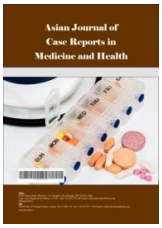

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Povidone-iodine Induced Fixed Bullous Eruption: A Case Report

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Authors' contributions

This work was carried out in collaboration among all authors. Author ZGK was the doctor in charge of this case and managed the diagnostic procedures. She wrote the first draft of the manuscript as well. Author SSH assisted the diagnostic procedures and revised critically the draft of the manuscript. Author TGA managed the literature search. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Fixed drug skin eruption to the iodine especially manifesting by bullous lesions is very rare. We present a case of a 73-year-old female who developed multiple blisters on the fingers of both hands with serous or serous-hemorrhagic content after a week of postoperative topical use of Povidone-iodine. Clinically diagnosed bullous eruption resolved in 12 days on the background of offending drug discontinuation and systemic steroid treatment but then it was reappeared at the same site after re-treatment of inflamed wound with the same antiseptic drug. Three months later after the complete resolution of the symptoms, diagnostic examinations such as patch-test and provocation were performed. On the basis of these test results, the diagnosis of a fixed bullous eruption caused by Povidone-iodine was confirmed.

Keywords: Bullous drug eruption; povidone-iodine; patch-test.

1. INTRODUCTION

Fixed drug eruption of the skin always recurs at the same sites on re-exposure to the causative drug [1,2]. The rare cutaneous reactions to iodine called iododerma usually manifest as acne-like skin rash and sometimes bullous skin eruption [3,4]. In the majority of cases iododerma is

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induced by iodine-containing radiographic contrast media or oral medications for iodine therapy [5-7]. The eruption due to topical use of iodine mainly manifests as allergic or irritant contact dermatitis at the application site. Only a few cases of this reaction have been found in the available literature [8-12]. Here we present the case of fixed bullous non-contact eruption of the skin after postoperative topical use of Povidone-iodine. According to our knowledge, this is the first case described in the available literature to present this rare type of reaction outside of the Povidone-iodine application area.

2. CASE REPORT

A 73-year-old female admitted to our clinic in October 2019 with a one-day complaint of bullous skin lesions on both hands, accompanied by expressed burning and slight itching. The patient reported having a surgery for recurrent breast cancer 7 days ago. The operative wound on the chest was dressed with 10% Povidone-iodine solution (Betadine, EGIS Pharmaceutical Ltd, Budapest, Hungary) daily since then. The wound care was done by surgical resident and the patient did not touch the solution with hands. She also mentioned that the lesion on the left thumb enlarged into a big bulla in a few hours. She had a medical history of breast cancer, that was diagnosed 12 years ago and mastectomy was performed followed by chemotherapy. During chemotherapy period, she was diagnosed with paraneoplastic dermatitis which was successfully treated by a dermatologist. The recurrence of breast cancer was diagnosed approximately 1 month ago by X-ray mammography at the follow-up visit.

During the physical examination, we revealed multiple blisters: there was a big bulla on the left hand with a diameter of 25 mm on the thumb with serous - hemorrhagic content and three small blisters on the index finger with serous content. A small blister with serous content was developed on the right thumb symmetrically (Fig. 1). The patient was afebrile, the vital signs were stable and the Nikolsky's sign was negative. The ESR of 36 mm/h and the eosinophil count of 7% were the only abnormalities in the routine workup. The systemic steroid treatment was prescribed to the patient (Dexamethasone - 4mg intravenously, once daily for 5 days) and the use of Povidone-iodine was discontinued. The lesions were fully resolved in 12 days, leaving only slight hyperpigmentation. The patient was advised to avoid the iodine-containing medications and visit the clinic after a month for causality assessment.

18 days after the first visit the patient returned with a complaint of itchy blisters on the right thumb at the same place as before (Fig. 2). The blisters appeared on next day she mistakenly started re-treatment of the inflamed operative wound with 10% Povidone-iodine. No other medications were used. The steroid treatment was prescribed again and the use of Povidone-iodine was discontinued. The blisters completely resolved within 4 days and did not recur in the next three months of follow-up.

