JOURNAL OF PHARMA INSIGHTS AND RESEARCH

CASE REPORT

A case report on drug-induced bullous pemphigoid in a cervical cancer patient undergoing chemotherapy

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Publication history: Received on 30th October; Revised on 27th November; Accepted on 2nd December

Article DOI: 10.5281/zenodo.10402458

Abstract: Bullous pemphigoid (BP) is an autoimmune disorder characterized by the development of fluid-filled blisters on the skin, and it is a rare but serious complication linked to specific medications, notably chemotherapeutic agents. This case details a 57-year-old female with stage-II cervical cancer who experienced widespread blistering lesions on her body after undergoing two cycles of chemotherapy involving paclitaxel and carboplatin. The patient noticed the appearance of multiple fluid-filled, reddish blisters on her hands, back, abdomen, and lower extremities, accompanied by a burning sensation, three days after the initial day of the latest chemotherapy session. Confirmatory histopathological and immunological assessments established the diagnosis of BP, an immune-mediated condition targeting the basement membrane zone through autoantibodies against bullous pemphigoid antigen-1 and antigen-2. The patient's symptoms were successfully managed with corticosteroids, and the implicated chemotherapeutic agents were discontinued. This case underscores the crucial importance of monitoring cancer patients undergoing chemotherapy for cutaneous adverse reactions, especially those presenting with blistering eruptions. It highlights the necessity for prompt recognition and appropriate management of drug-induced bullous pemphigoid in such cases.

Keywords: Bullous pemphigoid; Autoimmune disorders; Antibodies; Cancer; Chemotherapy

1. Introduction

Bullous pemphigoid (BP) is a rare autoimmune skin disorder characterized by the formation of fluid-filled blisters on the skin [1]. The epidermis, composed of pancake-shaped keratinocytes containing keratin protein, consists of a single layer of stem cells in the Stratum Basale, continuously producing new keratinocytes. Melanocytes within the Stratum Basale secrete melanin, a pigment-protein. Bullous pemphigoid is predominantly triggered by certain medications such as furosemide, captopril, penicillamine, NSAIDs, and antibiotics.

This condition represents a type II hypersensitivity reaction, wherein the immune system generates antibodies, specifically IgG antibodies produced by beta cells. The Fab region of these antibodies binds with proteins, including bullous pemphigoid antigen 1 (BPAG11 or dystonia) and bullous pemphigoid antigen 2 (BPAG2, BP180, or the 17 Collagen). Simultaneously, the Fc region activates the complement system, initiating a cascade that attracts mast cells, which release inflammatory molecules. Inflammatory cells like neutrophils, eosinophils, macrophages, and T cells are then attracted, leading to the destruction of hemidesmosome proteins (BPAG and BPAG2). [2] The destruction of hemidesmosome results in the separation of basal cells from the basement membrane, forming a split between the epidermis and dermis, without Nikolsky's sign and circulating IgG antibodies. The reported case involves a patient who developed bullous pemphigoid after receiving chemotherapy containing sulfhydryl group-containing cells, altering the antigenic properties of the cell surface. Autoantibodies, either circulating or tissue-bound, directed against bullous pemphigoid antigen 1 or bullous pemphigoid antigen 2, primarily cause this condition, with a higher incidence in women. Bullous pemphigoid typically presents with tense blisters or bullae over the trunk and extremities, accompanied by intense pruritus. Mucosal involvement is rare. The condition can be drug-induced, and distinguishing between Bullous pemphigoid (BP) and Drug-induced bullous pemphigoid (DIBP) poses a challenge. DIBP can be caused by various medications, including antihypertensives, nonsteroidal anti-inflammatory drugs, diuretics, antiarrhythmics, antidiabetics, antirheumatics, antibiotics, tumor necrosis factor inhibitors, vaccines, and other agents. [3,4]

