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## Steroid-induced diabetes mellitus in pemphigus vulgaris patient at Bali Mandara Hospital: a case report



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### ABSTRACT

**Background:** Pemphigus vulgaris (PV) is a blistering autoimmune disease of the skin and mucous membranes defined histologically by intraepidermal blister due to acantholysis. Systemic corticosteroids and immunosuppressive agents had greatly improved the prognosis of pemphigus. However, steroid use often leads to metabolic complications, such as diabetes mellitus. This case report describes steroid-induced diabetes mellitus in PV, where the side effect of long-term high dosages steroid used and the method to manage it can be used as a study case.

**Case report:** A 31-year-old man complained of new blisters from almost the entire body. He had a history of PV 1 year ago and no history of diabetes mellitus in the patient or family. He had a medication history of methylprednisolone 8 mg every 8 hours. Dermatological status showed erythema macules, extensive erosion almost on the entire body, the Nikolsky sign (+), and the Asboe-Hansen sign (+). Blood laboratory result: random blood glucose 451 mg/dl, HbA1c 12.3%. Histopathological examination: suprabasal blister, in which the basal cells still attached to the basement membrane show a "tombstone" appearance. The diagnosis was steroid-induced diabetes in pemphigus vulgaris. He was treated with steroids and insulin.

**Conclusion:** Steroid use in PV treatment can lead to metabolic complications, such as diabetes mellitus. Regularly monitoring is needed to prevent complications due to steroid use.

**Keywords:** Pemphigus vulgaris, autoimmune, steroid-induced diabetes mellitus

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### INTRODUCTION

Pemphigus vulgaris (PV) is a blistering autoimmune disease of the skin and mucous membranes defined histologically by intraepidermal blisters due to acantholysis. The blisters occur in the deeper part of the epidermis, above the basal layer.<sup>1</sup> Incidence of PV has a worldwide distribution and occurs in all races and ages.<sup>2</sup> PV is triggered by various factors such as drugs (captopril, penicillamine), infection (herpes simplex virus, Epstein-Barr virus, etc.), pesticides, ultraviolet radiation (UVR), thermal burns, stress, and food containing an allium, phenol, thiol, or urushiol.<sup>3</sup> PV results from autoantibodies (IgG) against desmoglein, a desmosomal adhesion molecule, resulting in loss of cell-to-cell adhesion. Desmoglein-1 is found in all epidermis layers, while desmoglein-3 is located in the parabasal and basal layers.

Patients with PV have antibodies targeted against desmoglein-1, and desmoglein-3.<sup>4</sup> PV was usually a disease with a 50% mortality rate in 2 years. Large areas of the skin lose their epidermal function, leading to the loss of fluids or secondary infection.<sup>5</sup> Management of PV depends on the severity and distribution of the disease.<sup>4</sup> Systemic corticosteroids and immunosuppressive agents had greatly improved the prognosis of pemphigus.<sup>5</sup> Nonetheless, systemic corticosteroids used in high dosages and long term can lead to metabolic complications.<sup>6,14</sup> Diabetes mellitus is one of the major complications because of impaired glucose metabolism by corticosteroids due to increased insulin resistance in tissues, increased glucose production in the liver, and impaired glucose consumption in muscles and adipose cells.<sup>5</sup> We present a patient with steroid-induced diabetes mellitus

in pemphigus vulgaris at Bali Mandara hospital, where the side effect of long-term high dosages steroid used in PV and the method to manage it can be used as a study case.

### CASE DESCRIPTION

A 31-year-old man came to the Emergency Department of Bali Mandara hospital with a chief complaint of new blisters from almost the entire body two days ago. Some of the blisters are broken and leave yellowish brown crusts. The patient complained of itch from almost the entire body and pain in the broken blisters. One year ago, the patient reported that the first blister wound appeared on the left wrist. The blister was about 0,1cm x 0,2cm. Afterward, blisters widen and spread to almost the entire body. Some of the blisters are broken and leave a similar

appearance to the type of wounds found on burn victims. The patient also reported he had a history of PV since one year ago. He had been admitted to the hospital with the same disease several times. The patient denies a history of diabetes mellitus, allergies, and a family history of diabetes mellitus. The patient reported a medication history of methylprednisolone 8 mg every 8 hours.

