Paraneoplastic Pemphigus: A Case Report and Literature Review

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Abstract
Pemphigus is a bullous autoimmune disease of skin and mucous membrane that may be acute or chronic.There are two major types pemphigus vulgaris and pemphigus foliaceus.These two types are rare.A variant of pemhigus vulgaris is paraneoplastic pemphigus which is associated with malignancy and is rarer.

Paraneoplastic syndromes refer to the disorders that accompany benign or malignant tumours but are not directly related to mass effects or invasion of the skin

We hereby present the case of Mrs A.R. an 80years old woman presenting with paraneoplastic pemphigus with a 30years history of simple goiter.

Keywords: paraneoplastic pemphigus, goitre

Case Presentation
Mrs A.R. is an 80-year old trader who presented to the dermatology unit of our hospital with one month history of body rashes and itching .The rashes started from the right forearm and progressed to involve the limbs, trunk and scalp, sparing the mouth, eyes and vulva. Lesions were vesicular and bullous: some containing clear fluid, others containing yellowish exudate. Each vesicle or bulla ruptured spontaneously forming an ulcer and new lesions came up in crops simultaneously. Generalised body itching also started one month prior to presentation, associated with intense itching that disturbed her sleep, with no previous history of itching or skin morbidity in the past.

There was a history of low grade fever one week before onset of body rashes, during which she used Nivaquine (chloroquine). There was no history of sulphonamide-containing drug use. She had diarrhoea a week prior to presentation with associated weight loss evidenced by loosening of clothing. She had had an anterior neck swelling for 30 years which had not been increasing in size, and for which she had never received treatment. Review of other systems were not contributory and there was no previous history of surgery. She was Para^{7+0} (7 alive), and 32 years post-menopausal. She had no known history of drug allergy or herb intake. She was 15 years a widow, did not smoke or use illicit drugs, and had no family history of such skin illness.

General examination revealed an elderly woman with pallor and a right axillary lymphadenopathy – medial group about 2 x 3 cm, firm, non-tender and mobile with pitting pedal oedema up to the upper third of both legs. The skin showed generalised scaly bullous eruption which were bilateral and symmetrical with ulcerated parts. There were a few bilateral discreet lichenoid eruptions on the lower third of both legs. Nikolsky sign was negative. There was crust on healing skin lesions with hypopigmented patches on the forehead, chin, neck and trunk, and upper and lower limbs with lesions more in the lower. There was exfoliation of her soles and palms and ridging of her fingernails. Her scalp was not affected, but she had arcus senilis with loss of eyebrows and eyelids. There was no oral or vulval involvement. Her pulse was 56/min, blood pressure 90/60 mmHg and she had normal heart sounds. Her chest was clinically clear and abdominal examination revealed hepatomegaly of 6 cm which was firm and smooth with blunt edges. Vaginal examination revealed normal atrophic female external genitalia, with no induration felt on cervix, and gloved finger was

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stained with yellowish mucus. Her central nervous system was grossly intact. A probable diagnosis of bullous pemphigoid was made, to rule out paraneoplastic pemphigus.

She was admitted, had a skin incisional biopsy done of a bullae on the anterior chest wall. She was commenced on intravenous hydrocortisone 200 mg stat and continued on oral prednisolone 15 mg and oral loratidine10 mg, all daily. She also received intravenous co-amoxicillin, daily potassium permanganate baths and intravenous infusion.

Her investigation results included a thyroid scan which showed generalised increase in parenchymal echogenicity, consistent with her age. No mass lesion or cystic lesions were noted within it. Her chest x-ray, fasting blood sugar and 2-hour post prandial, electrolytes, urea and creatinine, and urine microscopy were all normal. Her packed cell volume was 35%, white cell count 10.8^{x10}/L (neutrophils 67%, lymphocytes 25%, monocytes 8%), and platelets 460^{x10}/L. Erythrocyte sedimentation rate was 15mm/hr. Her HIV and VDRL screens were negative. Stool microscopy found mucus and dipstick urinalysis showed bilirubin and leucocytes. Thyroid function tests were not done due to financial constraints. Skin biopsy found skin with a subepidermal blister and underlying mixed inflammation including numerous eosinophils, consistent with the history of bullous pemphigoid. Correlation with immunofluorescence studies was advised but could not be done before her demise.

Discussion

The term paraneoplastic pemphigus was first used by Anhalt et al[1] in 1990 in the United Kingdom when he described five patients with bullous skin disease associated with underlying malignancy and atypical pemphigus-like autoantibodies in perilesional epithelium and serum.

