doi:10.21276/obgyn.2016.3.1.10 *ISSN Print- 2454-2334; Online- 2454-2342*

CASE REPORT

Pemphigus and ovarian neoplasm: a case report

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ABSTRACT

A patient initially diagnosed as pemphigus vulgaris four months back presented to our outpatient department. She also had large thyroid swelling and abdominal mass. A thorough workup embarked on manifestations implicating an intimate association. Pemphigus vulgaris like lesions coexisting with an ovarian neoplasm and multinodular goiter raised the possibility of paraneoplastic pemphigus, a well recognized yet rare entity. The purpose of this report is to stress upon the importance of preserving a broad outlook while confronting atypicality in any disease.

Keywords: Pemphigus vulgaris, Paraneoplastic syndrome, Ovarian neoplasm.

Pemphigus vulgaris (PV) is an autoimmune blistering disorder associated with blistering over the cutaneous and mucosal surfaces. IgG autoantibodies are produced against cadherin molecules desmoglein 3 and desmoglein 1. They appear on normal looking or erythematous skin, rupture easily to form large erosions and are usually not associated with pruritus or pain. Paraneoplastic pemphigus (PNP) is an autoimmune bullous disease characterized by severe mucous membrane involvement, polymorphous skin eruptions, and underlying neoplasms [1, 2]. In PNP, antibodies are directed not only against desmogleins but also against all members of plakin family. Desmosomes are important intracellular junctions that link plasma membrane to the cytoskeleton's intermediate filaments. They comprise of three protein families: desmosomal cadherins, armadillo proteins and plakins. Desmosomal cadherins comprise of desmogleins 1 & 3 and desmocollins. There are four types of protein family members in the plakin family: plectin, desmoplakin, envoplakin and periplakin. The mechanisms which induce tumours to produce autoantibodies to plakin proteins are not exactly known. Tumor cells probably produce autoantibodies that react to epidermal proteins. Cross-reactivity of tumor antigens and epidermal antigens and production of plakin proteins by the tumour, initiating an autoimmune response, are other possibilities. A dysregulated cytokine production by tumor cell, specifically interleukin 6, contributing to the autoimmune process is another hypothesis. The concept of epitope spreading, with which patients develop antibodies to multiple structurally related and unrelated proteins, may explain the multitude of antibodies produced in association with this disease [3].

Case Report

In the month of January, 2015, a 40 year old female cachectic patient, G_1P_1 was referred to our hospital by a

Received: 25th November 2015; **Accepted:** 3rd January 2016.

Dutta B, Mahela S, Barman K, Bhuyan K, Boro B, Datta B. Pemphigus and ovarian neoplasm: a case report. The New Indian Journal of OBGYN. 2016; 3(1): 51-54. *doi:10.21276/obgyn.2016.3.1.10*

Dermatologist with a clinical diagnosis of Pemphigus Vulgaris, to be initiated on Dexamethasone Cyclophosphamide pulse therapy. She mostly had post inflammatory hypopigmentation following irregular use of systemic steroids for the past four months. Within two days of her stay in our hospital, patient started developing intensely pruritic flaccid and tense, very superficial looking vesicles filled with clear fluid. Patient gave a history of menorrhagia lasting for 3 to 4 months a year back when she was diagnosed as a case of ovarian tumour. Surgery was planned twice, but had to be deferred on account of high T3, T4 levels. Patient was also presenting with an asymptomatic large neck swelling for the past twenty years which was clinically diagnosed as multinodular goiter, responsible for causing the hormonal irregularities.

