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CLINICAL FEATURES AND HISTOPATHOLOGIC EXAMINATION IN SUPPORTING THE DIAGNOSIS OF EXFOLIATIVE DERMATITIS SUSPECTED CAUSED BY CAPTOPRIL IN CHILD: A CASE REPORT

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ABSTRACT
Exfoliative dermatitis (ED) is a rare but severe skin condition in children, characterized by widespread erythema and scaling involving more than 90% of the body surface area. Drug-induced ED is uncommon in the pediatric population, with captopril rarely reported as a causative agent. Case Presentation: We report a case of a child presenting with generalized erythema, scaling, and desquamation of the skin after initiation of captopril therapy for a cardiac condition. The clinical course was marked by fever, irritability, and extensive skin involvement. Laboratory findings showed leukocytosis and elevated inflammatory markers. Histopathologic examination of a skin biopsy revealed parakeratosis, acanthosis, and perivascular lymphocytic infiltrate, consistent with features of exfoliative dermatitis. Captopril was discontinued, and the patient was managed with supportive care, including fluid balance, topical emollients, and systemic corticosteroids. Significant clinical improvement was observed within days after drug withdrawal. Conclusion: This case emphasizes the importance of recognizing the clinical and histopathological features of exfoliative dermatitis in children. Although rare, captopril should be considered as a potential cause, particularly when symptoms occur shortly after drug initiation. Early diagnosis and prompt discontinuation of the offending agent are crucial for patient recovery and prevention of complications.

Keywords: captopril; clinical feature; exfoliative dermatitis; histopatology

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INTRODUCTION

Exfoliative dhermatitis (ED) is defined as diffuse erythema and scaling of the skin involving more than 90% of the total body skin surface area. (Grant-Kels JM 2012) It is a reaction pattern and cutaneous manifestation of a myriad of underlying ailments, including psoriasis and eczema, or a reaction to the consumption of certain drugs. Though some experts believe it does not pose a significant risk of death, erythroderma is a potentially life-threatening condition that requires proper diagnosis, identification of underlying etiology, and management. (Austad SS 2022)Exfoliative dermatitis is an uncommon clinical entity in the pediatric age group, similar to adult ED, the etiology of ED includes pre-existing skin diseases, drug-induced, malignancy, and others. (Wisuthsarewong, 2017)Several factors have been implicated as triggers for erythroderma and can be grouped into several general categories, including preexisting dermatoses, drugs, and malignancies. Cutaneous drug eruptions are one of the most common types of adverse reaction to medications, with an overall incidence of 2–3 % in hospitalized patients. (Cesar A 2016) In particular, drug induced exfoliative dermatitis (ED) are a group of rare and more severe drug hypersensitivity reactions (DHR) involving skin and mucous membranes and usually occurring from days to several weeks after drug exposure. Drugs Involved in Exfoliative Dermatitis, one of the drugs that cause it is cardiac drugs such as captopril. (Yacoub MR 2016).

Captopril, an angiotensin-converting enzyme (ACE) inhibitors containing a sulfhydryl group and has occasionally been implicated in complex immunological diseases, this chemical group has been considered the culprit of allergic reactions to captopril. Captopril has recently been released for limited clinical use in the treatment of refractory congestive heart failure and severe hypertension. Cutaneous reactions are the most common side effects of this therapy include exfoliative dermatitis, angio-edema, anaphylactoid reactions, maculopapular eruptions, pitiryasis rosea-like rash, and toxic erythema. (Gaig P 2001)The classic presentation of ED is erythematous patches that increase in size and coalesce into generalized red erythema with a shiny appearance. By definition, ED involves more than 90% of the patient's skin surface. A few days after the onset of erythema, fine white or yellow scaling begins, classically arising in the flexures. Plate-like scaling may occur acutely and on the palms and soles. The scaling progresses further, giving the skin a dull red appearance. With chronicity, edema and lichenification lead to skin induration. (Tso S 2021)Diagnostic workup includes a complete history and physical examination, with careful analysis of pertinent clinical clues and dermatohistopathology. Other laboratory workup is often required and determined by clinical clues. (Austad SS 2022)Management of ED involves combining symptomatic relief with addressing the underlying etiology and potential systemic complications. In patient hospitalization is required in acute cases. (Austad SS 2022)

METHOD

This article is a case report study that provides diagnosis, clinical management, and patient follow up care. Data from this case report were obtained through anamnesis, physical examination, and supporting examinations conducted at Adam Malik General Hospital, Medan. The data obtained were then analyzed qualitatively and presented in narrative form. This case report discusses a a 16-year-old girl who experienced ED suspected by drug-induced due to captopril. This case report will describe the risk factors found, analyze individual case, and is expected to provide insights into clinical practice, especially regarding the problem of ED in children.

