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A Rare Case of Autoimmune Hemolytic Anemia after Implantation of a Drug Eluting Stent to Coronary Artery

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Abstract: ***We report a case of autoimmune hemolytic anemia following implantation of drug eluting coronary stent.71 years old diabetic and hypertensive male without any past hematological history presented with unstable angina. His coronary angiography revealed critical disease in LAD and LCx. Coronary angioplasty to LAD and LCx was done with DES (Resolute Integrity). In the 1st week following PTCA, patient developed dyspnoea for which check coronary angiography was done which showed patent stent. On further evaluation, he was found to have severe anemia. Extensive evaluation of the anemia proved it to be an autoimmune hemolytic anemia.***

Keywords: Autoimmune Hemolytic Anemia, Drug Eluting Stent, Coronary Artery

1. Case Report

71 years old male was admitted to this hospital with chief complaints of chest pain on exertion (NYHA class II) since 2 weeks before admission. He had chest pain on climbing a flight of stairs which was retrosternal pain radiating to left shoulder and used to last for 10-15 minutes and get relieved on taking rest. But, since last 4 days, he experienced similar chest pain at rest, without any precipitating factor. He denied any history of dyspnea, palpitations or fatigue. He visited this hospital with these complaints. On admission, patient was comfortable with temperature of 36.8 degree Celsius, HR of 84/min with multiple missed beats and BP was 132/86mmHg. His RR was 19/min. There was no pallor, cyanosis, palpable lymph nodes. His jugular venous examination was normal. Cardiovascular and respiratory system examination was normal. His ECG showed sinus rhythm with multiple ventricular premature complexes, without any ST-T changes. His 2 dimensional echocardiogram revealed no regional wall motion abnormality with LVEF 60%.

Past history – Patient is a case of essential systemic hypertension since 1999 and type II diabetes mellitus since 2000 for which he was on regular treatment. There is no history of any other significant disease including any hematological disease in past.

Personal history –He is non alcoholic, non smoker. His father has ischemic heart disease. There is no history of recent exposure to any toxic substance or drug.

His Hb on admission was 11.2 gm/dl, TLC was 10800/cu. mm, platelets were 2, 45, 000/cu. mm. Sr. Creatinine was 1.2mg/dl. BSL random was 347 mg/dl of blood.

Elective coronary angiography was done on 01/02/2017, which revealed 90% stenosis in LAD and 90% stenosis in LCx-OM. Thus, PTCA to LAD was done with 3.0*26mm resolute integrity stent and PTCA to LCx-OM was done with 2.75*26mm resolute integrity stent on the same day. He was treated with aspirin, ticagrelor, rosuvastatin. His post op recovery was uneventful and patient was discharged 2 days after the procedure.

On 04/02/2017, patient visited emergency room with complaints of chest discomfort and dyspnoea (NYHA class III). His HR was 116/min, BP 112/74 mmHg, RR 22/min. There were no crackles or rales on examination. He was appearing pale clinically. In view of this clinical picture and recent history of PTCA, he was taken for check coronary angiography which showed patent stents in LAD and LCx. His Hb was 5.2gm/dl, TLC 15261/cu. mm, Platelets 1, 89, 000/cu. mm. He was transfused 2 units PCVs. On evaluation of anemia, his stool for occult blood was negative, there was no hematoma at PTCA puncture site and CT pelvis did not show any retro peritoneal hematoma. His serum iron was 149mcg/dl (65-175), TIBC was 273mcg/dl (250-450), serum ferritin was 270.86ng/ml (30-300) and serum B12 was >2000. His LDH was 691U/L (86-227), serum total bilirubin was 3.41mg/dl (0-1), indirect bilirubin was 2.72mg/dl (0.1-1), direct bilirubin was 0.69mg/dl, SGOT was 38 U/L, alkaline phosphate she was 82U/L (46-116). In view of hemolytic picture, his direct and indirect coomb's test was done which were both positive (direct ++++ and indirect ++).

So, the diagnosis of autoimmune hemolytic anemia was made and he was treated with dexamethasone and azathioprine. Patient symptomatically improved. His Hb after 6 days of admission was 7.4 gm/dl, TLC was 10230/cu. mm and platelets were 1, 48, 000/cu. mm of blood. Patient was discharged on immunosuppression with stable hemodynamic status and without angina.

