

Role Of Clopidogrel In Catastrophic APLA With Aspirin Intolerance: A Therapeutic Challenge

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Abstract: Catastrophic antiphospholipid syndrome (CAPS) is a rare and fatal condition that is characterized by diffuse venous and/or arterial thromboembolism within a short period of time and histopathological confirmation of small-vessel occlusion in at least one organ or tissue in the presence of positive antiphospholipid antibodies. Here we discuss a case of a 28-year-old woman with CAPS. During the first week of her hospitalization, she was diagnosed with CAPS on the basis of skin necrosis, mesenteric ischaemia, renal dysfunction, and positive lupus anticoagulant. She was treated with corticosteroids and anticoagulants. In spite of getting adequate anticoagulation, thrombotic events did not subside, hence she was given clopidogrel as an antiplatelet agent. No further thrombotic events occurred. A loading dose of clopidogrel followed by maintenance therapy may be an effective treatment option for patients with CAPS.

Keywords: Antiphospholipid syndrome, clopidogrel, skin necrosis, CAPS

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I. Introduction

Anti phospholipid syndrome (APS) is a state of hypercoagulation that is characterized by recurrent venous or arterial thrombosis and/or morbidity during pregnancy. Antiphospholipid antibodies include three main antibodies: anticardiolipin, lupus anticoagulant, and anti-b2-glycoprotein. Infection, malignancy, and certain drugs may play a crucial role in triggering APS. However, the pathophysiology of this association is unclear (1).

Catastrophic APS is a rare, abrupt, life-threatening complication. It consists of multiple thromboses of medium and small arteries occurring (despite apparently adequate anticoagulation) over a period of days and causing stroke; cardiac, hepatic, adrenal, renal, and intestinal infarction; and peripheral gangrene. Acute adrenal failure may be the initial clinical event. Patients often have moderate thrombocytopenia and other features of thrombotic microangiopathies; erythrocytes are less fragmented than in the hemolytic uremic syndrome or thrombotic thrombocytopenic purpura, and fibrin split products are not strikingly elevated. Renal failure and pulmonary hemorrhage may occur. Tissue biopsy specimens show non-inflammatory vascular occlusion. Early diagnosis and aggressive treatment are important to save the lives of patients with CAPS.

II. Materials and Methods

Lipi Halder a 28 year old female, was diagnosed a case of antiphospholipid antibody syndrome 3 months back at another institution where she presented with left upper limb ischaemia along with history of recurrent spontaneous abortion in 1st trimester (3 episodes) and her left forearm had to be amputated. APLA profile was done there which was positive. She is also a known case of COPD. This time she presented at emergency with severe breathlessness along with dyspnoea and precordial and epigastric pain.

On presentation her saturation was 90%, blood pressure 100/60 pulse 110/min regular and jvp was raised with bilateral basal crepts and poor air entry. She was treated as a case of AECOPD with heart failure. Now in this current situation as the pain and distress did not resolve with failure management the case was suspected as complication of APLA Syndrome as the patient was not on any therapy to prevent the recurrent vaso occlusive episodes, which is common in APLA syndrome. Then in a very rapid course of events the patient's urine output decreased..and the serum creatinine was raised more than 50 % in 12 hours ,indicating

renal damage. The amputated stump also became dark in colour suggestive of tissue necrosis and the epigastric pain was suspected as mesenteric ischaemia which was confirmed by usg doppler. All these evidences were indicating towards the diagnosis of Catastrophic Apla Syndrome (CAPS). Hence the patient was given iv methylprednisolone 1gm along with anticoagulation. But as the response was suboptimal with adequate anticoagulation, antiplatelet therapy was added. But the patient being a known case of COPD and had a previous history of aspirin intolerance she was given a loading dose of CLOPIDOGREL which is a P2Y12 receptor antagonist and it responded well. Patient did not experience any more thrombotic episodes and was discharged with oral anticoagulation and antiplatelets.

APLA Profile

Lupus antioagulant	105.3	Reference value 25
Anti Beta 2 glycoprotein IgM	180	<12
IgG	>200	<12
Anti Cardiolipin antibody		
IgM	52	<20
IgG	>200	<20

III. Discussion

We reported the case of a 28-year-old female patient admitted with cutaneous necrosis. During the first week of her hospitalization, she was diagnosed with CAPS on the basis of skin necrosis, renal dysfunction, mesenteric ischaemia, and positive LA. She was treated with corticosteroids, and anticoagulants. And subsequently antiplatelet in the form of clopidogrel was added. No further thrombotic events occurred after the addition of clopidogrel.

Catastrophic antiphospholipid syndrome, a severe manifestation that is observed in a small number of patients with APS, is characterized by widespread thrombosis in many organ systems (3). Being a rare disease, an optimal treatment for CAPS is not yet available. Anticoagulation therapy is the first and most important step of treatment. Unfractionated heparin is an effective anticoagulation agent. Antiplatelet therapy, in particular, can be used in addition to anticoagulant treatment in patients with arterial thrombosis (4). LMWH therapy was initiated in the present study patient in conjunction with the emergence of necrotic skin lesions. Second-line treatments include plasmapheresis and/or immunomodulatory treatments. Plasmapheresis is very frequently used in patients with CAPS. In the present study patient, we have administered Methylprednisolone at a dose of 1 g/day for 3 days, followed by 1 mg/kg/day was initiated to treat the present study patient. But the breakthrough in this case was that the patient responded to a loading dose of clopidogrel with subsequent improvement.

IV. Conclusion

CAPS is a rare and life-threatening condition. It should be quickly diagnosed, and an aggressive treatment protocol is needed. Clopidogrel is one of the choices for the effective treatment of CAPS along with the previously available choices. Because of the rarity of the disease, optimization of the treatment protocol is difficult. Hence more data is necessary to create a protocol which significantly brings down the mortality rate of CAPS.

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