

**BULLOSIS DIABETICORUM INVOLVING AN UNUSUAL SITE-A DIAGNOSTIC DILEMMA; MANAGED SUCCESSFULLY WITH ANTIDIABETIC DRUGS: A CASE REPORT**Rakesh Tilak Raj<sup>1</sup>, Hemant Kumar<sup>2</sup>, Surinder Pal Singh<sup>1</sup><sup>1</sup>*Department of Dermatology, Venereology and Leprosy, Government Medical College and Hospital, Patiala (Punjab), India*<sup>2</sup>*Consultant Pathologist, Military Hospital, Patiala (Punjab), India*

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**Abstract**

A case of Bullosis diabeticorum (BD) affecting unusual sites involving anterior abdominal wall and axilla in a female with newly diagnosed type 2 diabetes mellitus (T2DM) without antecedent trauma and drug intake is being reported for its rarity. Dermatologists must be made aware of this under diagnosed possibility in diabetes whose status is unknown after considering direct immunofluorescence studies to exclude other similar histological and immunological entities.

**Key words:** Bullosis diabeticorum (BD); type 2 diabetes mellitus (T2DM); Oral hypoglycemic drugs**Cite this article:**

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**What is known?**

- Occurrence in long standing cases of diabetes as a complication
- Etiology is not well defined.
- Tense clear blisters on normal skin
- Treatment is conservative

**Introduction**

Bullosis diabeticorum (BD) is a rare, blistering condition of unknown etiology, being unique to long standing cases of diabetes [1]. Its yearly reported incidence is 0.16% in a tertiary diabetes care institute with a male preponderance ratio of 2:1 as compared to female [2]. The hall mark of the diagnosis is by exclusion of other similar entities by clinico-pathological correlation and after ruling out immunological components [3]. Although lack of control of diabetes is a predisposing factor in its causation yet glycemic control does not appear to have a direct correlation with bullae formation [1]. However, we report a rare case of BD with atypical presentation of nonacral haemorrhagic bullae on anterior abdominal wall and axilla in a female with newly diagnosed T<sub>2</sub>DM that responded to the glycaemic control with antidiabetic drugs.

**Case Report**

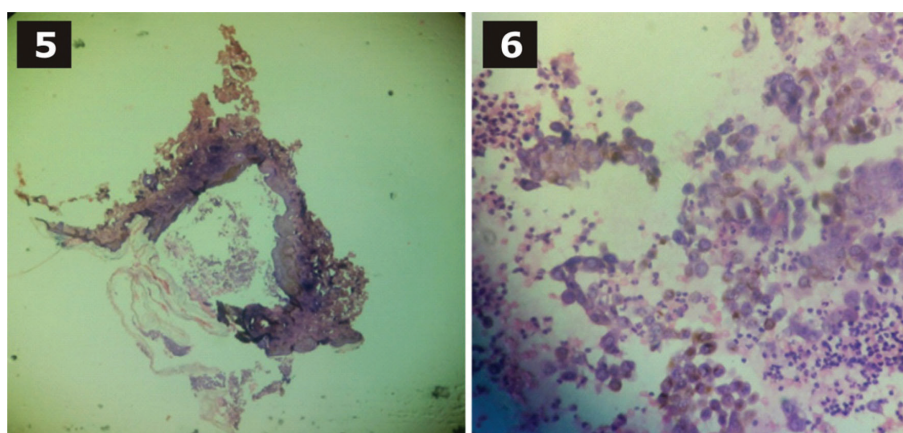
A 50 years old housewife reported in outdoor patient unit of Department of Dermatology, Venereology and Leprosy of Government Medical College and Rajindra Hospital, Patiala with complaints of multiple, painless, large, haemorrhagic blisters of 3 weeks duration developing overnight, involving the anterior abdominal wall and right axilla (Figs. 1, 2) without antecedent trauma, diabetes, photosensitivity or drugs intake. There was neither any medical illness nor family or personal history suggestive of autoimmune and allergic diseases. Cutaneous examination revealed multiple, discrete, large, semiflaccid and nontender bullae, of varying sizes measuring 5cm<sup>2</sup> to 10cm<sup>2</sup> in diameter containing haemoserous fluid. They had asymmetrical distribution along with collapsed blister roof. Some lesions were having red erythematous surface with central and peripheral haemorrhagic crusting.