2. Discussion

Common causes of anemia include hemorrhage, abnormal erythropoiesis in bone marrow and hemolysis. In this case, patient underwent a percutaneous coronary intervention with placement of two drug eluting stents in his coronary arteries. Following stunting, patient was prescribed dual anti platelet therapy with aspirin and ticagrelor to prevent thrombosis inside the stent. Considering this, one would consider possibility of hemorrhage as cause of anemia in this patient. But, there was no external visible hematoma at the puncture site and CT scan of abdomen and pelvis did not show any retro peritoneal or intra abdominal hematoma. He was not bleeding from any site and also, his stool did not show any occult or visible bleeding. So, possibility of hemorrhage was ruled out in this case.

Abnormal erythropoiesis in the bone marrow due to bone marrow depression also can lead to anemia. This will be reflected as decreased reticulocyte count in peripheral blood. But, in this case, reticulocyte count was elevated, which rules out bone marrow suppression as a cause of anemia.

In this case, serum iron and B12 levels were normal. Patient had elevated LDH levels and indirect hyperbilirubinemia, which favors hemolysis as a likely cause. Hemolytic anemia can be hereditary or acquired. In this case, his peripheral blood smear did not show any abnormal erythrocytes and he denied any past or family history of hemolytic disease, which rules out hereditary hemolytic anemia. Absence of abnormal erythrocytes also makes conditions like TTP, HUS unlikely. His direct and indirect Coomb's test were positive. This confirmed autoimmune hemolytic anemia as the cause.

Patient denied any history of recent exposure to a new drug or toxic chemical recently. He also did not receive any blood transfusion prior to anemia occurrence. Considering this, we came to a possibility of autoimmunity to anti platelet drugs of drug elated by the stents. Patient was started with aspirin and ticagrelor on the day of 1st admission and anemia occurred on the 5th day after starting anti platelets. So, this makes autoimmunity to these drugs unlikely. We finally came to a final diagnosis of autoimmune hemolytic anemia secondary to placement of drug eluting stent in coronary artery.

Stents used in this patient were Resolute Integrity. These stents release zotarolimus, which is a potent anti proliferative drug used to prevent re stenosis in coronary arteries. The Resolute Integrity stent is comprised of a bare metal stent made of cobalt alloy with a Parylene C primer coat and a coating that consists of a blend of the drug zotarolimus and the BioLinx polymer system. BioLinx is a blend of the Medtronic proprietary components C10 and C19, and PVP (polyvinyl pyrrolidone).

As one kind of Sirolimus analogue, zotarolimus belongs to the limus family. With strong anti-proliferative capacities, it works through an inhibition of mTOR (mammalian target of Sirolimus). As the target protein of Sirolimus, TOR is a key regulatory kinase of protein translation, cell cycle and cell proliferation. At the carboxyl group terminus, the target protein undergoes phosphorylation to lose its decomposing activity. As a result, a series of subsequent e ects are impacted so that the cells during G1 phase fail to enter into S phase and cell migration is simultaneously inhibited. A er blood absorption, 95% of Sirolimus is distributed in erythrocytes, its plasma content takes up merely 3% and its un-conjugated form is even smaller. There were evidences of sirolimus is associated with anaemia. Zotarolimus is an analogue of Sirolimus. After blood absorption, it is also predominantly distributed in erythrocytes. While conjugated with erythrocyte, zotarolimus may present as one kind of hapten forming a complete antigen jointly with erythrocytes. Autoimmune body reactions are elicited to induce the occurrence of anaemia. In addition, all packages of zotarolimus eluting stents mention anemia as one of the side effects. Therefore, the primary cause of anaemiain this case should be of haemolytic nature due to the inherent drug of DES. Wang et al also reported a similar case of hemolytic anemia after zotarolimus eluting stent placement in 2012.

3. Conclusion

If encountering the progressive post-stent decline of haemoglobin, a physician should consider many possibilities and conduct multiple examinations. An initial possibility of haemorrhage comes to mind since haemorrhage is one major etiologic cause for post-stent anaemia. But the examinations of haemolysis and bone marrow haematopoiesis should also be conducted. A physician may rule out quickly the possibility of haemorrhagicanaemia through a large battery of examinations. For the patients with a heavy load of thrombosis within coronary artery, the anti-platelet and anti-coagulation drugs should not be discontinued since a re-occurrence of cardiovascular event may be lethal.