A Rare Presentation of Arterial and Venous Thrombosis in a Case of Bullous Pemphigoid [Bp]

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***Abstract*—Bullous Pemphigoid (BP) is the most common autoimmune subepidermal blistering disorder. Bullous pemphigoid (BP) and pemphigus vulgaris (PV) share similar pathophysiology with venous thromboembolism (VTE) involving platelet activation, immune dysregulation, and systemic inflammation. It can be prevented by regular cardiovascular evaluation in patients with concomitant risk factors.**

I. INTRODUCTION

Bullous Pemphigoid (BP) is the most common autoimmune subepidermal blistering disorder.[1] It mainly affects the elderly population. The condition is distinguished by widespread itchy hives and tight blisters beneath the skin surface.[2] This condition is defined by the existence of IgG autoantibodies that circulate in the body and target BP180 and BP230, which are proteins found in hemidesmosomes responsible for maintaining the interface between the dermis and epidermis layers of the skin. BP180 antibodies have demonstrated their potential for pathogenesis by initiating an inflammatory pathway that results in tissue destruction and, eventually, the production of blisters beneath the epidermis.[3] Venous thromboembolism (VTE) is the occurrence of blood emboli in the veins, including deep vein thrombosis (DVT) and pulmonary embolism (PE). VTE is a multifaceted condition with multiple factors involved, and its underlying causes are poorly understood.The Virchow's triad and their respective anomalies comprise the stasis of blood flow, hypercoagulability, and vascular endothelial damage. Immune modifications and inflammation of blood vessels are also recognized to have a crucial impact on the formation of blood clots and development of VTE.[5,6] As a frequent characteristic of systemic autoimmune diseases, long-lasting inflammation is presumably the primary factor responsible for maintaining a dysfunctional endothelial system and encouraging a thrombophilic condition.[5,7] Treatment with high-dose corticosteroids in acute pemphigus flares are thought to be associated with an increased risk of venous thrombosis[1] but there is no reported incidence of arterial thrombosis .We describe the case of 75 year old female diagnosed with BP and having concomitant risk factors such as old age , female gender , diabetes mellitus, and treatment with steroids .We have to enhance the need for taking preventative measures by reducing secondary risk factors and recognizing life threatening complications like pulmonary embolism in order to save the patient.

II. CASE REPORT

A 75-year-old female was brought to dermatology OPD with chief complaint of developing multiple painful vesiculobullous lesions all over the body.

Past history- she has similar complaints in the past 6 months ago for which she was taken to local outside hospital and was started on low dose steroid and azathioprine. She has stopped taking medications for 2 weeks. Known case of type 2 diabetes mellitus and bronchial asthma. No addictions.

In hospital course-

Biopsy of the lesion was taken and patient was started on IV Dexamethasone 8 mg OD.

On day 4 patient developed pain, swelling, tenderness of left lower limb and slowly developed bluish discoloration of left foot.

On examination there were Multiple erosions with erythematous base and multiple post inflammatory hypo to hyperpigmented papules, with multiple fluid filled tense vesicles/bullae over chest, hands, legs and upper back. Swelling and tenderness of left lower limb and bluish discoloration of left foot.

INVESTIGATIONS

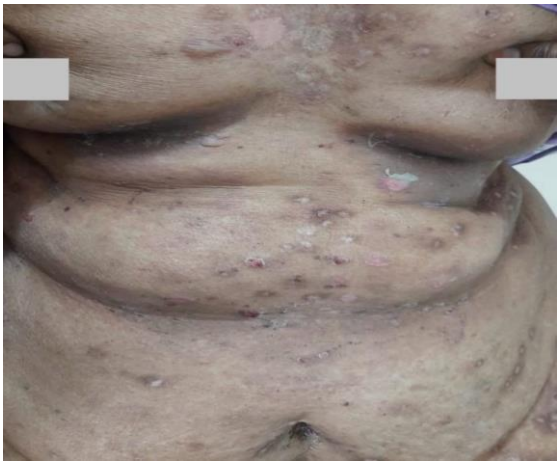
CBC, RFT, LFT, ECHO -Normal

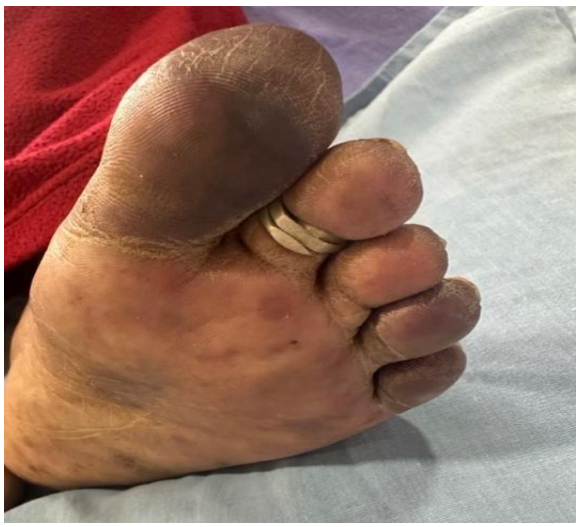
ANA - NEGATIVE
Dimer >4 microgram/ml
SMALL BIOPSY - suggested features of Bullous pemphigoid.