Three months after the complete resolution of the symptoms, the diagnostic tests were performed with the written informed consent and in accordance with principles of the Declaration of Helsinki. During this period the patient didn't have any intake or topical use of iodine-containing medication as well as other medicinal treatment and had iodine-limited diet. The application of Povidone-iodine on the 1cm^2 of nape was implemented with use of Finn chamber according to the current recommendations for the semi-open patch-test. This was also a topical provocation with Povidone-iodine solution [13,14] (Fig. 3).

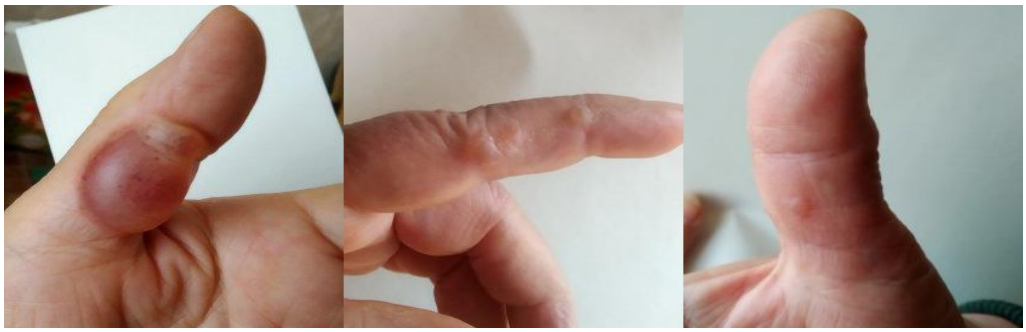

Fig. 1. Bullous eruptions on the fingers at the first visit

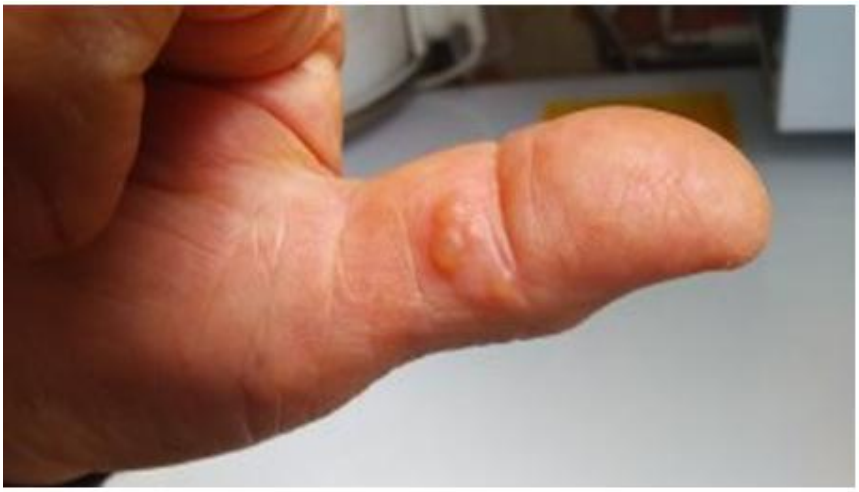

Fig. 2. Blisters on the right thumb after re-treatment with Povidone-iodine

Fig. 3. Procedure of semi-open patch-test and provocation with Povidone-iodine

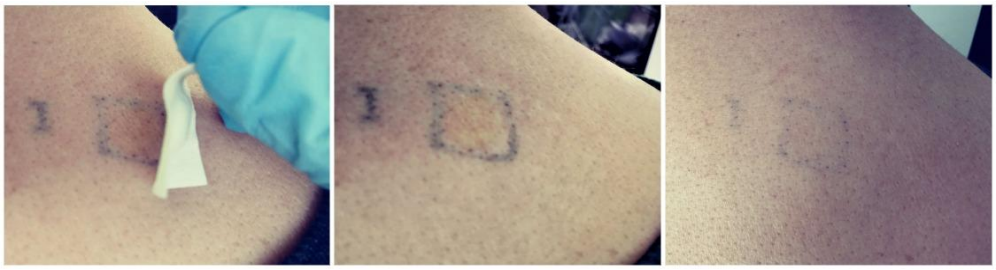

Fig. 4. Assessment of the patch-test at the moment of patch removal, after 48 hours and after 72 hours

