Acute Femoral Neuropathy, Shock and Abdominal Compartment Syndrome Secondary to Nontraumatic Retroperitoneal Hemorrhage Following Clopidogrel Therapy for Carotid Artery Stenting

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Abstract
An 85 year old women present with large retroperitoneal hematoma due to clopidogrel therapy after coronary and carotid stenting. A severe symptomatic femoral nerve compression syndrome and hemorrhagic shock with abdominal compartment syndrome occurred. A decompression laparotomy with packing and 48 hours delayed abdominal closure was carried out with full recovery. At 3 months follow-up an improvement in knee jerk function and paresis of the quadriceps muscle, without recovery of sensory on the lateral part of the thigh was detected. Retroperitoneal hematoma after antiplatelet therapy is rare but physicians must be aware of these complications.

Keywords: Clopidogrel; Retroperitoneal hematoma; Antiplatelets therapy complications

Introduction
Herein we report a case of retroperitoneal hematoma of the psoas muscle presenting with initially severe femoral neuropathy and secondary hemorrhagic shock and Abdominal Compartment Syndrome (ACS) in a patient receiving clopidogrel 6 months after successful carotid artery stenting.

Case Presentation
An 85-year-old woman was referred to our unit for treatment of severe left symptomatic carotid artery stenosis. The medical history revealed an insulin-dependent diabetes, hypertension and severe coronary artery disease treated by means of coronary stent placement with double antiplatelet therapy (clopidogrel 75 mg and aspirin 325 mg) one month early. No history of liver dysfunction or deficiency of coagulant factor was reported at medical history. Under local anesthesia and after heparinization (5.000 UI), a carotid wall stent (7 mm × 3 mm Boston Scientific) was successfully placed and patient was discharged in 3\textsuperscript{rd} postoperative day with the same double antiplatelet therapy for one month. At the one month follow up the aspirin therapy was stopped because of cutaneous rash and only Clopidogrel was continued.

Four months later the patient was recovered with severe pain in the left lower abdominal quadrant irradiating to left groin, thigh and leg with tenderness and nausea. No history of trauma, dysuria or haematuria was reported. Her blood pressure was 100/65 mmHg with a heart rate of 80 beats min. At physical examination abdominal tenderness without signs of local peritoneal irritation was revealed. A psoas test was positive and the pain was worsened by hyperextension of the thigh and knee. An absence of the knee jerk reflex and paresis of the quadriceps muscle with sensory loss on the lateral part of the thigh was detected. The rest of physical examination was normal. Laboratory investigation showed a hemoglobin level of 6.5 g/dl. Platelet count was within normal values. Urea nitrogen and creatinine were 28 and 1.9 mg/dl. Liver enzymes were normal.

A duplex scan examination was emergently performed showing a mixed echoic lesion within the left iliopsoas muscle. Angiography CT scan was carried out showing a large retroperitoneal hematoma of the psoas (Figure 1) and parietal muscles dissecting down to the pelvis (Figure 2). No hyperdensities were noted in the renal parenchima or perirenal space. The patient was resuscitated with intravenous fluids and received 5 units of packed red blood cells and 7 of platelets, despite the normal counts.

Patient was admitted to our intensive care unit for observation and analgesia with hemoglobin level of 9 mg/dl. Antiplatelet therapy was stopped and Enoxaparin 2000 UI was started to prevent in-stent thrombosis.
On the second day of admission patient become unwell with signs of abdominal compartment syndrome (worsening oliguria, confusion, acidosis, respiratory distress) and hypovolemia shock. A prompt intubation was carried out. His hemoglobin level dropped to 6.1 mg/dl. Arterial blood gas values at the intubation time were PH 7.14 with a partial pressure of carbon dioxide of 53 mmHg and partial pressure of oxygen of 79 mmHg. An emergent laparotomy was performed showing a large retroperitoneal hematoma within the left psoas, iliac and quadratus lumorum muscles. The groove between iliacs and psoas muscle was shallow with compression of the femoral nerve on the lateral margin of the same psoas. The iliac and psoas fascia were opened, the hematoma was evacuated and a packing was carried out. Her abdomen was closed with silastic silo (Dow Corning Corp, Midland, Michigan) and the patient was returned to the intensive care unit where she continued to improve. Postoperatively, urinary bladder pressure was followed and no elevation above 12mm HG was detected. Depacking was performed 48 hours later. Drainage was placed and the abdomen was closed. The postoperative course was normal with rapid resolution of abdominal compartment syndrome and shock. An improvement in knee jerk and paresthesia of the quadriceps muscle but without recovery of sensory on the lateral part of the thigh.

Discussion

The incidence of retroperitoneal bleeding into the iliopsoas muscle that seems to be predisposing to spontaneous Intramuscular bleeding, in patients submitted to heparin or warfarin therapy has been reported to be 6.6% [1].

In contrast retroperitoneal hemotoma due to antiplatelet therapy has been rarely described [2,3].

