

Fixed Drug Eruption Due to Ambroxol

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Abstract: **Introduction:** Fixed drug eruption (FDE) is a common cutaneous drug eruption characterized by the development of one or more annular, oval, erythematous and hyperpigmented patches as a result of systemic exposure to a drug. The lesion may recur at the same site and/or at the new sites with re-exposure to the offending drug(s). More than 100 drugs have been implicated in causing FDEs including ibuprofen, sulfonamides, naproxen and tetracyclines. There was only one case report fixed drug eruption due to Ambroxol in Japan. This is a second case report fixed drug eruption due to ambroxol. **Case:** A 37-years old Male came to Adam Malik Hospital Medan with the chief complaint an itchy, two similar violaceous macular lesions on the left back of the hand and erythematous macular lesion in his genital part. Three days ago, he was taking ambroxol that he buy over-the-counter for treating his sore throats. Then the cutaneous lesion in the left back of the hand appeared about one day later followed by a cutaneous lesion in his genital part. He recalled a history of 2 similar episodes in the same location 1 year and 6 months ago due to the same medication (ambroxol) that resolved about 7-10 days without any treatment, leaving post-inflammatory hyperpigmentation. This patient was given an education to avoid the offending drug (ambroxol) because this has been the third times he was experienced. Then he was given cetirizine 10 mg once daily and topical desoximetasone cream applied on the lesion twice daily. **Conclusion:** There is an increased risk of cutaneous drug reactions with expectorants containing ambroxol. We must increase awareness of fixed drug reaction cases due to the medications that are often used freely especially an over-the-counter medication.

1 INTRODUCTION

Fixed drug eruption (FDE) is a common cutaneous drug eruption characterized by the development of one or more annular, oval, erythematous and hyperpigmented patches as a result of systemic exposure to a drug and account for ~16% of all cutaneous drug eruption (Breathnach, 2004). The lesion may recur at the same site and/or at the new sites with re-exposure to the offending drug(s) (Ayanlowo, 2015). The reaction may be erythematous, eczematous, urticarial, bullous and pigmented with a necrotic center sometimes mimicking the target lesions of erythema multiforme. The lesion resolve with postinflammatory hyperpigmentation (Ayanlowo, 2015; Butler et al, 2015).

The number of diagnosed FDE cases is increasing steadily, due in part to increased awareness by physicians as well as increased

requests by patients to identify the precise cause of repeated eruptions and pigmentation (Lee, 2000). Fixed drug eruption is the second most common adverse cutaneous eruption reported in both in- and outpatients units, occurring at all ages and in all races (Ayanlowo, 2015). The list of drugs keeps growing with the introduction of new medications (Ayanlowo, 2015). Barbiturates, antibiotics (sulfonamides, tetracyclines, penicillin, and erythromycin) and non-steroidal anti-inflammatory drugs are common and well-known causative agents (Lee, 2000).

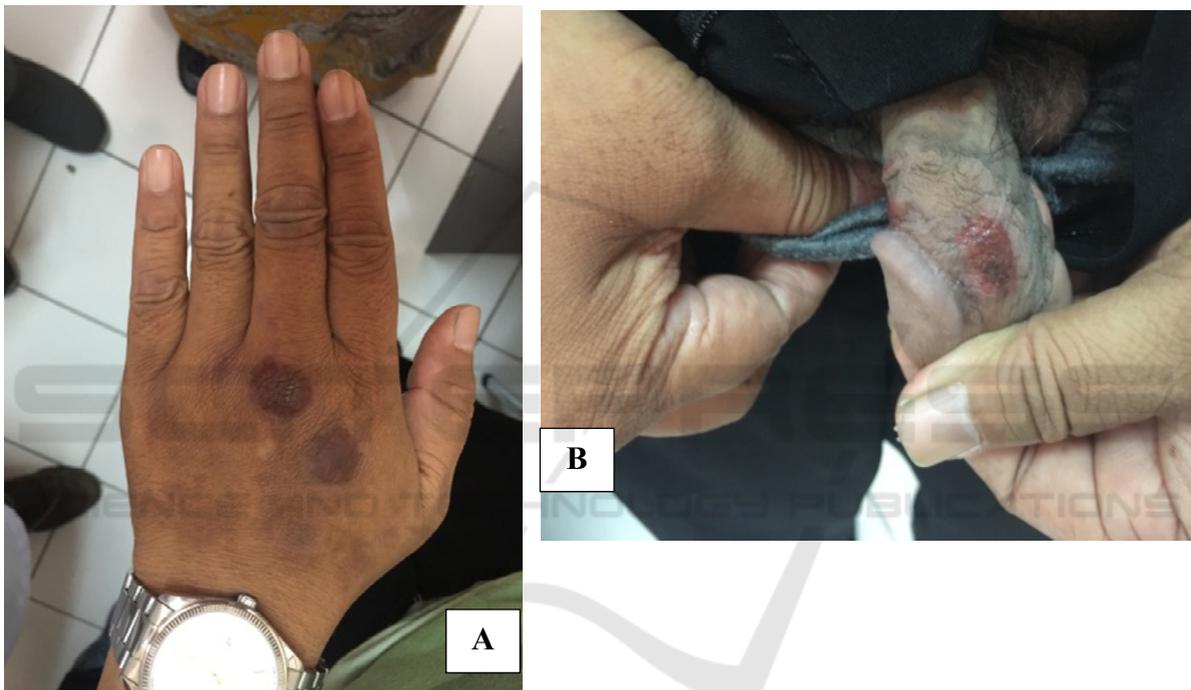
Mucoactive substances such as ambroxol, available in several countries as an over-the-counter medicines that used for the treatment of acute and chronic bronchitis.⁶ There was an old publication in 2006 about safety and usage pattern of an over-the-counter ambroxol cough syrup. This study confirms that ambroxol is used according to the advice given in the patient's leaflet and supports the already established safety and efficacy of this product in

acute bronchitis (Schulz et al., 2006). But in 2015, there was an emerge to update ambroxol safety because accumulating evidence from case reports and literature demonstrating that ambroxol is potentially responsible for severe cutaneous adverse reactions (SCARs) (Health Product Regulatory Authority, 2015).

