Case Report

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Churg Strauss Syndrome – Case Report

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Funding Source: None
Conflict of Interest: None
Received: Aug 08, 2022
Accepted: April 02, 2022

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A B S T R A C T

We report a 49 year old male patient who presented with swelling in both thighs without pain and dyspnea. Platelet count was low (13,000/mm3) with increased eosinophils (48.9%). The patient developed a pulmonary embolism. His ADAMTS 13 level was low and was therefore diagnosed as TTP. Treatment given was corticosteroid and plasma exchange. After a year he developed a lump in his skull. The histopathology report revealed vasculitis. Due to presence of vasculitis (TTP) along with eosinophilia, the patient was finally diagnosed as a case of Churg Strauss Syndrome (CSS).

Keywords: Churg Strauss Syndrome, Pulmonary function test,Vasculitis.

Cite this article as: Noreen N, Amanat ST, Jalil SW, Irfan R, Farooq A. Churg Strauss Syndrome – Case Report. Ann Pak Inst Med Sci.2022; 18(2):135-138.doi. 10.48036/apims.v18i2.561

Introduction

TTP is a very rare but life threatening micrangiopathy. Its diagnostic criteria include Microangiopathic Hemolytic Anemia (MAHA), thrombocytopenia with or without neurological or renal involvement, and it could be without any known cause.[1] TTP is characterized by deficiency of ADAMTS 13.[2] Plasma exchange is cornerstone of treatment. TTP had an overall mortality rate of >90%, but with treatment, especially plasmapheresis, the mortality has fallen to around 10%.[3]

Churg Strauss is an eosinophilic vasculitis of small blood vessels that involves many organs, such as cardiac, pulmonary, renal, vascular, and nervous systems.[4]

Case Report

A 49-year-old male, known case of thalassemia trait, was referred for haematology consultation for thrombocytopenia, following bacterial pneumonia for which he took treatment. His recent Blood Complete Picture report showed a platelet count of 5000 and total leukocyte count of 38,000, with predominant eosinophilia. Eosinphils were 46%, neutrophils 40%. Hemoglobin was 11g/dl while ESR was 5.

His previous chest X-ray showed medium dense patchy opacities, indicating pneumonia. He gave a history of dark brown to blackish lesions on the thighs, which were itchy. He self-medicated with topical steroid creams.

On general physical examination, no significant findings were found except diminishing dark brown to blackish lesions on his thighs. Lesions were approximately 5*2 cm in size, slightly raised and thickened. However, they were non-blanchable and non-tender. Considering thrombocytopenia, he was advised steroids, 1 mg per kg and was called for follow-up after one week.

He presented to the hospital after one week with complaint of breathlessness. Blood CP and X-ray chest, echocardiography along with serum LDH and CRP were done. CBCshowed platelet count of 13,000 and total leukocyte count of 38,000, predominantly showing 48% eosinophils and 40% neutrophils. Hemoglobin was 11.2g/dl with a reticulocyte count of 10%. LDH was 496. CRP was 24. Peripheral blood film showed marked RBC fragmentation as seen in Figure I (a)

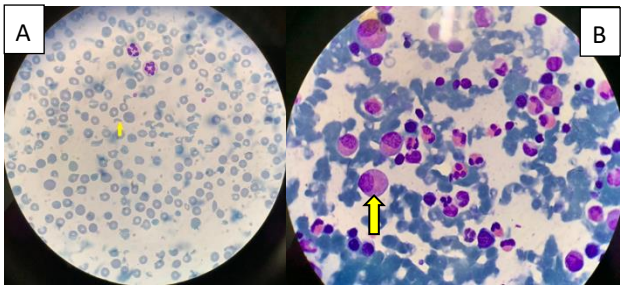

Figure I. (a) RBC Fragmentation and Thrombocytopenia, (b) Prominent Eosinophil Precursors in Bone Marrow.

Repeat X-ray chest showed cystic lesions in the lower lung zones, and the differentials were old TB and/or Infarcts. Echocardiogram was normal.

Considering on the lines of microangiopathic hemolytic anemia, most likely TTP (Thrombotic Thrombocytopenic Purpura), detailed investigations including complete autoimmune profile, D-dimers, PT, APTT, Protein C and S, ADAMS-13, Antithrombin III, Bone marrow aspirate, along with CT-pulmonary angiogram were carried out. As the tentative diagnosis was TTP, patient was admitted in the ICU and started on plasma exchange therapy.