Physical examination: *compos mentis* awareness, with GCS 4-5-6, blood pressure 111/67/72 mmHg, pulse rate 106 x/minutes, regular respiration rate 18x/minutes, regular axillary temperature 37.1°C. Bodyweight 50 kg, height 160 cm, body mass index 19.53 kg/m<sup>2</sup>, oxygen saturation 99% on room air.

In dermatological status, almost the entire body is found erythema macules with soft boundary, extensive skin erosion, erythematous base, generalized distribution, irregular shape, nummular, firm edge. In this patient is found a positive Nikolsky sign and positive Asboe-Hansen sign.

**Laboratory examination:** Random blood glucose 451mg/dl, urea 52 mg/dL, creatinine 0.43 mg/dL, liver function within normal limits. Electrolyte levels: sodium 130 mmol/L, potassium within normal limits. The patient's HbA1c has been examined, and the results are 12.3%. The histopathological examination in this patient shows a suprabasal blister, which the basal cells still attached to the basement membrane that shows "Tombstone" appearance.

Based on clinical manifestation and laboratory findings, the patient was

diagnosed with steroid-induced diabetes in pemphigus vulgaris. The patient was treated with IVFD NaCl 0.9% 20 drops per minute, insulin drip 4 unit/hour, pantoprazole injection one vial every 12 hours, ondansetron injection 8 mg every 8 hours, antacid syrup 10 ml every 8 hours, sucralfate syrup 10 ml every 8 hours, methylprednisolone injection 62.5 mg every 12 hours, cetirizine 10 mg every 24 hours, NaCl 0.9% compress three times a day for 10 minutes in wet lesions, topical gentamicin cream in new blisters after being compressed with NaCl 0.9%

## CLINICAL COURSE

On the second day of hospitalization, random blood glucose 191 mg/dl and blood glucose 2-hours postprandial 171 mg/dL. The insulin drip was stopped. The patient received additional insulin basal therapy 1x6 IU and rapid-acting 4 IU every 8 hours. The patient was planned to be received additional therapy, azathioprine as a sparing agent, but the patient did not agree due to side effect reasons. On the fourteenth day of hospitalization, random blood glucose 123 mg/dL and blood glucose 2-hours postprandial 140 mg/dL.

Management of PV in this patient, the methylprednisolone dose was gradually reduced. The initial dose is given 62.5 mg every 12 hours intravenously for seven days. After the lesion showed improvement and there were no new blisters, the dose of methylprednisolone was reduced to 62.5 mg once a day for eight days. In re-evaluation, the lesion improved, and there were no new blisters, the dose was reduced

to 48 mg orally in the morning for four days. Afterward, the patient was given an outpatient medication with a 48mg oral dose of methylprednisolone once a day. After one week of outpatient medication, the patient was being followed up in the polyclinic showed improvement, and there were no new blisters. The patient agrees to share information and photography for publication.

## DISCUSSION

This case report describes a patient diagnosed with pemphigus vulgaris and received high-dose methylprednisolone therapy, undergoing diabetes mellitus.

PV is the most common type of pemphigus. The incidence of pemphigus is 0.1-0.5/100,000 people per year and even higher in certain populations.<sup>7</sup> PV is rarely found in children.<sup>8</sup> PV usually occurs in patients between 40 to 60 years of age, with a higher incidence in men.<sup>4</sup> In this case, it was found that the patient was 31 years old, with a chief complaint of new blisters from almost the entire body for two days before the examination. The patient denied a history of diabetes mellitus, allergies, and a family history of diabetes mellitus. The patient reported a medication history of methylprednisolone 8 mg every 8 hours. This complaint shows symptoms in a patient with vesiculobullous dermatosis disorders, one of which is pemphigus.

Clinically, skin lesions in PV are rarely pruritic but are often painful. The initial lesion of PV is a flaccid blister, which may occur on any area of the skin surface. Rarely found intact blisters because these blisters are fragile. Even the new blisters are usually flaccid or become so quickly. The most common skin lesion in the patient is erosion, often painful, following a broken blister.<sup>1</sup> In this patient, the initial lesion is found on the left wrist. These complaints are increasing day by day, and the erosive become quite extensive.