RESULT

A 16-year-old woman, was consulted to the Dermatology and Venereology Department of H. Adam Malik General Hospital on September 1st, 2023 with reddish patches and exfoliative scaly on the skin all over her body accompanied by fever, puffy-looking face, itching, painful on the skin, had fatigue, malaise and was shivering since 4 days ago. Initially, 4 days before admission to the hospital, red patches were found on the patient's arms and body, then the patches were scaly and itchy, so the patient tended to scratch until the skin peeled off and the patches became itchy. So the patient tended to scratch until the skin peeled off and was stinging. The patient had a history of SLE and lupus nephritis who regularly took systemic steroids, and 5 days before hospitalization the patient received captopril due to high blood pressure conditions. After taking the drug, red patches began to appear followed by thickened scales which became more and more widespread. Then the patient went to the puskesmas and received itching medicine and ointment therapy, but said the patient had not improved. The drug was discontinued due to suspicion of captopril drug allergy since August 27, 2023.

There is no history of food allergies, nor a history of cancer or malignancy in patient or the family member. Past medical history, patients previously diagnosed with systemic lupus erythematosus (SLE) and lupus nephritis. History of suffering from other atopy diseases in the patient and family was denied. The physical examination revealed a shivering general condition, compos mentis consciousness, good nutritional status, the body weight of 51 kg and height of 155 cm, blood pressure of 130/90 mmHg, pulse frequency of 85 x/min, respiratory frequency of 22 x/min and body temperature of 37.6 °C. On dermatologic examination (Figure 1), patch erythematous are found in the fascialis, trunkus, and inferior

extremities, and scales were found in the fascialis, trunks, superior extremities, and inferior extremities (generalized).

Figure 1. A - E. Exfoliative Dermatitis. Erythematous macules with thickened scales were found in the fascial region, trunk, superior extremities, and inferior extremities (generalized).

Supporting examinations performed on the patient were complete blood laboratory tests, liver function, kidney function, electrolytes, and blood sugar. Laboratory abnormalities found in the patient include anemia with hemoglobin of 8,4 g/dL, hematocrit of 23,5 %. Type count examination in patients gives the impression of eosinophilia, low albumin test result. The patient was differentially diagnosed with exfoliative dermatitis suspected caused by captopril, exfoliative dermatitis caused by seborrheic dermatitis and exfoliative dermatitis caused by psoriasis. The working diagnosis based on physical and additional examination was exfoliative dermatitis suspected caused by captopril. Based on anamnesis, complaints appeared after the patient was given the captopril before hospitalized on H. Adam Malik Hospital. On physical examination, the patient was found to have a more dominant generalized scalling and on laboratory support examination, the impression of eosinophilia and hypoalbuminemia was found.The results of histopathological examination; Macroscopically: two pieces of biopsy tissue from a lump on the scapula area, yellowish white color, uneven surface, rubbery consistency, weight 0.09 grams, size 0.6 x 0.4 x 0.3 cm and 0.8 x 0.5 x 0.4 cm. Microscopically: Biopsy tissue preparation of a lump in the scapula area with an epidermal layer of stratified squamous cell epithelial layer that undergoes acanthosis, hyperkeratosis and minimal spongiosis. in the sub-corneum layer, there are foci of intraepidermal vasicles containing keratinized masses. in the sub-epidermis, there is an infiltration of inflammatory cells - lymphocytes and neutrophils in the papillae of the dermis. stroma consists of fibro-collagenous connective tissue. no dysplasia cells or signs of malignancy are found in this preparation. (Figure 2) Conclusion: Consistent with eksfoliative dermatitis.

