Dermatology Practical & Conceptual

Bridging Pemphigoid Gestationis and Parry Romberg Syndrome: New Perspectives on Autoimmune Disorder Interactions

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Introduction

Pemphigoid gestationis (PG) is an autoimmune pregnancy dermatoses characterized by sub-epidermal bullae, predominantly manifesting in the third trimester [1]. The incidence of PG ranges from 1 in 2,000 to 60,000 pregnancies, depending upon the prevalence of HLA haplotypes [2]. It manifests with severe pruritus and tense bullae with periumbilical predilection [1]. Parry-Romberg syndrome (PRS), also known as progressive hemifacial atrophy, is a rare condition causing atrophy of the skin and soft tissues of the face, predominantly on the left side. The exact etiology is unknown, but various factors (viral infections, trauma, and autoimmunity) act as potential triggers. Although both these disorders have a varying etiology, microchimerism has been suggested as the possible link between the two entities. Only one such case of co-occurrence of both has been reported so far [3]. Here we report another rare case of co-existence and explore the molecular pathogenesis.

Case Presentation

A 27-year-old secundigravida (22 weeks gestation) presented with pruritic, vesiculobullous lesions for 1.5 months, progressively involving the periumbilical region, abdomen, and limbs (Figure 1A). Similar lesions were present in the previous pregnancy. Histopathology demonstrated subepidermal split with perivascular inflammatory infiltration in the dermis (Figure 1B). Direct immunofluorescence (DIF) showed linear C3 deposition (2+) at dermoepidermal junction. IIF was negative for IgG and IgG4 antibodies. The serum BP180 IgG antibody levels were 69 U/ml [ELISA- reference range: normal (negative)- less than 9 U/ml; increased (positive)- 9U/ml and greater]. Anti-BP 230 antibodies were negative. The

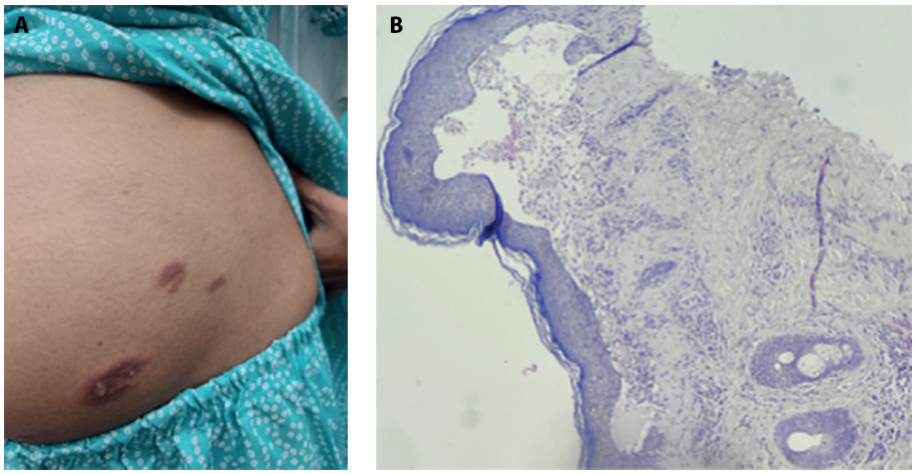

Figure 1. A: Presence of clear fluid-filled vesicles and bullae along with crusted plaques on the abdomen. B: Histopathology (H&E x10) from the vesicobullous lesions demonstrating subepidermal split along with perivascular lymphocytic, neutrophilic, and eosinophilic infiltration in the dermis.