Vesicles and bullae were mostly present in groups and were seen over the forehead, submandibular

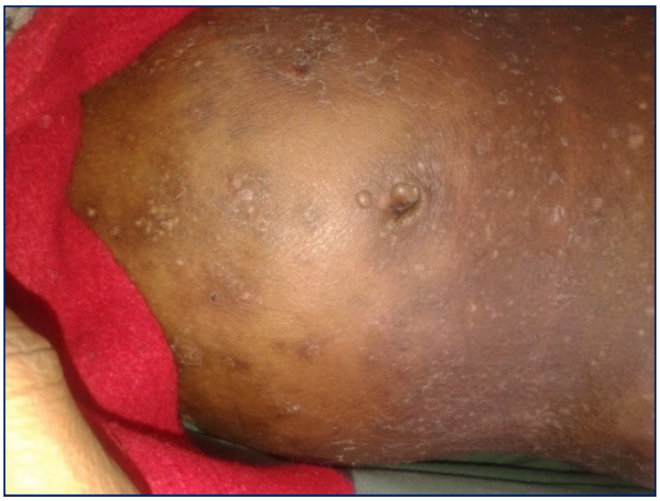

Figure 1: Vesicles and bullae were seen over abdomen, periumbilical region

region, neck, chest, abdomen, periumbilical region (figure1), back, forearms, lower legs and ankles. Lesions were also seen over unusual sites like vermilion border of the lips (figure 2), and the web space of fingers, palms and soles. Most of the lesions were in the range of 2 to 3 mm, with few larger lesions over the legs. On Abdominal Examination, there was a large solid mass in the (R) lower abdomen; per rectal examination revealed a hard mass in the anterior aspect. Per vaginal examination showed cervix as drawn up; there was a hard and immobile lump in the pouch of Douglas. Within two days of her stay, patient presented with frank haematuria which continued for two days and subsided with supportive care.

Her blood parameters showed anemia and a raised ESR. Tzanck smear done from the lesions was consistent with Pemphigus. Biopsy taken from an intact vesicle over the leg showed acantholyis of the epidermis, and intraepidermal bulla with lymphocytes, eosinophils and few large detached acantholytic cells, consistent with a diagnosis of pemphigus vulgaris. FNAC of the neck mass showed cytomorphological features consistent with nodular goiter. T3 was 3.61ng/ml, T4 >30 micrograms /dl and TSH 0.035micro IU/ml. FNAC from the abdominal mass showed cytomorphological features suggestive of adenocarcinomatous cells in a fluid and haemorrhagic background. Tumour markers were tested for with the following findings, Carcinoembryonic Antigen (CEA) 2.59ng/mi, HCG 608 mIU/mi, alpha feto protein 0.242, CA 125 38.80. HRCT Thorax and Abdomen showed a large heterogenous mass with solid and cystic components in pelvic cavity extending to the level of umbilicus, measuring approximately 161x 150 mm. The mass could not be visualized separately from uterus and ovaries. Bilateral hydronephrosis was noted due to pressure effect on ureters by the mass. Thyroid gland was enlarged predominantly over the left lobe with popcorn calcification. Enlarged mediastinal lymph nodes were seen measuring up to 15 mm x 10 mm. Well defined nodular opacities were noted scattered over both lung fields, measuring upto 20 mm x 16 mm, suggestive of metastasis.

A diagnosis of paraneoplastic pemphigus with ovarian malignancy (adenocarcinoma) with multinodular goiter was considered. Direct and indirect immunofluorescence tests from perilesional skin and blood respectively for detection of antiplakin antibodies as a further diagnostic tool for PNP, and biopsy from the abdominal mass for confirming the FNAC diagnosis of adenocarcinoma were planned.

Unfortunately, poor general health of the patient, late presentation, time and financial constraints prevented us from proceeding further. Patient suddenly developed severe respiratory distress seven days following her admission and expired the same day.

Discussion

Both benign and malignant neoplasms are associated with PNP like, non-hodgkin lymphoma, chronic lymphocytic leukemia, castleman disease, thymoma, waldenström macroglobulinemia, hodgkin lymphoma, various carcinomas, sarcomas, and malignant melanoma.Underlying lymproliferative neoplasms were considered mandatory for diagnosis.