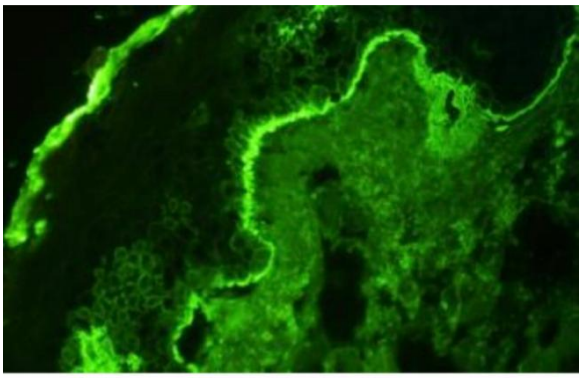
DIRECT IMMUNOFLUORESCENCE - 3+ linear positivity along Dermo epidermal junction (n serration pattern) for Ig G and C3. favoring Bullous Pemphigoid.

DOPPLER (left lower limb)- Deep venous thrombus of superficial femoral vein & popliteal vein.
Left Anterior tibial artery - echogenic focus with no flow and spectral wave pattern.

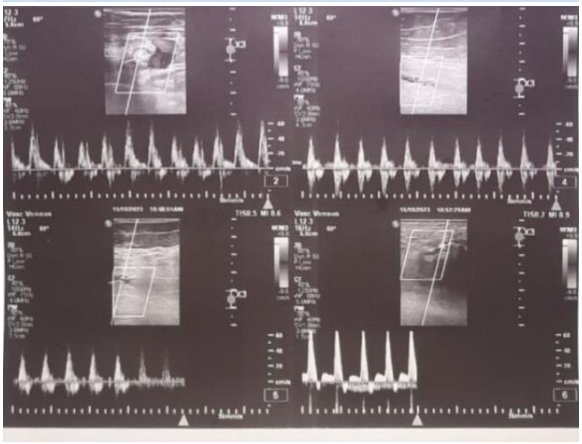
She was referred to cardiology department for further management.Patient couldn't be thrombolysed and a decision was made to initiate anticoagulants and was discharged on Tab Apixaban 5mg twice daily.







IgG



III. DISCUSSION

Risk of incident venous thromboembolism in BP patients due to its disease pathogenesis is known but their is no documented evidence of simultaneous arterial and venous thrombosis. This is a rare and first ever documented case of both arterial and venous thrombosis in a case of BP. An earlier meta-analysis conducted in 2018 examined the correlation between BP and VTE and found a strong positive relation.[7] Numerous cohort studies have examined the likelihood of VTE in individuals with BP.[9,10,12,15] Asians had a lower occurrence of VTE.In addition to genetics, old age , sexual predispositions for developing cancer , and patients undergoing surgeries are at elevated risk for developing VTE but also various other medical conditions such as cardiovascular, renal, hepatic, and chronic obstructive pulmonary diseases have been identified as risk indicators for VTE.[8]A number of autoimmune skin diseases have a higher likelihood of developing thrombosis , with BP presenting a significant risk factor.[5] Bullous pemphigoid (BP) has been linked to

a higher risk of venous thromboembolism (VTE); however, the precise timeline remains uncertain.[16] Although the majority of the conducted studies established a positive relationship between BP and VTE, two studies have indicated that BP may be an insignificant risk variable for VTE.[11,14]. Primary factors for developing thrombosis are chronic inflammation leading to endothelial dysfunction thereby maintaining an increased blood clotting tendency. [17,18] oxidative stress [13,19] leading to further endothelial damage. Coagulation pathways have been reported to been activated in BP subjects. [20] Individuals with BP has high levels of thrombin production and fibrin breakdown. [21,22] Moreover, it was observed that individuals with BP exhibited elevated levels of various proinflammatory cytokines. This indicates that BP can be classified as an autoimmune disorder characterized by widespread inflammation. [23,24,25] Type 2 inflammation is considered to initiate the production of autoantibodies in BP. [26] Eosinophils present in BP are also thought to play a role in activating blood clotting at the skin level.[27] Additionally, antiphospholipid antibodies have been identified in individuals diagnosed with BP.[28,29] Prophylactic anticoagulation may be necessary for individuals with BP, especially if they have additional VTE risk indicators, including cancer or recent hospitalization.[9]Glucocorticoids are used as the initial treatment option because they quickly produce therapeutic benefits and alleviate the acute episode. However, prolonged use may result in significant negative consequences that surpass the advantages.[30] Rituximab and other anti-CD20 antibodies have the ability to eliminate B cells that produce autoantibodies. The combination of rituximab and short-term systemic corticosteroids is currently regarded as the primary therapeutic approach.[31]

IV. CONCLUSION

BP is associated with increased risk for venous thrombosis and also arterial thrombosis. Preventive approaches and cardiovascular evaluation should be considered especially within first few years after diagnosis. Prophylactic anticoagulation and multidisciplinary care could be considered in patients with concomitant risk factors.

V. CONSENT

The consent was taken and signed by respective patient.

VI. CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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