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Case report

A case report of atraumatic splenic rupture after coronary stenting and dual antiplatelet therapy: Causality or relationship?

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ABSTRACT

Introduction and importance: Atraumatic splenic rupture(ASR) is a rare event with challenging management, due to absence of clinical history of trauma and delayed diagnosis. Current clinical report could provide detailed information regarding clinical presentation and management to physicians.

Case presentation: A 61 years-old woman underwent percutaneous coronary intervention(PTCA) after ST elevation myocardial infarction(STEMI). In the first day after PTCA epigastric abdominal disconfort was reported, and new PTCA excluded early complication. During hospitalization, due to anemization and hypotension CT scan was performed which revealed ASR with large hemoperitoneum. Emergency surgical splenectomy was performed. Postoperative course was uneventful and patient started 90 mg Ticageclor twice daily in the first post-operative day(POD) plus low molecular weight Heparin and restarted dual antiplatelet therapy(DAPT) the seventh POD. During follow up, patient underwent to assessment of platelet function showing normal level of DAPT inhibition. Due to the lack of pathological aggregation activity, DAPT was maintained.

Clinical discussion: ASR is mainly linked to oncological, malformative, inflammatory and thromboembolic conditions. Despite anticoagulant and anti-aggregating drug-related ASR has been already described, we report the first case of drug-related ASR as immediate complication of PTCA due to DAPT. After surgery, careful anti-aggregating management was required to balance in stent restenosis and hemorragic risk. Assessment of platelet activity was performed to design a tailored anti-aggregating therapy.

Conclusion: Drug-related ASR is dangerous complication due to the high mortality rate and misleading symptoms. After major bleeding events, such as drug-related ASR, evaluation of platelet function could provide a tailored DAPT.

1. Introduction

Splenic rupture (SR) is the most common trauma related injuries [1]. Conversely, atraumatic splenic rupture (ASR) is a rare event and represents an even more challenging management, due to the absence of clinical history of trauma and delayed diagnosis [2].

Little is known about patients' characteristics, incidence, and etiology of ASR. Thromboembolic infarction, infectious diseases (e.g. mononucleosis, malaria), inflammatory disorder (e.g. immuno-rheumathologic), chronic infiltrative diseases (e.g. amiloidosis, haematologic), and neoplasms (e.g. Acute myelogenous leukaemia, Myeloproliferative disorders) have been variously associated in the literature with ASR, but data on clinical outcome are limited [3,4].

Drug-related ASR is even more a rare nosology. Despite some cases of antithrombotic/anticoagulant related ASR has been already described in literature, they usually occur under chronic treatment or after previous trauma [3,5], and no prior evidence of drug-related ARS as immediate complication of percutaneous transluminal coronary angioplasty

Abbreviations: SR, splenic rupture; ASR, atraumatic splenic rupture; PTCA, percutaneous transluminal coronary angioplasty; AMI, Acute Myocardial Infarction; DAPT, dual antiplatelet therapy; SCARE, Surgical CAse Report; ED, Emergency Departme; ASA, acetylsalicylic acid; LAD, Left Anterior Descending Artery; EKG, Electrocardiogram; STEMI, ST-Elevation myocardial infarction; DES, Drug-eluting stent; CT, computed tomography; LMWH, low molecular weight Heparin; POD, postoperative day; COVID-19, Coronavrus Disease 2019; LTA, light transmittance aggregometry; PRP, platelet-rich plasma; ADP, adenosine diphosphate.

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(PTCA) for Acute Myocardial Infarction (AMI) was described in literature. Hence, we report a case of hemorragic ASR in a patient undergoing double antiplatelet treatment (DAPT) in the 4th day after PTCA. The work has been reported in line with the SCARE 2020 guidelines [6].