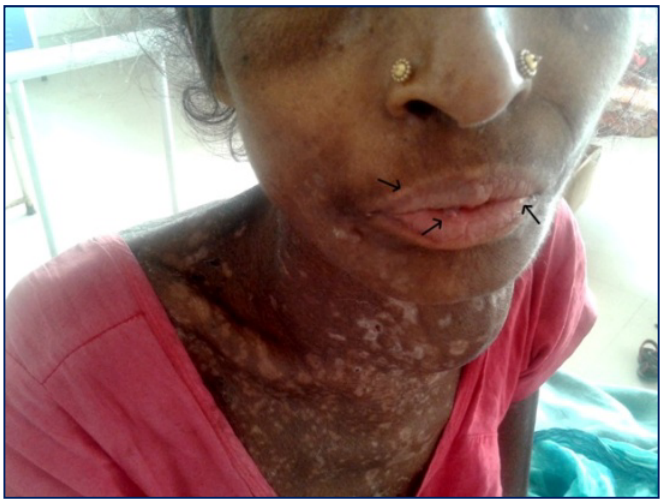

Figure 2: Vesicles and bullae were seen over vermilion border of the lips

But, patients with solid tumors like, pancreatic adenocarcinoma , bronchogenic squamous cell carcinoma and uterine squamous carcinoma have been reported [4-8]. In PNP, patients often present with painful oral erosions, which are severe and intractable involving even the lateral tongue and vermilion. Though painful progressive stomatitis has been proposed as a criteria for diagnosis, an atypical case associated with endometrial carcinoma without mucosal lesions has been reported [9].

A generalized cutaneous eruption often accompanies mucosal lesions which manifest a wide range of morphologies. Manifestations could be like pemphigus, pemphigoid, erythema multiforme, graft versus host disease, and lichen planus. Both blisters and lichenoid lesions affecting the palms and the soles, as well as the paronychial tissues, are common; they help to distinguish PNP from PV, in which acral and paronychial lesions are uncommon. Additionally, some patients report pruritus or pain. Our patient had cutaneous involvement of multiple sites including palms, soles and vermilion border of lips with associated intense pruritus. Respiratory involvement by PNP lesions is a significant cause of mortality. It causes obstructive lung disease, manifests as dyspnea, or maybe subtle without any radiographic findings, progresses to bronchiolitis obliterans and culminates in death. The sudden death of our patient could be attributable to the same cause.

Introduction of corticosteroids and immunosuppressive agents has greatly improved the prognosis of pemphigus vulgaris. Cases of PNP associated with benign neoplasms can improve dramatically when the tumor is resected, owing to the decreased production of autoantibodies. Administration of tumour specific chemotherapy may result in complete resolution of the malignancy and a slow resolution of skin lesions; mucosal lesions are very refractory to treatment [10, 11]. Our patient probably stood a chance of a better prognosis had she successfully undergone surgical removal of the ovarian neoplasm earlier, without the existing thyroid anomalies.

Conclusion

The existing findings of lesions at atypical sites, intense itching, underlying ovarian malignancy preceeding the cutaneous eruption and sudden death following an acute episode of respiratory distress are highly suggestive of the two entities being interrelated rather being a happenstance association. Her poor health and preceeding malignancy should have evoked an earlier attention to her existing problem. Failure to do so, coupled with her late and advanced stage of presentation before us and financial constraints

culminated in an unfavourable and inconclusive outcome. More diagnostic evidence is definitely warranted to establish the case as Paraneoplastic Pemphigus. Yet the existing clinical and laboratory evidence definitely points towards a diagnosis of Paraneoplastic pemphigus or neoplasia induced pemphigus. The purpose of reporting this case is to sensitize specialists with this unusual condition so that an early integrated management approach is planned which will allay delay in diagnosis and ensure a much better outcome.

Conflict of interest: None. **Disclaimer:** Nil.

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