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Paraneoplastic Pemphigus Presenting as Toxic Epidermal Necrolysis

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Abstract

Polymorphous skin lesions have classically been described in paraneoplastic pemphigus (PNP), but it can present as toxic epidermal necrolysis (TEN) though this type of presentation is extremely rare. We report a case of PNP presenting as TEN in a young male patient. Patient had history of fever and diarrhoea six weeks before starting of lesions in oral cavity, for which he was treated with injectable medicines. Then patient developed generalized necrosis and peeling of skin with involvement of conjunctiva, oropharynx and genital mucosa. For this, the patient was given intravenous dexamethasone considering it as TEN, but after transient improvement initially skin lesions recurred when dose of dexamethasone was reduced. On seventh day, patient developed few circular deep ulcers over arms and back. Nikolsky sign was positive with tzanck smear showing acantholytic cells. Hence, we added PNP as one of the differential diagnosis. On further investigations patient was found to have B cell lymphoma in mediastinum and skin biopsy and direct immunofluorescence were confirmative of PNP. Unfortunately, patient then succumbed to death due to multi-organ failure and electrolyte imbalance. The onset of PNP can be as acute as TEN and clinical picture being initially undistinguishable, high index of suspicion is required in diagnosis.

Key words: Acantholysis; fluorescent antibody technique, direct, pemphigus; stevens-johnson syndrome

Introduction

Paraneoplastic pemphigus (PNP) or paraneoplastic autoimmune multiorgan syndrome (PAMS) is characterized clinically by polymorphic skin lesions with neoplasia. As described by Anhalt GJ et al PNP has mucocutaneous and systemic presentation.[1] PNP presenting as Toxic epidermal necrolysis (TEN) is very rare.[2,3] Most common malignancy reported with PNP is B cell lymphoma.[4,5]

Hisopathology from lesion showed acantholysis, suprabasal cleft, dyskeratotic keratinocytes, basal cell vacuolization and exocytosis of inflammatory cells. The distinctive feature of PNP is presence of dyskeratotic keratinocytes in all layers of epidermis and around zone of acantholysis. Though immunoprecipitation is highly sensitive, direct immunofluorescence (DIF) showing combination of intercellular and subepidermal deposition of immunoreactants is a clue to diagnosis. DIF in case of TEN shows diffuse intraepidermal deposition of immunoreactants.[6]

Camisa C et al has revised diagnostic criteria for PNP.[7] Major criteria include polymorphic skin eruptions, neoplasia and immunoprecipitation of specific antibodies. Minor criteria include histological evidence of acantholysis, DIF showing intercellular and basement membrane staining and indirect immunofluorescence (IIF) staining with rat bladder epithelium. Three major or two major and two minor criteria are needed for diagnosis.