2. Case presentation

A 61 years old female patient smoker of 15 packs/year was admitted to our Emergency Department (ED) for chest pain. Family history was positive for cardiovascular disease, but she had no family history for ASR or any genetic abnormalities. Past medical history included hypertension under medical treatment (Atorvastatin 20 mg, olmesartan 20 mg and amlodipin 5 mg daily). She had a previous episode of AMI at the age of 49, treated with left anterior descending (LAD) coronary stenting. After this procedure, the patient received acetylsalicylic acid (ASA) 100 mg daily, and no bleeding episodes were reported during follow up. Patient reported never discontinued ASA therapy after LAD coronary stenting in 2009. ED admission blood test revealed Serum hemoglobin (HB) 13.7 g/dL and platelet count 143,000/mm3. Admission electrocardiogram (EKG) revealed anterior acute ST-Elevation myocardial infarction (STEMI). Patient received ASA 300 mg prior the admission and Ticagrelor 90 mg and underwent PTCA within two hours since reported symptoms. A new Drug-eluting stents (DES) (Nevo, Cordis, Johnson & Johnson, New Brunswick, NJ USA) was placed upstream of the one previously implanted on LAD. After procedure, patient received 5000 UI of low molecular weight Heparin (LMWH) and Ticagrelor (180 mg) and then she was put on long term DAPT with ASA (100 mg, daily) and Ticagrelor (90 mg, twice a day).

Twenty-four hours after PTCA patient began to complain of epigastric abdominal discomfort. On suspicion of in stent restenosis, a new coronary angiography was performed in the second postprocedural day without signs of early postprocedural cardiac complications (e.g. Embolization, in stent restenosis, coronary laceration, occlusions of side branches). During hospitalization, patient continued to complain the same abdominal discomfort, but the abdomen was treatable without peritonism, Blumberg sign was negative, and no melena nor hematemesis were reported. In order to rule out abdominal causes of this symptoms, in the 3rd postprocedural day a complete abdomen ultrasound was performed which was negative for suspicious finding, but strongly impaired by intestinal meteorism. However, in the 4th postprocedural day HB levels dropped from 13.7 g/dL upon admission to the hospital to 6.7 g/dL with progressive hypotension. The abdomen became poorly treatable with no signs of peritonism and contrast enhancement abdominal computed tomography (CT) was performed which revealed SR with active bleeding with 11 × 12 cm peri-splenic hematic collection and hemoperitoneum with perihepatic, perigastric, parietocolic gutters bilaterally, and pelvic hematic collection (Fig. 1).

Patient was referred to the surgeon, which performed urgent laparotomic exploration. Surgery was performed by an attending surgeon with more than 30 years of experience (D·V). A large hemoperitoneum was observed with clots and multiple fracture of the spleen (Fig. 2). Due to the large hemoperitoneum and the multiples tears on the spleen surgeon decided to avoid splenoraphy and performed splenectomy. Clamp and cut of the splenic hilum was performed with Ligasure Impact (Covidien, Dublin, Ireland). A surgical drain was placed in left hypochondrium. After surgery DAPT was interrupted for 12 h and substituted with LMWH 4000 UI twice daily.

Postoperative course was uneventful for surgical or medical and no further major haemorrhagic events were found so the patient restarted 90 mg Ticagrelor twice daily plus LMWH in first postoperative day (POD). In the 7th POD surgical drain was removed, LMWH was suspended, and patient restarted DAPT. During the hospitalization, in the