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The incidence of bullous pemphigoid is 0.2 to 3 per 100,000 person-years, and it is less common than pemphigus vulgaris in India. Bullous pemphigoid is a chronic autoimmune disorder caused by antibodies targeting BP180, a type XVII collagen, and HD1 (BPAG1), a 230-kDa glycoprotein. The word 'pemphigoid' is derived from the Greek word 'pemphix,' meaning 'pustule,' and 'oid' means 'to resemble. Oral lesions, which are challenging for oral physicians to diagnose, occur in the oral cavity following the onset of pruritic papules in the extremities. These ulcers are usually multiple and exhibit chronicity due to the autoimmune destruction of hemidesmosome proteins, anti-BP 180 and BP 230, targeting the basement membrane zone. Pruritic rashes on the skin often precede the occurrence of oral lesions [5, 6. Left untreated, bullous pemphigoid follows a course of spontaneous remissions and exacerbations, and advanced age increases vulnerability to the adverse effects of corticosteroids and immunosuppressive agents commonly used for management. Ciprofloxacin, while generally exhibiting few side effects, has been associated with ciprofloxacin-induced bullous pemphigoid in only a few reported cases [7, 8]. The objective of this case report is to document and elucidate the development of bullous pemphigoid in a 57-year-old female with stage-II cervical cancer following chemotherapy with paclitaxel and carboplatin.

2. Case presentation

2.1. Subjective evidence

The presented case depicts a 57-year-old female patient admitted to the Dermatology (DVL) ward of GSL General Hospital, Rajahmundry, presenting with widespread fluid-filled blisters covering approximately 40% of the body surface area (BSL) accompanied by a burning sensation. The patient medical history reveals a recent diagnosis of cervical cancer, for which she underwent two cycles of chemotherapy comprising paclitaxel and carboplatin, with the last session occurring on 10/04/2023. Notably, she experienced a similar episode of blistering eruption following the first chemotherapy session, which resolved with hyperpigmentation. Comorbidities of long-standing diabetes and hypertension managed with telmisartan and metformin were noted in the patient's history.

2.2. Clinical investigations

Laboratory investigations revealed derangement in random blood sugar (293mg/dl), reduced hemoglobin (10.6g/dl), and leukocytosis (WBC: 12000 cells/cumm). Examination unveiled asymmetrical, multiple fluid-filled bullae on the upper and lower limbs and trunk, characterized by a clear fluid content, erythematous base, and resistance to rupture. Additionally, erosions and desquamation were observed on different body part along with bluish discoloration of the tongue, anagen effluvium of the scalp, and negative Nikolsky's sign. Based on the clinical presentation and investigation, a diagnosis of drug- induced bullous pemphigoid (chemotherapy -induced pemphigoid) was established. The mechanism involves the interaction of chemotherapy drug with immune system, leading to autoantibodies targeting bullous pemphigoid antigen and subsequent blister formation.

2.3. Treatment

The therapeutic approach included systemic management with Omnacortil (20mg OD), Pan (40mg OD), Bilastine (20mg OD), Dazit (5mg OD), along with local application of momate cream over the lesions. Additionally, insulin (Actrapid, TID) for diabetes control, Telma (40mg OD) for hypertension, and Azithral (OD) were prescribed. Acute symptomatic relief was sought through the administration of avil (2CC stat).

3. Discussion

The presented case illustrates a complex scenario of a 57-year-old female diagnosed with cervical cancer undergoing chemotherapy, subsequently developing drug -induced bullous pemphigoid (DIBP). The association between chemotherapy agents such as paclitaxel and carboplatin and onset of Bullous pemphigoid is rare but has been reported in literature, implicating the immune-modulating effect of these drugs in triggering autoimmune reaction leading to skin blistering. The patient's clinical presentation aligns with classic manifestations of bullous pemphigoid, characterized by fluid-filled bullae over an erythematous base, localized predominantly on the extremities and trunk. The absence of Nikolsky's sign, a characteristic feature of pemphigus vulgaris, reinforces the diagnosis of bullous pemphigoid [9]. furthermore, the patient's history reveals a previous episode of similar blistering eruption following the initial chemotherapy cycle, suggesting a drug-induced etiology.

Laboratory findings indicating leukocytosis and reduced hemoglobin are non-specific but relevant in the context of an immune-mediated condition, reflecting possible systemic inflammation and ongoing autoimmune response. The presence of bluish discoloration of the tongue, desquamation in genital areas, and anagen effluvium of the scalp signifies the diverse mucocutaneous involvement associated with bullous pemphigoid. Management primarily involves a multidisciplinary approach targeting both the underlying cancer and the dermatological manifestations [10]. Systemic corticosteroids (omnacortil) serve as the cornerstone in suppressing the immune response and mitigating blister formation. Supportive therapy with antihistamine (bilastine, pain), along with insulin (Actrapid) for glycemic control and other medications for comorbid condition, was initiated.