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Case report

A 26-year-old male patient was referred to department of dermatology from another tertiary care hospital. Patient had history of oral ulceration for last six weeks which had started after treatment for episode of fever and diarrhoea with unknown injectable medicine at primary care centre. Evaluation of case record of referring tertiary care hospital revealed that patient was treated with intravenous 12 mg dexamethasone along with other supportive therapy. But patient then developed generalized skin necrosis and peeling of skin (>90% BSA- body surface area) along with involvement of conjunctiva, oropharynx and genital mucosa as the dose of dexamethasone was reduced to 8 mg after 7 days. So, dose was escalated to 12 mg of dexamethasone without remarkable improvement and patient was referred to our centre. We continued patient's management with injectable 12 mg of dexamethasone, intravenous fluid replacement, broad spectrum antibiotics keeping TEN as our primary differential diagnosis. On 7th day of presentation patient developed few circular deep ulcers of < 1 cm size over back and upper limb over background of necrosed skin (Figure 1). There were few bullous lesions along with multiple erosions in palms and diffuse peeling in planter surface (Figure 2). Nikolsky's sign was positive. Hence, we added PNP as one of the differential diagnosis. Patient had low haemoglobin (8.8 gm/dl), electrolyte imbalance (Sodium-126.5, potassium 3.3, chloride-93.1 mmol/L), ESR-42 mm/hour and pus culture and sensitivity showed methicillin resistant *Staphylococcus aureus* and multidrug resistant *Klebsiella.* Tzank smear showed multiple acantholytic cells. Skin biopsy showed dyskeratotic keratinocytes, suprabasal clefts with loss of intercellular junctions between suprabaslal keratinocytes and mixed inflammatory infiltrate in superficial epidermis. DIF showed IgG positivity in intercellular space in epidermis and at basement membrane zone (Figure 3). Computed Tomography (CT) scan (plain and contrast enhanced) scan showed mass of 8.8 x 6.7 x 12 cm in posterior mediastinum with multiple subcentrimetric lymph nodes in bilateral axillary region. CT guided biopsy of same was suggestive of lymphoma. Immunohistochemistry of same showed positivity for LCA and CD-20 suggesting B cell lymphoma (Figure 4). Patient was started on intravenous 12 mg of dexamethasone, cefipime-tazobactum 1.125 mg thrice daily, linezolide 600 twice daily along with other supportive therapy and local care. Despite of fluid replacement with normal saline patient had persistent hyponatremia. Serum Anti-diuretic hormone estimation was not done because of non-availability at our centre. Patient's haemoglobin also decreased gradually to 4 gm/dl because of blood loss from erosions for which two packed cell volumes (PCV) was given. Patient's general condition continued to deteriorate hence chemotherapy could not be started. Eventually patient succumbed to death due to metabolic acidosis (pCO2: 27.9, HCO3: 18.2, Lactic acid: 3.02) and multi-organ failure on 13th day of admission.

Discussion

Most of the cases of PNP are reported beyond the age of 45 but our patient was quite young, only 26 years of age. [1,2,3,8]

Initially our patient had generalized skin necrosis and peeling of skin with multiple mucosal sites involvement and presence of misguiding history of taking some

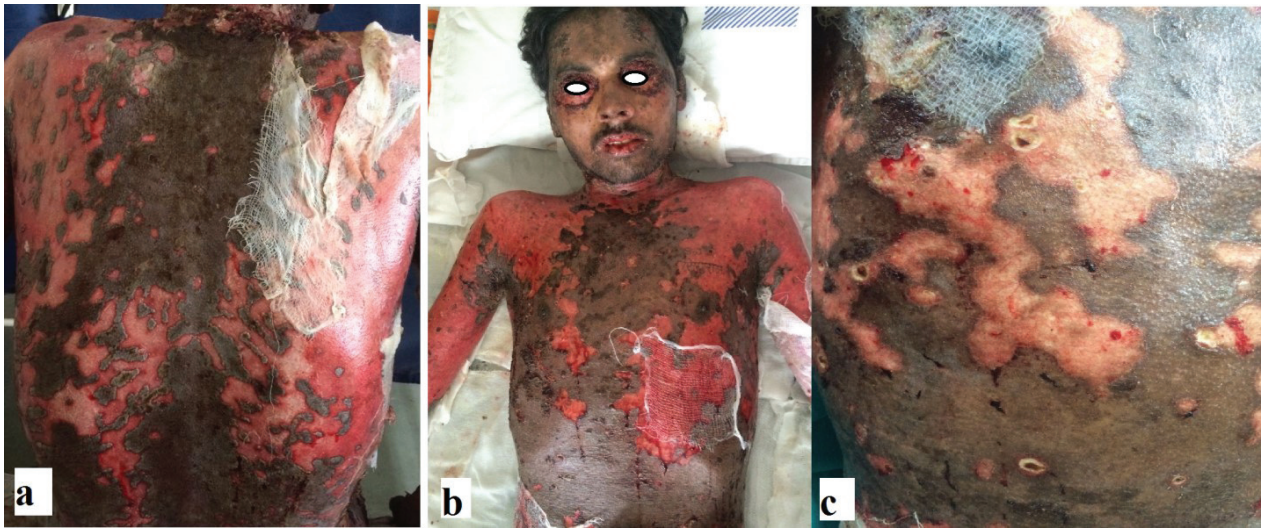

Figure 1: (a,b) Generalized skin necrosis with mucosal involvement (c) Development of circular deep ulcers over back on 7th day of admission.