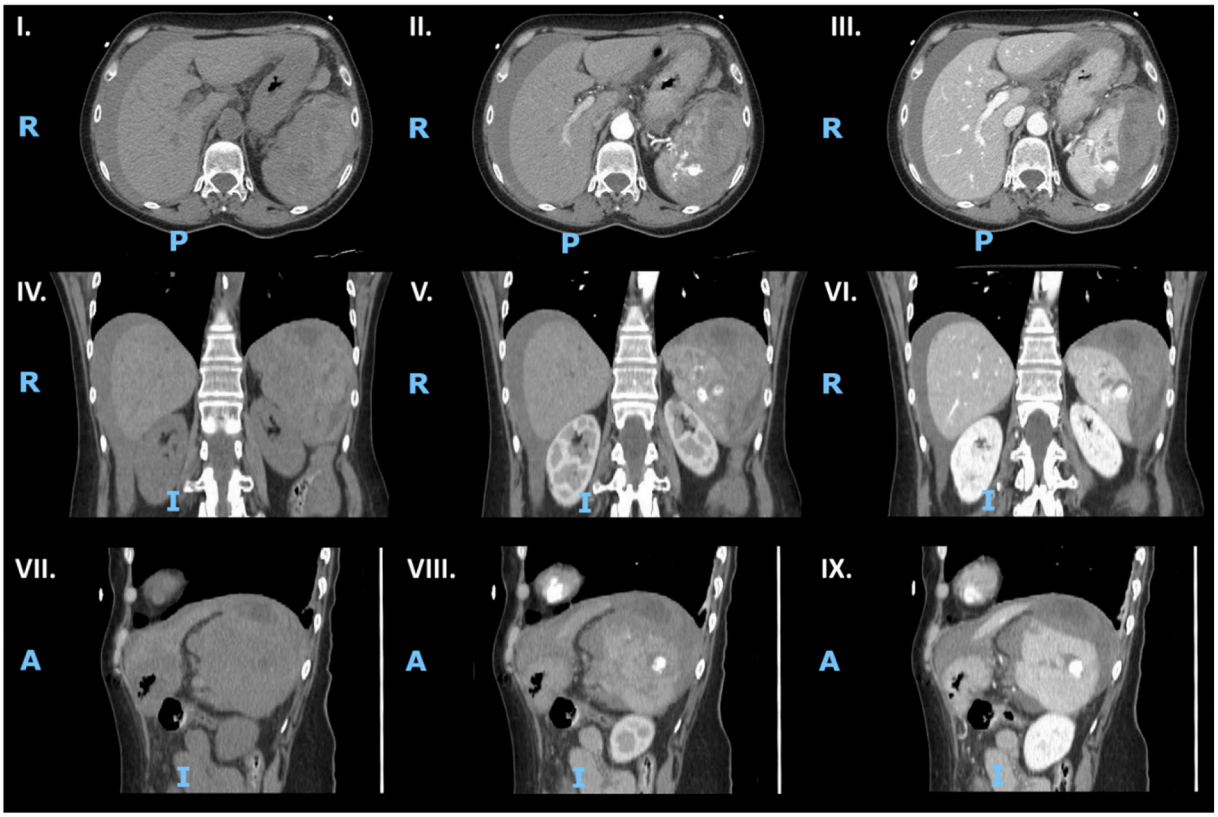

Fig. 1. Contrast enhancement CT showing splenic laceration with multiple extravasation of contrast enhancement in the early arterial phase and late arterial phase with 11 × 12 cm peri-splenic collection, hemoperitoneum with perihepatic, perigastric, parietocolic gutters bilaterally, and pelvic fluid collection. Inferior Vena cava is collapsed. From left to right I-IV-VII: baseline; II-V-VIII: early arterial phase; III-VI-IX: early arterial phase. From top to bottom: I-II-III: transverse view; IV-V-VI: frontal view; VII-VIII-IX: parasagittal view. A: anterior; R: right; P: posterior; I: Inferior. CT: computed tomography.

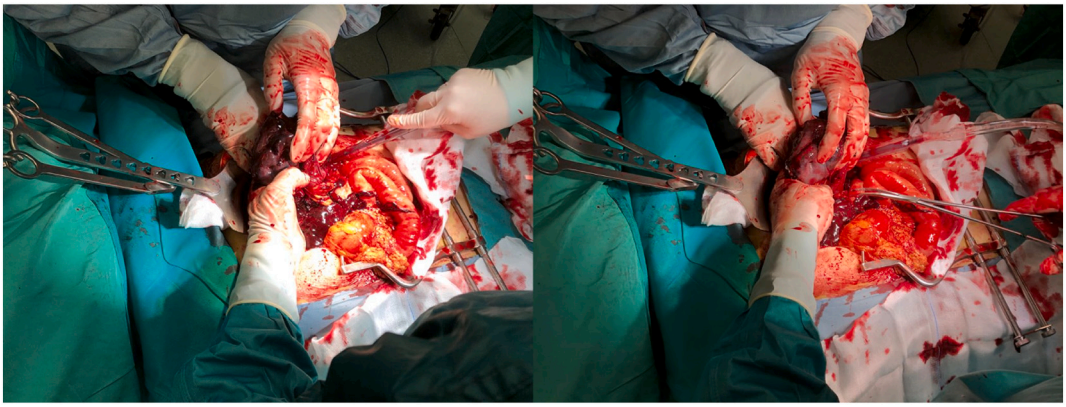

Fig. 2. Surgical splenectomy operatory room pictures. On the left: emoperitum, spleen with multiple fractures and attending surgeon exposing the ilum of the spleen. On the right: attending surgeon (D.V.) clamping splenic artery and splenic vein.