In 1995, in France, Rodot S *et al.*[2] reported a 71year old man with chronic lymphoid leukaemia of 4 years duration who developed a severe mucocutaneous bullous eruption. In 1996, also in France, Fournier B *et al.*[3] also reported a similar case of paraneoplastic pemphigus in a 62years old man with chronic lymphoid leukaemia. In 1996, in Japan, Izaki S *et al.* [4] also reported paraneoplastic pemphigus in a 56 year old Japanese with chronic lymphocytic leukaemia. In 1998, in France, Joly P *et al.*[5] reported lichenoid erythrodermic bullous pemphigus in three Senegalese patients and stated that autoimmune bullous skin diseases such as paraneoplastic pemphigus or bullous lupus erythematosus may also be associated with lichenoid eruption.

In 2000, Allen C et al [6] in the USA reported paraneoplastic pemphigus as a relatively rare but highly significant acquired mucocutaneous disorder. In 2004, Powell A M *et al.* [7] reported a patient with chronic lymphocytic leukaemia who developed paraneoplastic pemphigus soon after the initiation of fludarabine therapy. In November 2008, Edgin W.A et al[8] described pemphigus vulgaris and paraneoplastic pemphigus as life-threatening, autoimmune mucocutaneous bullous conditions that may be encountered by oral health providers. In 2010, Hayanga A J *et al.* [9] working in the USA noted that because of the rarity of paraneoplastic pemphigus, it is frequently misdiagnosed as Stevens-Johnson Syndrome or toxic epidermal necrolysis.

These references show that paraneoplastic pemphigus though a rare bullous disease has a wide geograghical distribution from western Europe to eastern Asia and northern America, but there were no reports from the Caribbean and southern America. The 3 Africans reported (Senegalese) were outside the continent, in France and were probably immigrants. To the best of our knowledge, no reports had been documented from sub-Saharan Africa, and Nigeria in particular.

Table 1 illustrates the summary of these cases.

Table 1

LOCATION	PRESENTATION	ASSOCIATED MALIGNANCY	PATIENTS ORIGIN OR ANCESTRY	REPORTER
United Kingdom	Bullous skin disease associated painful mucosal ulcerations and polymorphous skin lesions.	Varied Malignancies	Caucasian	Anhalt *et al.*
France	Severe mucocutaneous bullous eruption	Chronic Lymphoid Leukaemia	Caucasians	Rodot S *et al.*
France		Chronic Lymphoid Leukaemia	Caucasians	Fournier B *et al.*
Japan	Extensive erosive mucocutaneous lesions.	Chronic Lymphocytic Leukaemia	Japanese	Izaki S *et al.*
France	Lichenoid eruption, erythrodermic bullous eruption.		Senegalese(African)	Joly P *et al.*
Netherlands	Severe oral and cutaneous erosions progressing to unusual hyperplastic papillomatous lesions affecting the inner aspect of lips and buccal mucosa	Chronic Lymphocytic Leukaemia	Caucasians	Powell A.M. *et al.*
Michigan, USA	Desquamation.Acute diffuse blistering	Low grade Lymphoma	Native Americans	Hayanga AJ *et al.*

Paraneoplastic pemphigus associated with thyroid mass was not found in literature.

Paraneoplastic pemphigus is an autoimmune acantholytic mucocutaneous disease associated with an occult or confirmed neoplasm. It is an autoimmune bullous disease described by precise clinical,histological and immunological features[3]. Patients with paraneoplastic pemphigus have IgG auto-antibodies against cytoplasmic proteins that are members of the plankins family (e.g.desmoplakins I and II.bullous pemphygoid antigen I, envoplakins, periplakins and plectin) and cell surface proteins that are members of the cadherin family (e.g. Dsg3 and Dsg2). Passive transfer studies have shown that autoantibodies from patients with paraneoplastic pemphigus are pathogenic. Mrs A R on presentation was not a known patient with any malignancy, and a clinical search for an occult malignancy was inconclusive. She however had a simple goitre of 30 years duration which may have undergone mitotic transformation to a thyroid cancer, for which her age and sex were risk factors. Since she requested for an early discharge due to financial constraint, the plan was to monitor her for malignancy on follow up but she died a day before her first follow up appointment.

Also, while the literature associated paraneoplastic pemphigus with lymphoreticular disease, this patient did not have such, neither was her bullous eruption linked to the intake of any drug. It is also worth nothing that her paraneoplastic pemphigus had associated lichenoideruption, similar to the finding of in the three Senegalese reported outside the African continent. This corroborates the statement that paraneoplastic pemphigus may also be associated with lichenoid eruptions, perhaps among Africans. In literature the modalities of treatment include corticosteroid therapy for up to one year, repeated plasmapharesis with improvement, immunosuppressive agents and mycophenolate mofetil with low-dose prednisolone. In this patient corticosteroid therapy was employed with initial clinical improvement until she agitated for early discharge (due to financial constraints) and died 13days after.

Conclusion

Paraneoplastic pemphigus is a rare autoimmune bullous disorder with poor prognosis.

References

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