parenteral medicine followed by development of oral and skin lesions prompted us to suspect TEN. Development of multiple ulcers, blisters and poor response to therapy made us to revise our differential diagnosis. In our patient clinical presentation was strongly suggestive of TEN. Malignancy can be aetiology for both TEN and PNP, so it was difficult to differentiate both only on clinical presentation. Despite of extensive search we could only find two cases of PNP mimicking TEN reported till now.[2,3] Martín García et al has described confluent area of denudation involving 60% BSA in PNP mimicking TEN though lesions were polymorphic to start with.[8]

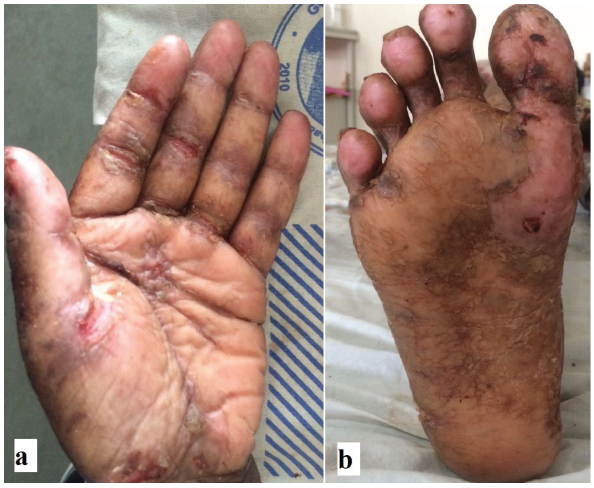

Figure 2: (a) Bullous lesions with erosions over palm (b) peeling of skin over soles.

According to revised criteria for diagnosis of PNP proposed by Camisa C et al, our patient initially fulfilled only one major criteria (neoplasia) with two minor criteria of histological acantholysis and positive DIF.[7] On 7th day of admission when patient developed bullous lesions in hand and ulcers over back and hand, another major criterion in the form of polymorphic lesions was fulfilled.

Mortality and morbidity are high in patients of PNP owing to its multiorgan involvement. Persistent hyponatremia despite of proper fluid management as in our patient may be because of paraneoplastic syndrome adding further complication in managing a patient with skin failure. Respiratory complications and failure are high in patients of PNP.[9] Our patient developed metabolic acidosis and eventually succumbed to death because of multiorgan failure.

Serum ADH level, immunoprecipitation and IIF was not done in our patient because of its non-availability at our institute as well as in our state. But, cases of PNP without detection of auto-antibodies has also been reported[10,11] with a suggestion that pathophysiological mechanisms may not be limited to humoral immunity when bullous lesions predominate, it may resemble graft versus host disease or lichen planus when cell mediated mechanisms are present.[12]