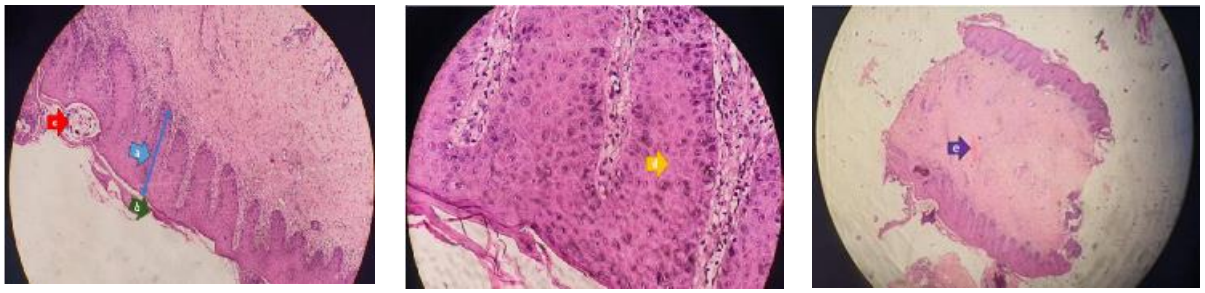

Figure 2. Histopathology of skin from the scapula region showing ; A) a. acanthosis an epidermal layer; b. hyperkeratosis an epidermal layer; c. infiltration of inflammatory cells - lymphocytes and neutrophils in the papillae of the dermis. B) d. minimal spongiosis an epidermal layer (x20 magnification Haematoxylin & Eosin). C) e. stroma consists of fibro-collagenous connective tissue. (x20 magnification Haematoxylin & Eosin).The therapy given to this patient is Intravenous fluid replacement, intravenous methylprednisolone pulse 125 mg/daily until 3 days and stop giving methylprednisolone tablets, intravenous ampisilin 1500

gr/6 hours, intravenous gentamisin 250 mg every 24 hours, albumin correction with albumin 25% 8.5 cc in 4 hours, intravenous paracetamol 500 mg three times daily, intravenous ranitidine 50 mg every 12 hours/day, cetirizine 10 mg twice daily, fusidic acid 2% cream twice daily in erosions lesions, desoximetasone 0,25% cream twice daily in erythematouslesions, and atopiclair® cream twice daily. And also it is recommended to do a bacterial culture examination (Table 2).

Table 2.
The results of bacterial culture to antibiotic sensitivity

Chemistry	Result
Ampicilin	R
Ciprofloxacin	R
Erythromycin	R
Gentamicin	R
Linezolid	S
Oxatilin	R

R = Resistance; S = Sensitive

On the 17th day of hospitalization, Patient felt the skin lesions had improved much. The patient had no complaint. The dermatological examination, erythema and scales on generilized were no longer visible on the body (Figure 3).

Figure 3. A - E. Exfoliative Dermatitis. Erythema and scales on generilized had been reduced significantly.

The therapy given to this patient from our department including atopiclair® applied to the whole body twice daily and desoximetasone 0,25% cream twice daily. The patient was discharged with markedly clinical improvement 13 days after admission. The patient was advised to follow up at the Dermatology and Venereology Clinic of Adam Malik General Hospital, Medan.

DISCUSSION

Exfoliative dermatitis is a generalized skin erythema involving more than 90% of the body surface area with varying degrees of of scaling. Some cases are associated with erosions, crusts, and hair and nail changes. Generalized exfoliative dermatitis is often known as with erythroderma. Patients with erythroderma can be clinically stable with an acute, subacute, chronic or life-threatening disease course. Generally generalized exfoliative dermatitis affects the whole body and is associated with with life-threatening complications, namely sepsis, hypovolemic shock, and acute renal failure secondary to cutaneous fluid loss. (Reynolds KA 2021) The patient in this case report presented with a general condition of chills with skin manifestations that were first encountered in the form of erythematous plaques accompanied by thickened and thorough scales, in accordance with the description of exfoliative dermatitis A detailed history is essential to diagnose dermatitis exfoliativa generalized and finding the underlying etiology, including comorbidities, allergies, previous skin diseases, history of drug consumption, and timing of the of symptom onset. In general, the onset of symptoms is acute and faster for generalized exfoliative dermatitis is often found in drug induction, whereas

primary skin diseases have a slower course. Its characteristic clinical features are erythematous plaques with well-defined borders and enveloping scuama. (Simpson EL 2019