4th POD, due to a direct contact with a COVID-19 patient, ten days of hospital was performed and patient was discharged in the 14th POD with COVID-19 negative nasopharyngeal swab. One week after discharge, the patient was stable from surgical and cardiological points of view with HB 8.3 g/dL and platelet count 669.000/mm3 as a result of splenectomy.

No signs of splenic infarction or other abnormalities (inflammatory, infiltrative or neoplastic disorders) were found at histopathological analysis. Moreover, after surgery patient's history was investigated and no trauma history was reported by the patient or during hospitalization and SR was thus classified as ASR.

One month postoperative follow up no abdominal complains were reported with stable HB levels (13.3 g/dL), normal count of white blood, and platelet (530.000/mm3).

An assessment of platelet function was performed during the follow up by light transmittance aggregometry (LTA) on platelet-rich plasma (PRP) by adenosine diphosphate (ADP) 10 μM, Arachidonic acid 1 mM, and collagen 10 μg/mL,. LTA assessment was compatible with DAPT administration, thus showing a reduced risk of hemorrhage after graded re-initiation of DAPT.

After three months we contacted the patient, who reported that she was in good health and that she had resumed a normal lifestyle and stopped smoking.

Table 1
Renzulli's ASR classification. ASR: Atraumatic Spleen Rupture.

1. Neoplastic disorder
   - Malignant haematological disorders (e.g. Acute myelogenous leukaemia)
   - Non-malignant haematological disorders (e.g. Histiocytosis)
   - Primary neoplastic disorders (e.g. Angiosarcoma)
   - Secondary metastatic neoplastic disorder (e.g. Lung cancer)
2. Infectious disorder
   - Viral infectious disorder (e.g. Infectious mononucleosis)
   - Bacterial infectious disorder (e.g. Endocarditis)
   - Protozoal infectious disorder (e.g. Malaria Tertiana)
   - Fungal infectious disorder (e.g. Aspergillosis)
3. Inflammatory, non-infectious disorders
   - Local inflammatory and neoplastic disorders (e.g.Chronic pancreatitis)
   - Amyloidotic disorders (e.g. Primary amyloidosis)
   - Vascular disorders (e.g. Polyarteritis nodosa)
   - Genetic disorders (e.g. Haematological disorders)
   - Autoimmune disorders (e.g. Rheumatoid arthritis)
4. Drug- and treatment-related disorders
   - Drug-related splenic rupture (e.g. Granulocite colony-stimulating factors)
   - Dialysis-related splenic rupture (e.g. Haemodialisys)
5. Mechanical disorders
   - Pregnancy-related splenic rupture
   - Congestive splenomegaly (e.g. Liver Cirrhosis)
6. Normal spleen
   - With no triggering factor
   - With triggering factor

3. Discussion

ASR is a relatively rare event and mainly linked to oncological, malformative, inflammatory and thromboembolic conditions. In 2009, Renzulli et al. published a systematic review that reported 926 cases of ASR and classified in six different categories (Table 1) [3]. Previously, the absence of standardized nomenclature plus the rarity of the pathology led to a lack of high quality of evidence regarding patient characteristics and risk factors, incidence, etiology, outcomes, and crucially no guidelines to ease the clinical management [7,8]. Notwithstanding splenic artery embolization is an option for definitive therapy and it is described in literature [7,9], splenectomy represents the most common choice in the clinical practice [3,8].

Despite of anticoagulant and anti-aggregating drug-related ASR has already been described in literature as a dangerous complication with an high mortality rate, due to the rarity of the disease, anticoagulant and anti-aggregating drug-related ASR are usually collected together although different indications, pharmacology, and side effects [10]. In fact, regarding anti-aggregating therapy drug-related ASR, only four cases of splenic rupture on Ticlopidine [5] and three during DAPT were reported as chronic complication, respectively after 14 days, 4 weeks, and 7 months [2,9,11].