2 CASE REPORT

A 37-years old Male came to Adam Malik Hospital Medan with the chief complaint an itchy, two similar

violaceous macular lesions on the left back of the hand and erythematous macular lesion in his genital part. Three days ago, he was taking ambroxol that he buy over-the-counter for treating his sore throats. Then the cutaneous lesion in the left back of the hand appeared about one day later. He recalled a history of 2 similar episodes in the same location 1 years and 6 months ago due to the same medication (ambroxol) that resolved about 7-10 days without any treatment, leaving post-inflammatory hyperpigmentation.



Picture 1. (A) two similar violaceous macular lesions, circumscribed, annular, on the dorsum manussinistra. (B) Erythematous macular lesion, circumscribed, annular with a central necrotic on the corpus penis region

From a dermatology examination we found two similar violaceous macular lesions, circumscribed, annular, on the dorsum manussinistra, and single erythematous macular lesion, circumscribed, annular with a central necrotic in corpus penis region. From a physical examination, we found the awareness is compos mentis, blood pressure was 110/60 mmHg, heart rate was 90x/minute, respiratory rate was 22x/minute and the body temperature was 37°C. The nutritional status was good and no abnormalities was found in other physical status.

This patient was given an education to avoid the offending drug (ambroxol) because this has been the

third times he was experienced. Then he was given cetirizine 10 mg once daily and topical desoximetasone cream applied on the lesion twice daily.

3 DISCUSSION

The number of diagnosed FDE cases are increasing steadily, due in part to increased awareness by physicians as well as increased requests by patients to identify the precise cause of repeated eruptions and pigmentation.(Lee, 2000) Fixed drug eruption is the second most common adverse cutaneous

eruption reported in both in- and outpatients units, occurring at all ages and in all races. (Ayanlowo, 2015; Sehgal et al., 2006)

Acute FDE lesions can develop within 30 minutes to 8 hours after drug administration. Lesions are clinically characterized as single or multiple, sharply demarcated, round or oval erythematous patches or plaques that may become vesicular or bullous. Because of the diversity of clinical pictures, the correct diagnosis may sometimes be difficult to achieve. But the FDE is characterized by recurrence the same lesion at the same site after repeated exposure to a causative drug. With repeated exposure, new lesions can appear, and the previous lesions may increase in size. In our case, this patient has complained an itchy, two similar violaceous macular lesions on the left back of the hand and erythematous macular lesion in his genital part. These lesions appeared one day after he took ambroxol that he buy over-the-counter. The lesions in the left back of the hand appeared first followed by the lesion in his genital. He recalled a history of two similar episodes in the same location 1 years and 6 months ago due to the same medication (ambroxol). Fixed drug eruption are commonly found on the genitalia and in the perianal area, although they can occur anywhere on the skin surface. (Shear NH & Knowles SR, 2012)

The diagnosis of a cutaneous drug eruption involves the precise characterization of reaction type. Some cutaneous reaction such as FDE, are almost always due to drug therapy. Timing of drug exposure and reaction onset, course of reaction with drug withdrawal or continuation, timing and nature of recurrent eruption on rechallenge, a history of a similar response to a cross-reacting medication and previous reports of similar reactions to the same medication are helpful to diagnosed. (Shear & Knowles, 2012) Clinical history is most important in diagnosing FDE, but patch tests and drug challenge tests are also helpful and are used frequently for a more objective diagnostic approach. We didn't do a drug challenge test in this case because our patient clearly remembered that the cutaneous lesions appeared after he ingested ambroxol.

Ambroxol belongs to a group of medications called mucolytic. Ambroxol works by thinning down the mucus in the airway passages, thus making the mucus less sticky and it also facilitates the removal of the mucus from the airways. Ambroxol is available for pain relief of sore throats and available over-the-counter in many countries includes Indonesia. The review of ambroxol safety was

initiated following post marketing reports of hypersensitivity reactions including anaphylactic reactions and accumulating evidence from case reports and literature demonstrating that ambroxol is potentially responsible for severe cutaneous adverse reactions (SCARs). (Sehgal et al., 2006; Shear & Knowles, 2012). The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has completed a review of the safety of ambroxol and bromhexine-containing medicines. The PRAC considered that ambroxol and bromhexine are associated with a small increased risk of hypersensitivity reactions and possibility of a risk of SCARs. The PRAC was considered that the risk of SCARs should be addressed by its inclusion in the product information accompanied by a warning for patients and caregivers to recognise the prodromes of SCARs and to discontinue treatment immediately in the event of such signs. (Shear & Knowles, 2012)

4 CONCLUSION

There is an increased risk of cutaneous drug reactions with ambroxol. We must increase awareness of fixed drug reaction cases due to the medication that are often used freely especially an over-the-counter medication.

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