Nikolskys sign was negative and remaining skin was normal, with no involvement of any of the mucous membrane. There was nothing suggestive of neuropathy or symptoms of intermittent claudication. Physical, neurological and mental status examination were normal. The patient was investigated and all other laboratory tests were normal except fasting blood sugar levels which was 320 mg/dl; urine sugar was 4+ with traces of albumin. No ketone bodies were found, HbA1c was 10.8% and had a normal anion gap. Urine for uroporphyrins, smears and cultures for bacteria, fungus were negative. A 4mm incisional skin biopsy of the lesion showed stratified squamous epithelium lining exhibiting hyperplasia, hyperkeratosis and thinning at places of epidermis. Evidence of subcorneal bullae showing many acantholytic cells along with infiltrate consisting

predominantly of polymorpho-neutrophils (Figs. 5, 6). Dermis showed collagenized odematous stroma along with skin appendages. Immunofluorescence and ANA titre studies were negative excluding immunobullous and autoimmune diseases. On the basis of histopathology, immuno-fluorescence and diabetic status; the patient was diagnosed as a case of Bullosis diabeticorum. The patient was treated with a combination of oral metformin 500mg with glipizide 5mg per day. Patient recovered uneventfully in two weeks with residual dyspigmentation (Figs. 3, 4) but without any scarring and her fasting glucose levels were 110 mg/dl at the time of discharge. The follow-up of patient for 6 months did not show any recurrence of BD, while HbA1c (6.0%) and other routine tests were in normal range.



**Figure 1 - 4.** 1. Multiple, large, collapsed, blister roof over erythematous base at baseline (Day 1); 2. Multiple, large, collapsed, blister showing haemorrhagic crusting; 3. Lesions in healing phase after two weeks of oral hypoglycemic treatment; 4. Lesions in healing phase after six months of follow-up.



**Figure 5 and 6.** 5. Histopathology of Bullosis diabeticorum showing subcorneal and focally intraepidermal split (Hematoxylin and eosin stain, X100); 6. Higher power view of subcorneal bullae showing many acantholytic cells along with infiltrate consisting predominantly of polymorpho-neutrophils (Hematoxylin and eosin stain, X 400).

## Discussion

Bullosis diabeticorum (BD) is a rare dermatosis occurring in 0.5% of diabetic patients with 112 cases described in literature [4,5]. It commonly occurs in long standing type 1 diabetes mellitus [T<sub>1</sub>DM] with vascular or neurological complications but it may also occur in T<sub>2</sub>DM [1,4,6]. The common findings of these blisters are that they vary in size from a few millimeter (0.5cm) to several centimeters (10cm), tense, nontender, arising on normal skin, containing clear fluid, involving the acral and distal extremities. They resolve within 2-5 weeks without scarring and most of the cases have recurrences [1,5,6]. Though feet and distal extremities are often effected, blisters can occur rarely on trunk [3,6,7]. In this case, there was non acral presentation which was rare. However, various hypotheses have been proposed regarding the production of bullae i.e., lower threshold for suction that induced blister formation, trauma, ultra violet exposure, nephropathy, alterations in carbohydrate metabolism, immunoglobulin mediated vasculitis and ischemic cationic imbalance due to diabetic nephropathy [1,8]. Larsen et al [1] suggested that poor regulation of blood glucose to be an important factor and Wilson et al [10] confirmed development of new bullae in patients with hyperglycemia when their blood glucose levels varied between 79 mg/dl-340 mg/dl suggesting a correlation between hyperglycemia and bullae formation. Histopathologically, hemorrhagic bullae have the cleavage plane below the derma- epidermal junction and they heal with scarring, atrophy and with destruction of anchoring fibrils [1]. In this case, blisters were multiple, large, semi-flaccid, haemorrhagic, subcorneal bullae with many acantholytic and polymorphic neutrophilic cells that were at variance with cases described earlier in literature i.e., it involved nonacral sites, in a prediabetic female diagnosed as T<sub>2</sub>DM without any features of dermatopathy, neuropathy or nephropathy and with a histopathology of acantholytic cell. The Immunofluorescence and anti-nuclear antibody (ANA) titre studies were negative excluding immunobullous and autoimmune diseases. The

response to oral hypoglycaemic drugs within two weeks, with dyspigmentation and without having any recurrence or scarring during the six months follow-up suggests the diagnosis of BD, which is a diagnosis of exclusion. It may have occurred spontaneously or as a result of complication of diabetes posing a diagnostic dilemma and needs further research to establish causal relation with diabetes.

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### What is new?

- The truncal involvement is a rare presentation of this disease occurring in a newly diagnosed female of T<sub>2</sub>DM
- No neuropathic, nephropathic, dermatopathic features.
- Haemorrhagic Bullae with acantholytic cell on histopathology.
- Response to antidiabetic drugs.