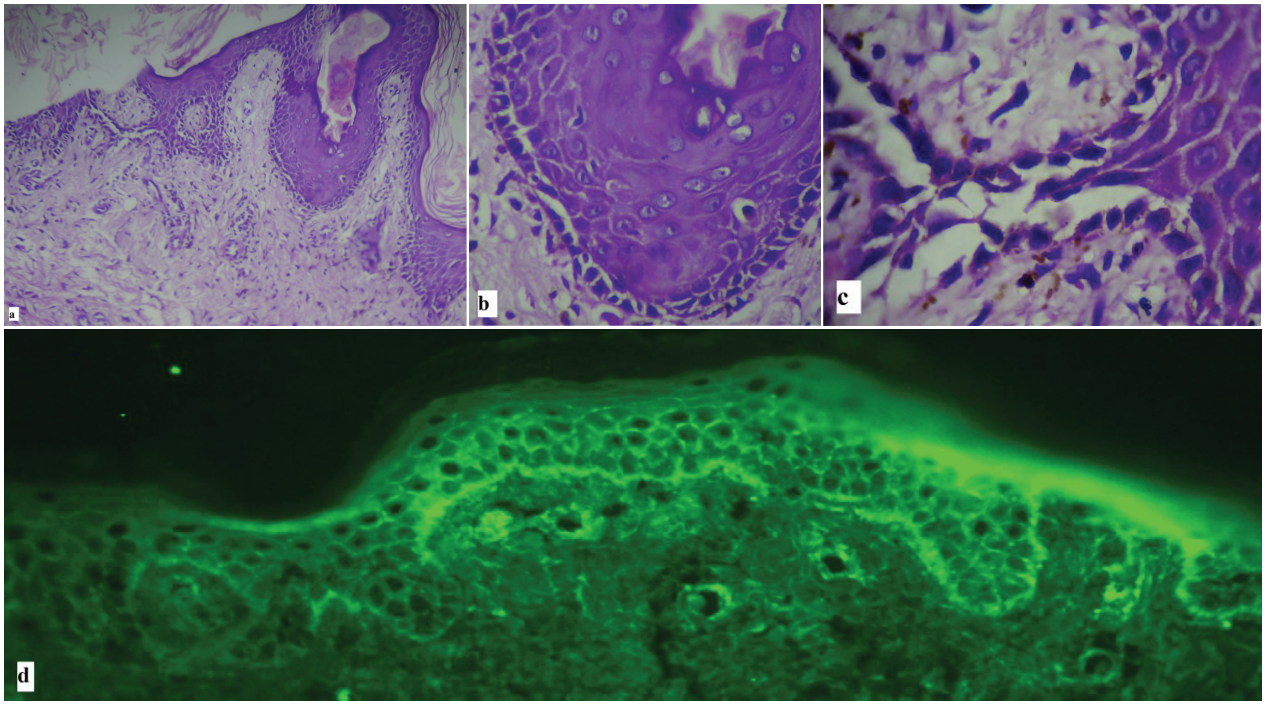

Figure 3: (a) Suprabasal clefts with dyskeratotic keratinocytes. (b,c) Suprabasal acantholysis with loss of intercellular junctions between keratinocytes in basal cell layer. (d) direct immunofluorescence showing positivity of IgG in intercellular space in epidermis and at basement membrane zone.

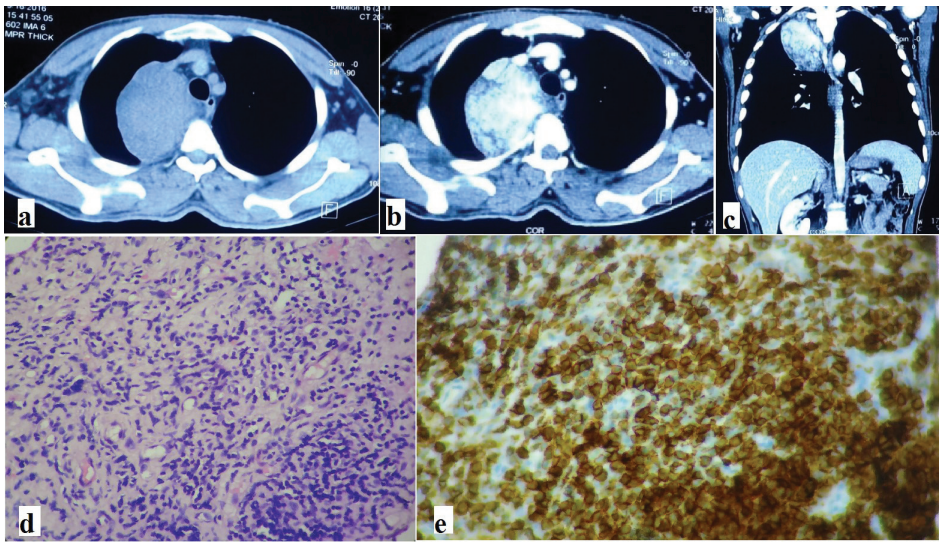

Figure 4: (a,b,c) Computed tomography showing mediastinal mass. (d) Histopathology suggestive of Lymphoma. (e) CD-20 Positivity in same.

Conclusion

Criteria for diagnosis of PNP have not been revised since long. TEN like presentation of PNP may not fulfil clinical criteria for diagnosis. TEN like presentation of PNP is very rare so high index of suspicion is required for diagnosis. Immunoprecipitation and indirect immunofluorescence are not readily available in most of developing countries and it further adds to diagnostic difficulty.

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Conflict of interest to disclosure: None declared.

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