of high density lipoprotein [14]. Furthermore, deconditioning frequently limits functional capacity assessment. Markers of RA disease severity associated with the patient in this case including longstanding RA, prior arthroplasty and evidence of radiographic joint destruction, along with other indicators of inflammatory activity such as the presence of rheumatoid nodules, extra-articular disease and seropositivity, were shown by a large longitudinal cohort study to be strong correlates with future cardiovascular events [24]. Core assessments of RA disease activity include counts of swollen and tender joints, global and pain assessments with the inclusion of acute phase reactants such as CRP [6]. Previous authors have demonstrated that elevated RA disease activity scores predicted cardiac risk more accurately when biomarkers including measures of arterial stiffening such as central systolic pressure or augmentation index were used [19]. Importantly, these authors found that patients in disease remission were indistinguishable from non-RA controls. A summary of these findings are listed in Table 4.

Because prospective data is lacking, validated perioperative management guidelines for this high risk cohort do not exist. Peters et al. introduced a series of evidence based recommendations for managing cardiovascular risk in RA patients not specifically addressing the perioperative setting [18]. These authors suggest that RA be considered a cardiovascular risk factor and urge adequate control of RA disease activity with proven targeted antirheumatic drug therapies. These authors also recommend cardiovascular risk assessment and management based on available national guidelines along with incorporation of a multiplication factor specific for RA into traditional CHD risk screening models [18]. More recently, authors have suggested RA be utilized as a risk

Table 3 Select creatinine data from the patient's labs

	POD 2	POD 5	POD 7
Creatinine	0.89	1.54	1.19

Table 4 Markers of RA severity and activity potentially useful in preoperative CHD risk assessment*

Markers of RA disease severity and activity	i.e. longstanding RA, prior total joint replacement, presence of joint destruction on radiograph, rheumatoid nodules, extraarticular disease, seropositivity
Biomarkers	i.e. Acute phase reactants (i.e. CRP); measures of arterial stiffening (i.e. central systolic pressure, augmentation index)

*a) Solomon DH, Kremer JM, Curtis JR, et al. Explaining the cardiovascular risk associated with rheumatoid arthritis: traditional risk factors versus markers of rheumatoid arthritis severity. *Ann Rheum Dis* 2010;69: 1920–1925 b) Provan SA, Semb AG, Hisdal J, et al. Remission is the goal of cardiovascular risk management in patients with rheumatoid arthritis: a cross sectional comparative study. *Ann Rheum Dis* 2011; 70: 812–817.

modifier to current ACC/AHA perioperative guidelines [1]. None of these recommendations, however, have undergone long-term validation. There is insufficient trial data to support the routine perioperative use of beta-blockers and aspirin in RA patients without established CHD undergoing non-cardiac surgery. Evidence based on existing clinical trials such as POISE for beta blockers [4] along with prevention guidelines and trial data for aspirin use in at risk patients [17, 28] can be utilized in lieu of direct evidence to develop individual risk versus benefit decisions for their use taking into account the role of RA as a CHD equivalent. Along with controlling traditional risk factors, there is compelling evidence that targeted therapies for controlling the effects of inflammation in RA may help to attenuate perioperative risk. Large registry studies, not specifically addressing the perioperative period, demonstrated tumor necrosis factor antagonist biologics, disease modifying anti-rheumatic drugs such as methotrexate and statins significantly lower cardiovascular risk [10, 13, 16].

In conclusion, we emphasize that traditional CHD screening may not optimally detect all cases of subclinical coronary artery disease in rheumatic patients undergoing intermediate risk surgical procedures. A comprehensive perioperative management approach including traditional risk factors assessment and management based on available evidence, therapies aiming to control RA disease activity and vigilant hemodynamic monitoring is recommended (Table 5). There is insufficient evidence to support the routine pre or postoperative testing of inflammatory biomarkers to predict perioperative cardiovascular outcomes

Table 5 Summary of literature based perioperative recommendations for RA patients

1. Traditional cardiovascular risk assessment screening and management
2. Control of RA disease activity with the goal being remission using targeted anti-rheumatic therapies
3. Vigilant perioperative monitoring

in RA patients given the lack of clinical trials. Further prospective studies are needed to validate preoperative CHD risk assessment tools that incorporate rheumatic disease specific factors.

Disclosures

Conflict of Interest: James J. Calloway, MD; Susan M. Goodman, MD; Wesley Hollomon, MD; Linda A. Russell, MD; Daniel Krauser, MD declare that they have no conflict of interest.

Human/Animal Rights: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

Informed Consent: Informed consent was waived from all patients for being included in the study.

Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

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