Captopril, an angiotensin converting enzyme inhibitors (ACEIs), has recently been released for limited clinical use in the treatment of refractory congestive heart failure and severe hypertension. The only major dermatologic side effects from this medication have been either an urticarial or an erythematous, maculopapular eruption. (Esen 2020) The severe systemic allergic reactions are often referred to as anaphylactic reactions representing serious and potentially life-threatening reactions, presented with rapid onset within minutes to hours. (Mistry 2015) In some instances, the evolution of anaphylactic reactions may be delayed, and cardiovascular collapse and/or respiratory failure can occur up to eight hours after symptom initiation. Therefore, the initial and usually milder symptoms should not be ignored. (Linuwih S 2016) The patient was differentially diagnosed with exfoliative dermatitis suspected caused by captopril, exfoliative dermatitis caused by seborrheic dermatitis and exfoliative dermatitis caused by psoriasis. The working diagnosis based on physical and additional examination was exfoliative dermatitis suspected caused by captopril. Based on anamnesis, complaints appeared after the patient was given the captopril before hospitalized on H. Adam Malik Hospital and a rash appeared after 2 days.

The patient was treated in cooperation with pediatric. Treatment from the pediatric included stopping all suspected drugs (captopril). Intravenous fluid replacement, intravenous ampisilin 1500 gr/6 hours, intravenous gentamisin 250 mg every 24 hours, intravenous paracetamol 500 mg three times daily, intravenous ranitidine 50 mg every 12 hours, methylprednisolone 4 mg 1-0-1 tablet/day (8 mg), cetirizine 10 mg twice daily, The patient was also observed every 6 hours for vital signs and fluid balance and was given high-protein diet. The treatment from our department such as normal saline wet dressing four times daily, fusidic acid 2% cream twice daily in erosions lesions, desoximetasone 0,25% cream twice daily in erythematouslesions, and atopiclair® cream twice daily. Based on the literature, management of DEG includes providing nutrition, controlling skin hydration, preventing scratching, and triggering factors such as the use of drugs, as well as treating the underlying disease and preventing complications. Topical therapy modalities that are the first line for DEG are oatmeal bath, wet dressing, topical emollients, and topical corticosteroids. As for systemic therapy, sedative antihistamines can be given, oral antibiotics if a secondary infection is found, diuretics if peripheral edema is found and fluid replacement therapy to avoid electrolyte balance disorders. (Grant KJM 2012) Inflamed skin can be given moisturizers or mild potency topical steroids, while systemic corticosteroids are only used in DEG caused by atopic dermatitis and DEG caused by drug eruptions with a slow dose reduction to minimize the risk of rebound flares. Systemic corticosteroids 1-2 mg/kg/day with tapering off are effective to manage inflammatory reactions on the skin. (Tso S 2021) The use of corticosteroids in high doses and long term can cause suppression of adrenal gland function, suppression of the immune system, kaposi's sarcoma, and psychiatric disorders. The use of corticosteroids that are stopped suddenly can cause withdrawal symptoms in the form of fatigue, joint pain, muscle weakness, loss of appetite, nausea, hypoglycemia and dehydration. Consideration of some of these symptoms is the purpose of tapering off in systemic corticostaroid administration. (Dennis MW 2018).

The prognosis in this patient was quo ad vitam bonam, quo ad functionam bonam, quo ad sanationam dubia ad bonam. The clinical condition improved until follow-up 2 weeks after treatment. Many factors influence the clinical course and prognosis of erythroderma, including age, etiology, comorbidities, speed of onset of erythroderma, and early initiation of therapy. The patient in this case report was educated to discontinue and careful about vaccne use, informed of her drug allergy, and given a note of any suspected drugs that could give her an allergic reaction in case of future treatment. (B.C Kang 2014)

CONCLUSION

Exfoliative dermatitis (ED) is defined as diffuse erythema and scaling of the skin involving more than 90% of the total body skin surface area. Histopathologic examination is important to exclude differential diagnosis. Management involves a multidisciplinary specialist approach, immediate discontinuation of the suspected drug, administration of corticosteroid agents, and supportive care.

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