Patient started to improve clinically after two sessions of plasma exchange therapy. His autoimmune profile including C-ANCA and P-ANCA were negative. PT, APTT, protein C and protein S were all normal. ADAMS-13 was found to be 59.4, which was mildly reduced. Bone marrow showed trilineage active marrow with increased megakaryocytes and increased eosinophil precursors as seen in figure 1 (b)

However, his D-dimers were markedly increased, levels approaching more than 7,000. CT-pulmonary angiogram showed multiple hypodense filling defects in bilateral multiple branches of pulmonary arteries, suggesting pulmonary thromboembolism. Focal lung infarction in the right lower lobe was seen.

There was bilateral distention of the superficial femoral and popliteal veins with hypodense filling defects, concerning for DVT (deep venous thrombosis). Doppler lower legs was done, which showed deep venous thrombosis of left lower limb. Right lower limb was normal, and there was no evidence of DVT.

In view of normal Protein C and S, Antithrombin-III and ADAMS-13(59.4), which was only slightly below the normal value, and no neurological signs, likelihood of TTP diminished. Due to the presence of DVT, pulmonary embolism and unexplained eosinophilia, suspicion was shifted towards vasculitis. Patient was put on oral anticoagulants. He was started on Xeralto 15mg BD, which was then increased to 20 mg OD. He was also started on Imuran 50mg BD, along with steroids.

Patient improved clinically, his platelet count gradually increased to 226,000 and D-dimers were reduced down to 5280, LDH 279, total leukocyte count 11,000 with normal eosinophils (6%) and neutrophils (26%). However, his fasting and post meal blood sugar levels were raised, due to which his steroids were tapered, and a medical consultation regarding diabetes was taken.

On 30th august, 2019 he was discharged on oral anticoagulants with a gradual tapering of steroids. He was clinically stable, Blood CP showed platelet count of 296,000 and normal leukocyte count with normal morphology. LDH and D-dimers were also within normal range. Investigation parameters are shown in figure II. Patient was advised to come for follow up.

Table 1: Investigations

INVESTIGATIONS	RESULTS
CBC	TLC: 38,300/mm^3 Neutropjils:33.2% Lymphocytes:14.3% Monocytes: 3.3% Eosinophils: 48.9% (18,728.7/mm^3) Hb: 11.6g/dl Platelets: 13,000x10^9/L
Peripheral Film	RBC fragmentation Leukoerythroblastic picture
PT, APTT	Normal
LDH	497 units/L
CRP	24
D-dimers`	>7000
Protein C, S	Normal
p-ANCA	Negative
c-ANCA	Positive
ADAMTS 13	(59.4) reference range >66.8
BM aspiration and Trephine	Increased megakarycotes. Increased eosinphilic precursors Peripheral consumption/ destruction of platelets.
CT Angiogram chest	Pulmoanary thromboembolism. Focal infarcts in posterior basal segment of right lower lobe.
CT Venogram of lower limbs	DVT in superficial femoral and popliteal vein.
Histopathology of scalp lump	Thick walled vessels with numerous eosinphils, a diagnosis of vasculitis, most likely Churg Strauss Syndrome. (ERG positive, CALDESMON positive) (highlights vessel wall media layer).

On follow-up visit he presented with shooting pain and tingling in legs and feet, on examination an enlarged cervical lymph node, and a skin lesion on the scalp was noted. The lesion was 3*2 cm in size, firm, dome shaped, flesh to yellowish in color. He was referred to the surgeon, who labeled the lesion/cyst as sebaceous cyst and planned its removal under local anesthesia. During the procedure the surgeon noted grayish to pinkish colored granulation tissue. The tissue was excised and sent for histopathological examination. The histopathology report showed; eosinophilic granulomatous inflammation of small vessels and perivascular area, marked fibrinoid necrosis of vessel walls in the presence of numerous eosinophils, lymphocytes and macrophages. The findings were suggestive of Churg-Strauss Syndrome. Histopathology report thus aided in finalizing the diagnosis of this patient, which had proved to be a challenge so far.