The case highlights the importance of vigilant monitoring for adverse cutaneous reaction in cancer patients undergoing chemotherapy. Dermatological manifestation like bullous pemphigoid can significantly impact the patient's quality of life and treatment trajectory. Collaborative effort between oncologist, dermatologist, and other specialities are imperative to manage such complex cases effectively [11, 12].

4. Conclusion

The case illuminates the rare yet critical association between chemotherapy and drug-induced Bullous pemphigoid in a cervical cancer patient. Timely recognition of this adverse cutaneous reaction is pivotal, enabling prompt intervention and multidisciplinary management. The comprehensive approach, integrating systemic corticosteroids and supportive therapies, aims to address both the underlying malignancy and dermatological manifestation. Collaborative efforts among oncologists and dermatologist remain imperative in navigating such complex clinical scenarios. This case highlights the significance of vigilance for drug-induced complication in cancer care, emphasizing the necessity for proactive monitoring and tailored therapeutic strategies to optimize patient outcomes and alleviate the burden of cutaneous adverse effects.

Compliance with ethical standards

Acknowledgement

We extend our sincere gratitude to Mr. Amit Kumar, Associate Professor at Aditya College of Pharmacy, Surampalem (Department of Pharmacy Practice), for his invaluable assistance. His willingness to help, along with the pleasant environment and insightful knowledge he provided, greatly contributed to the completion of our case report. Additionally, we express heartfelt thanks to the compassionate parent of our subject for facilitating our study, sharing information on the subject's daily experiences, and allowing us to conduct observations. We also acknowledge the support and cooperation of all teaching and non-teaching staff members during our follow-up and research. Our appreciation is extended to everyone who contributed to the successful completion of this case report project.

Conflict of interest statement

All authors declare that there is no conflict of interest.

Statement of informed consent

Informed consent was taken from the patient.

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Author's short biography

Mukesh Kumar Gupta

Pharm-D intern with a dedication to ongoing professional development within the dynamic field of pharmacy. Currently enrolled in a Pharm-D program with a specific emphasis on drug therapy optimization and patient counseling, he is keen to apply theoretical knowledge in real-world clinical settings. Mukesh has also earned a certificate in Diabetology from the Vertued Academy International platform under the guidance of Dr. Ankita Kashyap, MBBS, MD, MCTAA (UK)

Neerupalli Bhavya

Pharm. D student with a passionate interest in the convergence of healthcare, pharmacy, and the pharmaceutical industry. With a solid academic foundation, my goal is to apply pharmaceutical knowledge to enhance patient well-being. I am dedicated to promoting a compassionate and evidence-based approach in pharmacy practice. I enthusiastically welcome challenges, constantly seeking opportunities to learn and contribute to the dynamic landscape of modern healthcare. Additionally, I have participated in various conferences and workshops organized by Avenida Innovations under the guidance of Dr. Karthik Rakam. Furthermore, I have earned a certificate in Nephrology from Dr. C. Yashwanth, MBBS, DM & MD (Nephrology) at GSL General Hospital

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I am a Pharm. D candidate deeply passionate about the interconnectedness of the pharmaceutical, pharmacy, and healthcare sectors. Armed with a robust academic foundation, my objective is to leverage my pharmaceutical knowledge to enhance patient outcomes. Committed to fostering a compassionate and evidence-based approach in pharmacy practice, I eagerly anticipate embracing new challenges, acquiring additional skills, and contributing to the ever-evolving landscape of contemporary healthcare

Amit Kumar

Amit Kumar is a highly accomplished professional in the field of pharmacy, possessing a B. Pharmacy and M. Pharmacy, and has submitted his Ph.D. Presently, he holds the position of Associate Professor and serves as the Head of the Pharmacy Practice Department at the NAAC A accredited Aditya College of Pharmacy in Surampalem. His commitment to advancing pharmaceutical knowledge is evident in his extensive publication record, boasting 33 articles published in various reputable Indian and international journals. His research contributions cover a diverse range of topics within the pharmaceutical domain, highlighting his expertise and unwavering dedication to the field