Interestingly, regarding ASR, our case report represents the first case of DAPT drug-related ASR as an immediate complication after PTCA, which occurred in the days immediately following primary PTCA and the beginning of DAPT, requiring emergency surgical procedure and careful management of DAPT after surgery.

After PTCA with DES placement, DAPT is the standard of care to prevent in stent restenosis, which could occur up to 2–10% [12]. In light of this evidence our patient was firstly investigated with coronarography after the onset of acute epigastric abdominal pain and only after worsening abdominal pain, anemia and hypotension performed contrast enhancement CT scan demonstrating ASR [13].

Additionally, careful DAPT management after surgery was required to balance in stent restenosis and hemorragic risk [14] with early reintroduction Ticagrelor therapy [13]. Despite higher risk of bleeding than other anti-aggregating drugs [15], Ticagrelor was chosen in this case due to the shorter half-life when compared with other anti-aggregating drugs [16,17].

In fact, DAPT was discontinued and reintroduced as soon as the hemorrhagic risk was acceptable according to the clinicians. Despite the discontinuation, postoperative course was uneventful for in stent restenosis or reinfarction, as confirmed in a recent study published by Cao et al. where perioperative interruption of anti-aggregating therapy was not associated with adverse cardiac events in 1092 non cardiac

surgical procedures performed within 1 year of PTCA [14].

In order to assess the risk of thrombotic and bleeding complications in our patient and to underline a possible causal relationship between DAPT and drug-related ASR, LTA on PRP test was performed Introduced in the 1960s, LTA is considered the gold standard [18,19], to assess high on-treatment platelet reactivity (insufficient P2Y12-inhibition) or low on-treatment platelet reactivity (high P2Y12-inhibition) [15]. In clinical practice both clinical conditions could result in serious complications such as trombotic events (high on-treatment platelet reactivity), or major bleeding such as ASR (low on-treatment platelet reactivity) [15]. Even if not routinely used, several authors endorsed a wider application into clinical practice of LTA [15], and recommendations for aggregation activity assessment and genotypic study in patients undergoing PTCA has been recently published [20]. However, in the current case, LTA assessment resulted in an aggregation activity compatible with DAPT administration without any other abnormalities.

The objective of this exam was to design a patient-based anti-aggregating therapy with Clopidogrel or Prasugrel as substitute of Ticagrelor [11], but in our case, due to the lack of any pathological aggregation activity finding on LTA, ASA plus Ticagrelor was maintained.

Moreover, a postoperative thrombocytosis is an expected transient event after splenectomy [21], which could potentially determine sub-optimal levels of anti-aggregating effect or conversely temporary hiding an excessive platelet inhibition in patient at risk.

In our case due to the lack of previous trauma we believe that ASR could have been caused by DAPT plus LMWH after PTCA, even without evidence of low on-treatment platelet reactivity status.

4. Conclusion

Drug-related ASR represents a rare but dangerous complication due to the high mortality rate and misleading symptoms. To our knowledge we present the first case of drug-related ASR as immediate complication after PTCA. Further studies are necessary to clarify ASR physiopathology. Low level of evidence supports the discontinuation of DAPT in non-cardiac surgery in emergency setting and further clinical evidence are needed to design safest DAPT discontinuation during surgical emergency.

In conclusion the aim of this case report is to emphasize the usefulness of evaluating platelet function with LTA after bleeding events to ensure that the patient receives a tailored anti-aggregating therapy avoiding further hemorrhagic major events. We believe that functional test as LTA should be routinary implemented in the clinical setting to avoid severe complication as ASR.

Registration of research studies

Not required for this manuscript (not first in man).

Guarantor

Dario Venditti.

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Ethical approval

For this study, ethical and ethnical approval are not required.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

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CRediT authorship contribution statement

Paolo Boccanelli: Conceptualization; Roles/Writing - original draft.
Marco Materazzo: Conceptualization; Writing - review & editing.
Francesca Santori: Data curation.
Marco Pellicciaro: Data curation.
Dario Venditti: Project administration; Writing - review & editing; Guarantor.
Michele Grande: Supervision; Writing - review & editing.

Declaration of competing of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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