Clopidogrel is an antiplatelet agent introduce as a secondary prevention therapy in patients at high risk of cardiac or cerebral thrombotic events that inhibits platelet aggregation leading to prolong bleeding time and delays in clot retraction by adenosine diphosphonate.

White cell disorders and hemorrhagic complications with thrombocytopenia and platelet dysfunction seem to be the major adverse reaction [4]. In the CAPRIE and CURE studies the rate of bleeding disorders was 9.27% (1.38% major) and 8.5% (3.7% major). Major bleeding episode were due to gastrointestinal hemorrhages or punctures arterial access bleeding. No cases of spontaneous retroperitoneal hemorrhage were reported [5,6]. Hepatotoxicity or arthritis is less frequent reported adverse effect [7].

In our case we believe that the hemotoma was due to clopidogrel therapy. Indeed no history of trauma, liver dysfunction or hemotologic disorders was report in preoperative assessment and during the follow-up. The access during carotid stenting was on the right side, excluding the possibility of catheter misdiagnosed lesion on femoral/iliac arteries, the interval time between intraoperative heparin and onset of clinical sign was >6 months and aspirin therapy was stopped for cutaneous rash five months earlier. No interaction with other medications, including postoperative antibiotics, seems to be justified as potentates of clopidogrel action.

In our case femoral compression neuropathy, abdominal compartment syndrome and hypovolemic shock occurred. Femoral compression neuropathy into iliopsoas muscle hemotoma has become a well described complication of anticoagulant therapy [8]. Femoral neuropathy can results from compression of femoral nerve that origin from lumbar roots 2, 3, 4 behind the psoas muscle. It runs down between psoas and iliacus muscle and passes into the femoral canal behind the inguinal ligament covered by an inextensible iliac fascia, where compression generally occurred. The neuropathy seems due to compression of the nerve into the hematoma in the psoas body and under the iliac fascia, but the low blood supply due to the same hematoma seems to be lead to ischemic damage of the nerve [9]. Femoral neuropathy is characterized by weakness of the iliopsoas, paralysis of quadriceps femoris, patellar hyperreflexia and hypoesthesia on the anterior aspect of the tight like report in our case. Diagnosis of retroperitoneal hemotoma is easy performed by means of Angiography-CT scan.

The best treatment still remains controversial. Some authors suggest a conservative approach showing a resolution of the symptomatology in more of 68% of cases with the only discontinuation of anticoagulant/antiplatelet therapy in association with blood and platelet transfusion replacement therapy [10]. Surgery should be reserve only in cases of severe worsening of femoral neuropathy, especially in young patients or in presence of hemodynamic instability due to rapidly expanding hemotoma. Although these approach can lead to an high percentage of patients with residual disability due to irreversible nerve damage,
especially after fibrosis of hematoma can occur [11,12]. In selective cases some authors have suggest the use of the percutaneous drainage in association with lumbar embolization to avoid major surgical trauma especially in high risk patients in which the discontinuation of the same antiplatelet therapy can predispose to major cardiovascular events [13].

Abdominal Compression Syndrome (ACS) can adversely affect the cardiovascular, pulmonary, renal, gastrointestinal and intracranial system leading to renal, respiratory and cardiac failure and bacterial translocation with intestinal necrosis. ACS is generally due to increased intraperitoneal volume from edema, bowel distension, ascites, tumor, bleeding or massive fluid resuscitation, but also occurs from retroperitoneal hematoma [14]. Urinary bladder pressure according with Kron technique is the most and easiest method to determining the Intra abdominal Pressure (IAP) and a bladder pressure of 25 mmHg with renal failure not responsive to volume expansion as an indication for surgical abdominal decompression [15]. A temporary closure with Silastic bag generally protects the viscera without increasing the IAP. A delayed fascia closure can be performed when the patient has stabilized and ACS has resolved [16].

In our case the synchronous presence of severe femoral neuropathy, ACS, retroperitoneal active hemorrhagic and the need to discontinuation of antiplatelet therapy in high risk patient for stent thrombosis lead to severe issues debate regarding the best algorithm treatment. In our opinion the interruption of antiplatelet therapy should be mandatory and use of prophylactic dose of low molecular weight heparin seems to be auspicious reducing the risk of in-stent thrombosis with very low risk of worsening bleeding. A conservative management should be performed as soon as possible reserving the surgery only in cases rapidly expansive hematoma with Hemodynamic instability and ACS. In our opinion the decompression for treatment of the only femoral neuropathy seems to be more questionable especially for very high risk patients. The retroperitoneal packing lead to safe hemorrhage control and delayed closure permit a good treatment of ACS with minimal incidence of wound breakdown after 48 hours.

Conclusion

Although rare, retroperitoneal hematoma due to antiplatelet therapy is a possible and serious complication. A promptly discontinued to prevent further bleeding is needed and a surgical approach only in large, symptomatic or rapidly expanding hematoma or in presence of ACS seems to be suggest.

References