Patient is currently stable, his treatment regimen
1. Xeralto 20 mg 1 OD, 2. Inderal 10 mg 1 OD
3. Steroids 1/2 tab on alternate days, 4. Amaryl

Figure I: Variation in investigations with time; (a) Platelet Count variation, (b) Hemoglobin variation, (c) LDH variation, (d) D-Dimer variation

Discussion

Thrombotic Thrombocytopenic Purpura (TTP) is a type of microangiopathic hemolytic anemia (MAHA). TTP is classified into idiopathic and secondary causes. Almost half of the cases of idiopathic TTP show severe deficiency of disintegrin, and metalloproteinase ADAMTS 13 (level or activity <10%).[5] Our patient had anemia, reticulocytosis, thrombocytopenia, schistocytosis, raised LDH level and low level of ADAMTS 13.

Treatment options for TTP are plasmapharesis, FFP transfusion, steroids and immunosuppression.[6] All these treatment options were used in our patient.

Association between Thrombotic Microangiopathy (TMA) and Hyper Eosinophilic Syndrome (HES) has been reported in literature. HES (marked eosinophilia of unknown origin, >1500x106/L for more than 6 months with end organ damage) causes tissue damage due to activation of eosinophils and release of toxic substances.[7] In our case, patient was having persistent eosinophilia which initially presented as TMA, later on diagnosed as CSS.

Eosinophilic Granulamotosis with Polyangitis (EGPA), now more commonly known as Churg Straus Syndrome (CSS) is a systemic disorder which presents with eosinophilia, necrotizing vasculitis of small and medium sized arteries, and extravascular granulomas.[8] The disease was first described in 1965. It is usually associated with asthma and tissue eosinophilia.[9] Other symptoms like myalgia, fever, weight loss, sinusitis, skin involvement and pulmonary infiltrates may also be present. CT scan of chest may show consolidation, bronchial wall thickening and ground glass opacities.[10] Peripheral neuropathy, cardiac disease, gastrointestinal symptoms and renal disease may also be present. Our patient had skin lesions as well as pulmonary infiltrates.

The diagnosis of CSS often proves to be a challenge. While many patients present with asthma, it is not easily diagnosed as asthma due to CSS. CSS usually starts as asthma or allergic rhinitis, and in time it progresses to vasculitis with eosinophilia.[11] Therefore the disease can be said to present in three phases:

1) Allergic rhinitis/ asthma. 2) Peripheral eosinophilia with frequent recurrences. 3) Systemic vasculitis.

However this is not always the case as vasculitis may sometimes develop early on in the disease. Different diagnostic criteria have been proposed, including one by American Rheumatology Association[12], but none of them is definitive as patients may present with mild features, or very few features suggestive of the disease. Patients usually have increased ESR along with an increase in eosinophil count. Histopathology also aids in the diagnosis as it can give evidence of vasculitis, granulomas and tissue eosinophilia.

There is an association of CSS with anti-neutrophilic antibodies. About 40-75% of patients who have symptomatic disease, test positive for ANCA.[13] Therefore

CSS can be divided into two distinct groups, ANCA positive and ANCA negative. Research has shown that ANCA positive cases have more chances of developing glomerulonephritis, peripheral neuropathy and purpura; while those who are ANCA negative may go on to develop cardiomyopathy.[14] It has also been demonstrated that cases which test positive for ANCA have more probability of a biopsy proven vasculitis[15], as was the case in our patient. Thus it can be said that ANCA positive patients have more prominent features of small vessel vasculitis, while in ANCA negative patients, the clinical manifestations are dominated by presence of eosinophilic infiltration.[10]

The exact pathophysiology of CSS is not completely understood, although it is now known that CD4+ T cells have a role to play in the pathogenesis. These T cells and other cells including epithelial cells release cytokines and chemokines which may activate eosinophilic reactions.[16] The mainstay of treatment is corticosteroids, along with immunosuppressants.[17] Prognosis is very good, with patients responding very well to treatment. Relapses are common but can usually be treated with increased dose of steroids or immunosuppresants.

Conclusion

We conclude that Churg Strauss Syndrome is a type of vasculitis, can present with features of microangiopathic haemolytic anemia just like TTP. Overall prognosis of a treated case of CSS appears good with adequate treatment with immunosuppressive medications and steroids.

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