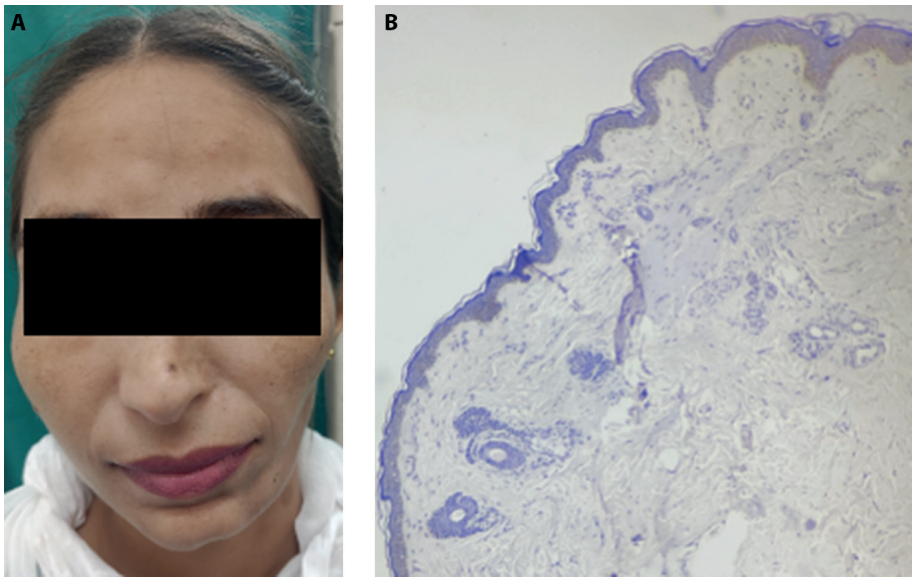

Figure 2. A Presence of deformity on the left side of face, associated with hypoplasia of the underlying zygomatic, maxillary, mandibular, and temporal area, along with malocclusion of teeth, and lifting up of the left angle of mouth. B. Histopathology (H&E x10) from the facial lesions demonstrating epidermal atrophy with loss of rete ridges and an increase in fibro-collagenous tissue along with preservation of adnexa.

investigations were consistent with Pemphigoid gestationis. Concurrently, the patient had progressive facial asymmetry since puberty. Deformity on the left side of face included hypoplasia of the zygomatic, maxillary, mandibular, and temporal areas, along with dental malocclusion and lifting up of the left angle of mouth (Figure 2A). Histopathology demonstrated epidermal atrophy, loss of rete ridges, and increased fibro-collagenous tissue with preserved adnexa (Figure 2B).

Conclusion

PG is an uncommon, self-limiting disorder, generally appearing in late pregnancy or shortly postpartum. PRS, a localized form of scleroderma, involves progressive craniofacial asymmetry due to subcutaneous tissue, muscle, bone, and cartilage atrophy, typically appearing in second decade and often within the trigeminal nerve territory. The association

between these entities has been attributed to microchimerism as the probable catalyst. Microchimerism refers to the presence of two separate and genetically distinct congregations of cells in an individual or an organ. It can occur naturally (pregnancy, abortion, sexual intercourse) or artificially (organ transplantation or blood transfusion). Apart from cell-free substances, transplacental cellular exchange also occurs in pregnancy. While this can contribute to immune tolerance during pregnancy, it might also be implicated in the pathogenesis of immune diseases such as PG and PRS. This phenomenon, termed "bad microchimerism" or "immune-cell microchimerism," has been linked to the ultimate destruction of maternal tissue. It is proposed that fetal cells trigger an autoimmune reaction in maternal circulation, leading to the onset of PG lesions. The resolution of lesions after delivery coincides with the disappearance of the triggering fetal cells from the circulation [3]. Similarly, nearly all the women with scleroderma have been found to have HLA-compatible fetal cells and Y chromosome-positive cells in the fibrotic maternal tissue indicating "fetal microchimerism," the most plausible trigger for autoimmunity [4,5]. The occurrence of PRS in childhood or early adolescence is further supported by the fact that probable sources of acquired foreign cells could be maternal or genetic material from a vanished twin or from a twin or older sibling which lie dormant in the fetal circulation, until an unknown trigger leads to disease. To date, only one other case documenting the concurrent presentation of both the conditions has been reported in literature [3]. Both these cases demonstrate classical clinical and immunopathological findings consistent with PRS and PG in a multigravida, including characteristic subepidermal blister formation, linear deposition of complement component C3 at the dermo-epidermal junction, and elevated serum anti-BP180 IgG antibodies. However, there was no history of an obvious trigger of PRS in the present patient (chicken pox was mentioned as a probable trigger in the previous report). Furthermore, the present patient reported the history of PG in the previous pregnancy as well, with positive fetal outcome (no history of vesiculobullous disease in the first child), and onset of similar lesions in the second trimester of the current pregnancy, coinciding with the onset of fetal cell transfer into maternal circulation, which usually intensifies with the gestational age and regresses postpartum (parallel to the course of PG in pregnancy). These similarities and distinctions underscore the clinical heterogeneity and potential coexistence of autoimmune conditions.

Herein, we make an attempt to explore the molecular pathogenesis and identify the missing link between these two disorders. However, this association remains conjectural, and further research is required to establish a link between these disorders so as to contribute towards the management of these unrelated disorders having a potentially unified etiology.

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