The following results were registered:

- within 24 hours – moderate burning sensation at the sites of previous bullous lesions and not at the test site, started approximately 12 hours after application.
- after 48 hours – the patch was removed and there was no reaction at the test site while slight burning at the site of previous bullous lesions was present.
- after 72 hours – no reaction and no burning were present (Fig. 4.).

3. DISCUSSION

The most common sites of fixed drug eruption are the lips, genital area, hands and feet. Antibiotics are the most common cause, especially sulphonamides and tetracyclines but many other causative drugs have been reported [1-3]. The fixed drug eruption to iodine is very

rare. Although iododerma usually presents as acne-like rash with pustules, it can be bullous with either clear or blood-filled blisters [4] as in our case. The pathogenesis of iododerma is not clear. It usually develops after long-term exposure to topical or oral iodine and resolves slowly over weeks after ceasing the drug due to slow excretion through the kidneys [3,14]. Acute or chronic renal failure is a risk factor, particularly for acute iododerma development in cases of oral or intravenous administration of iodine-containing radiocontrast media [5-7]. There was no iodine oral intake history in our case but the patient had numerous mammographic examinations with the use of contrast media a month prior to the reaction so a sensitization to iodine is possible. The increased eosinophil count in peripheral blood also can be suggestive of hypersensitivity. In available literature we have found only a few reports on iododerma due to topical use of iodine describing the blisters or plaques near or in the place of iodine exposure [8-12]. In contrast to these reports, no skin changes were seen on the place of iodine use in our case but only on the fingers symmetrically.

Bullous drug eruptions are nearly always diagnosed clinically [1,2,15]. In our case, the biopsy of skin wasn't performed because of the patient's refusal and the initial diagnosis was made clinically.

Treatment may involve the use of intravenous fluids and diuretics to increase iodine excretion, topical or systemic corticosteroids and cyclosporine in severe cases. The formation of iododerma seems to involve the accumulation of the iodine as well as a hypersensitivity so the best way of symptom resolution is the iodine avoidance [3]. In our case, we stopped the use of Povidone-iodine and prescribed a systemic use of corticosteroid (Dexamethasone) both times. The interesting point is that after the first reaction the connection with iodine was not proved and only on the basis of assumption about its probable causative significance Povidone-iodine was discontinued. As such reactions especially caused by Povidone-iodine are extremely rare the probability of a recurrence of the reaction to iodine was not taken into account by the surgeon when treating an inflamed wound.

The provocation with the possible agent (after allowing for a possible refractory period) is usually performed for confirmation of the diagnosis when the patch-testing with the agent elicits a positive response [2,13,14]. It is interesting that patch-test with Povidone-iodine was negative but the slight relapse of symptoms (burning) at the sites of previous lesions in 24 hours after application of Povidone-iodine was mentioned by patient. Although the symptoms were subjective, we assessed them as positive response to the provocation keeping into account that previously, the reappearance of blisters on the left thumb was induced (we can call it "provoked") by re-treatment with Povidone-iodine. Therefore, the causality of Povidone-iodine in the development of fixed eruption was confirmed.

4. CONCLUSION

The pathology for which the surgery was performed is much more serious than the developed skin lesion in the postoperative period. However, we consider it very important to identify Povidone-iodine as a causative factor, since this will allow avoiding an even more severe reactions to this drug in the future. Finally, this is the first case discovered in the available literature to show that topical application of Povidone-iodine can cause rare fixed bullous non-contact cutaneous reactions outside the application area.

CONSENT

Patient has given the consent for publication of her case.

ETHICAL APPROVAL

The authors declare that all the diagnostic procedures have been examined and approved by the Committee of Bioethics of Yerevan State Medical University after Mkhitar Heratsi (Approval № 5/13.12.2018) and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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