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Case Report

A patient who received clopidogrel with an indwelling epidural catheter☆

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Abstract A patient with a drug-eluting stent placed 18 months earlier received a thoracic epidural for perioperative analgesic control as part of her thoracotomy. Postoperatively, the patient was started on clopidogrel for secondary prevention. After consultation with the Hematology service and a platelet function assay, the patient was transfused two pools of platelets and the epidural catheter was removed on postoperative day 4. The patient then underwent hourly neurologic checks for 24 hours and was discharged several days later without any negative sequelae. If neuraxial techniques and the need for clopidogrel prophylaxis come into direct conflict, vigilance is necessary for warning signs of epidural hematoma and platelet transfusion should be considered to reverse the effects of the drug.
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1. Introduction

Patients receiving preoperative anticoagulants pose an increasingly common challenge for anesthesiologists. The anesthesiologist should be aware of the current evidence and guidelines regarding the continuation, discontinuation, and reversal of perioperative anticoagulation. A patient with a drug-eluting cardiac stent placed 18 months earlier received a thoracic epidural for perioperative analgesic control for thoracotomy. On postoperative day (POD) 1, she was started on clopidogrel with the epidural catheter still in place.

2. Case report

An 80 year old woman presented for bronchoscopy, right video-assisted thoracoscopy (VATS), and upper lobectomy for a suspected pulmonary malignancy. Her comorbidities included noninsulin-dependent diabetes mellitus, hypertension, chronic kidney disease, history of bleeding gastric ulcers, and coronary artery disease that required the insertion of a drug-eluting stent in the left anterior descending coronary artery 18 months before surgery. After placement of the drug-eluting stent, the patient underwent

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12 months of dual antiplatelet therapy with clopidogrel and aspirin, which was stopped 6 months before surgery based on the advice of her cardiologist.

The Pain Medicine service was consulted for placement of a thoracic epidural catheter for postoperative analgesia. The catheter was inserted atraumatically at the Th_6 - Th_7 level before induction of anesthesia. The case proceeded without incident during general anesthesia and the patient was successfully extubated in the operating room. In the Postoperative Care Unit, the epidural catheter was connected to a patient-controlled epidural analgesia (PCEA) pump that was programmed with a standard infusion.

On POD 1, unbeknownst to the Pain service, the patient was started on clopidogrel 75 mg by the primary surgical team. On POD 3, the Surgical service requested removal of the epidural catheter. On review of the patient's most recent laboratory tests and her current medications, it was discovered that the patient had already received three doses of clopidogrel. After discussion with the surgical team, a Hematology consult was requested; platelet function testing with the VerifyNow P2Y12 Assay (Accumetrics, Inc., San Diego, CA, USA) was recommended to assess the degree of platelet inhibition. The test was performed on POD 4 and demonstrated 161/326 P2Y12 reaction units (PRUs), corresponding to a 51% platelet inhibition. The Hematology consult also recommended administering one single donor platelet pack (approximately 6 units); however, after further discussion and review of the literature, the Pain service transfused two platelet packs and remove the epidural catheter immediately. Hourly neurologic checks were instituted for 24 hours, and the patient was discharged from the hospital several days later without any neurologic sequelae.

3. Discussion

The management of perioperative anticoagulation has been the subject of much research and the evidence is continually evolving. The most current guidelines recommend that dual antiplatelet therapy be continued for 4 to 6 weeks after placement of a bare metal stent, and one year after placement of a drug-eluting stent [1]. Patients who are unable to complete this course of therapy are recommended not to undergo reperfusion therapy, as the risks of in-stent rethrombosis outweigh the benefits of intervention (a ninefold increase in year-one mortality [2]). Given the high mortality associated with in-stent rethrombosis, many cardiologists are continuing therapy longer than one year so as to prevent very late stent thrombosis with a drug-eluting stent [3]. For patients who are currently receiving therapy, the risk of thrombosis must be weighed against the elevated risk of bleeding associated with planned or unplanned surgery [4] while anticoagulated. The American College of Chest Physicians (ACCP) states that surgeons need to be cognizant of the actual clinical risks of bleeding compared with stopping antiplatelet therapy in patients deemed to be at high risk for cardiovascular complications [5]. In patients within 6 weeks of bare metal stent placement or one year of drug-eluting stent placement, the ACCP recommends continuing dual antiplatelet therapy through the perioperative period; bridging therapy with short-acting anticoagulants is not recommended within the dual antiplatelet therapy window unless the procedure is emergent. For those patients outside the critical window but who are considered to be at higher risk for rethrombosis, the guidelines recommend stopping clopidogrel at least 5 days before elective surgery while continuing aspirin through the perioperative period if surgery contains a high risk of perioperative bleeding; in patients at low risk for rethrombosis, the recommendation is to hold aspirin so as to decrease surgical bleeding. In reference to resumption of dual antiplatelet therapy, the guidelines indicate that whatever was discontinued should be restarted within 24 hours after the procedure, assuming hemostasis has been achieved.

In addition to potentially affecting surgical bleeding, the continuation of antithrombotic therapy has implications for anesthetic techniques. Epidural catheter infusion is a common and effective modality for providing perioperative analgesia. The American Society of Regional Anesthesia (ASRA) guidelines for the insertion and removal of epidural catheters [6] suggest stopping clopidogrel for 7 days prior to placement or removal of epidural catheters. This recommendation is based on the consideration that irreversible platelet inhibition occurs with clopidogrel and the lifespan of a platelet is approximately 7 to 10 days. In spite of these guidelines, there is little concrete evidence about the specific risks of epidural hematoma-associated placement or removal of epidural catheters for patients receiving antiplatelet therapy, or the actual time frame necessary to mitigate this risk.

The overall risk of epidural hematoma following neuraxial anesthesia is estimated to be approximately one in 150,000 cases [7], and evidence from case reports indicates that patient coagulation abnormalities increase this risk. Specifically, the ASRA guidelines quote several case reports of epidural hematoma in patients receiving clopidogrel combined with other anticoagulants. In contrast, one study of 306 patients who received epidural anesthesia while also receiving clopidogrel found no events of hematoma or other complications, despite the presence of baseline sensory deficits in a large fraction of their patients [8]. Unfortunately, that series was grossly underpowered given the very low incidence of clinically significant epidural hematoma. In addition, the low incidence of epidural hematomas renders determination of the specific thresholds for safe interventions virtually impossible.

In this case, the hematologist recommended a platelet function assay to guide management. The current standard, platelet aggregometry, has shown consistency in selected studies [9]; however, it is highly operator-dependent, with poor standardization among the few centers equipped to perform the assay [10]. The test also requires a control

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