CLINICAL VIGNETTE

The Approach to Medical Management in Aspirin Allergic Patients Presenting with Acute Coronary Syndromes

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Case Report

A 38-year-old male with no prior medical history except for an allergy to aspirin (urticaria) presented to the Emergency Department with accelerating back pain that had progressed over the week prior to admission. His primary care physician suggested he take non-steroidal anti-inflammatory medication but his pain persisted. The day prior to admission, his wife gave birth to their first child. On presentation, his EKG revealed ST elevations in the anterior leads and he was taken emergently to the cardiac catheterization lab (Figure 1). Coronary angiography revealed severe coronary artery disease with 90% stenosis with thrombus in the left anterior descending artery (LAD), 85% hazy lesion in the right coronary artery (RCA), and 60-70% stenosis in the left circumflex artery (LCx). He was treated with Heparin, Abciximab and Clopidogrel, and percutaneous coronary intervention (PCI) was performed. Two drug eluting stents were deployed to his mid LAD (Figure 2) and subsequently to his distal right coronary artery. After discussions between the patient and his providers regarding his post-intervention therapy options, the decision was made to proceed with dual antiplatelet treatment. The Allergy-Immunology service was consulted for aspirin desensitization and he was maintained on both aspirin and clopidogrel after discharge.

Figure 1: EKG showing acute myocardial infarction.

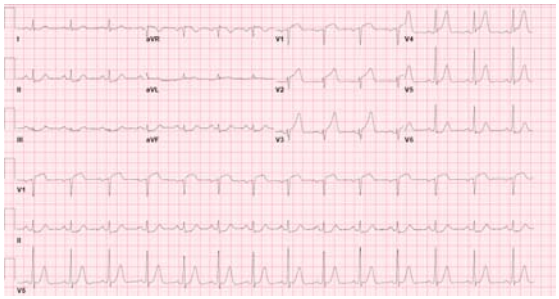
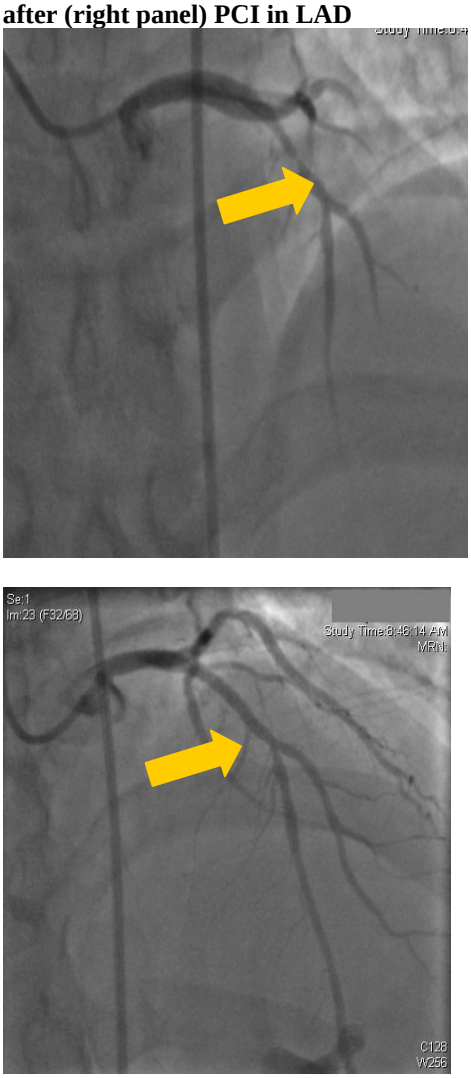


Figure 2: Angiogram before (left panel) and after (right panel) PCI in LAD



Discussion

Approximately 10% of the population reports allergy to aspirin with symptoms including rhinorrhea, angioedema, urticaria and asthma exacerbation[1]. This causes problems in patients with obstructive coronary disease undergoing

percutaneous coronary intervention. Aspirin is critical in the secondary prevention of atherothrombotic events following stent implantation[2]. Drug-eluting stents are associated with lower rates of restenosis when compared to bare metal stents, but warrants a longer duration of dual antiplatelet therapy. Historically, aspirin allergic patients have either been treated with thienopyridine monotherapy or with Clopidogrel and other anti-platelet agents such as Cilostazol despite the absence of clinical data supporting this approach[3]. Alternatively, aspirin desensitization prior to dual anti-platelet therapy has been shown to be a safe and effective method[4,5].

Aspirin hypersensitivity reactions are mediated by two concurrent mechanisms involving aspirin directed antibodies as well as excessive leukotriene production[1]. The goals of desensitization are thus to down-regulate leukotriene receptors as well as to curb antibody and leukotriene production. Numerous desensiti-zation protocols have been previously described, but all require a prolonged desensitization period lasting up to twenty-four hours. This time frame, while sufficient in certain clinical situations, is not ideally suited to patients with acute coronary syndromes. A novel desensitization technique described by Rossini et al. in 2007 is the largest to date and involved the gradual up-titration of aspirin over an approximately 6 hour period[3]. Patients were not pre-treated with diphenhydramine (Benadryl) or steroids per protocol (Table 1). The study involved 26 of 1,014 patients undergoing percutaneous coronary intervention (PCI) who had an aspirin allergy, and all of these patients received drug-eluting stents. The majority (61.5%) presented with acute coronary syndrome with 4 patients presenting with ST elevation myocardial infarction (STEMI). The STEMI patients underwent desensitization post-intervention. Of the 26 patients, the desensitization procedure was successful in 23 (88.5%).

Table 1: Aspirin Desensitization – Rossini Protocol.

Time (minutes)	**Aspirin Dose (mg)**
0	1
30	5
60	10
90	20
210	40
330	100

Disadvantages of the Rossini Protocol include a peak aspirin dose of 100mg, which precludes higher aspirin doses up to the more commonly used 325mg daily. In addition, although the duration of treatment is significantly shorter than previously protocols, it still exceeds five hours.

The Wong Protocol circumvents these concerns, with rapid titration of aspirin every thirty minutes to a peak dose of 325mg with completion within three hours.[6] Nine out of eleven patients were successfully desensitized in the study. This study used a liquid aspirin solution administered in fifteen to thirty minute intervals as shown in Table 2. Unlike the Rossini Protocol, these patients were pre-medicated with diphenhydramine (Benadryl) although there have been case reports of patients doing well without pre-medication.

Table 2: Aspirin Desensitization – Wong Protocol

Time (minutes)	Aspirin Dose (mg)
0	0.1
15	0.3
30	10
45	30
60	40
85	81
110	162
135	325

Peri-procedural Considerations:

Prior to aspirin desensitization, it is recommended that patients undergo pulmonary function testing (PFTs) since respiratory compromise can be an early manifestation of aspirin intolerance. Ideally, FEV1 should be greater than 70% predicted with a volume greater than 1.5 liters[5]. The procedure should be conducted in an intensive care setting with continuous monitoring under the guidance of an Allergy-Immunology specialist. If the patient develops asthma, a decrease in FEV1 by 25% or other allergic symptoms, the process should be discontinued and prompt treatment administered[7]. The need for aspirin therapy should ideally be re-assessed with an alternative protocol instituted if necessary.

It is important to note that if there is an interruption in the daily aspirin regimen for longer than a few days, aspirin sensitivity may return and the patient will need to be desensitized once again[7]. Despite the inter-

vention, there is an increased likelihood of a breakthrough reaction in the future[7].

Conclusion

Aspirin desensitization is a relatively safe and effective method that helps facilitate the administration of dual antiplatelet therapy to patients after PCI.

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