Both Nikolsky and Asboe-Hansen sign are found positive in PV. A positive Nikolsky sign is because of the acantholysis process. Asboe-Hansen sign is positive because of decreasing adhesion between keratinocytes or between the basal epidermal cells and the dermal connective tissue. To elicit the Nikolsky sign by pressing and sliding the skin between two



**Figure 1.** Patient's initial condition

bullae, the skin layer will shear off. Asboe-Hansen sign is said to be positive if the blister expands when the blister is being pressed.<sup>2,9</sup> In numerous patients, erosions tend to develop granulation tissue and crusting.<sup>1</sup> Clinically, this patient has the same result as described in theory. The primary blister of the patient was found on the left wrist, measuring about 0,1cm x 0,2cm, which is progressively expanding and increasing in number. The blisters are spread all over the body. Erosion caused by brittle blisters dominates the patient's skin. In many areas of the erosion has developed to crust. The erosion causes itch in the patient, although it is rarely found in PV in theory. Besides, there are positive Nikolsky and Asboe-Hansen sign in this patient.

A loose blister, which is easily broken, differentiates PV from other vesiculobullous diseases such as bullous pemphigoid, pemphigus foliaceus, or dermatitis herpetiformis. A fragile and broken blister will become erosion.<sup>10</sup> In this patient, there are erythematous macule, blister, extensive erosion, generalized distribution, irregular shape, nummular, firm boundaries.

The gold standard in diagnosing PV is a histopathological examination taken by skin biopsy of the new lesion to determine the location of blisters.<sup>10</sup> Histopathological examination in PV shows suprabasal blister with acantholysis. Above the basal layer, epidermal cells lose the adhesion between cells and form blisters. The basal cells stay attached to the basement membrane, but the adhesion between basal cells may lose. As a result, there is maybe a "row of tombstones" appearance.<sup>1</sup> In this patient, the histopathological examination taken by skin biopsy shows suprabasal blister, which the basal cells still attached to the basement membrane, that shows "row of tombstone" appearance.

This patient was given therapy as the patient's complaint, where the main therapy in this patient is a steroid, methylprednisolone 62.5 mg orally every 12 hours. Methylprednisolone dosage is decreased gradually when there is no new blister. Based on the consensus for PV therapy, the basis of PV therapy is steroids because they are immunosuppressive and anti-inflammatory potent.<sup>11</sup> The

most commonly used typed of steroid is methylprednisolone and dexamethasone.<sup>10</sup>

Based on the British Association of Dermatologists, a steroid in PV typically takes several weeks to achieve (median three weeks). One steroid that can be given is methylprednisolone at 1.5 mg/kg/day. However, a steroid is given at a high dosage intravenously (>2 mg/kg/day) to attain better efficacy.<sup>10-12</sup> In this case, intravenously, methylprednisolone is given at a high initial dose. After being evaluated, the condition is controlled, defined as there is no new lesion, and the lesion shows improvement, the dose is slowly reduced until it can be given orally.

Although the steroid is an effective treatment for PV, the morbidity and mortality are still significant due to complications of therapy. One of the major complications is diabetes mellitus. Steroid causes impaired glucose metabolism due to increased tissue insulin resistance, increased glucose production in the liver, and impaired glucose consumption in muscles and adipose cells.<sup>5</sup> The mechanism of impaired glucose metabolism after steroid therapy is similar to type 2 diabetes mellitus, up to 60-80% depending on the dosage and the type of steroid used.<sup>13</sup>

In this case, a patient with PV is given steroid therapy at a high dosage, leading to diabetes mellitus as a complication. There was no history of diabetes mellitus in the patient or family.

The diagnosis of steroid-induced diabetes mellitus (SIDM) is made when there is an abnormal increase in blood glucose associated with steroids in a patient with or without a preceding history of diabetes mellitus. Based on the American Diabetes Association, diagnosing criteria for diabetes mellitus: random blood glucose  $\geq 126$  mg/dl, blood glucose 2-hours postprandial  $\geq 200$  mg/dl, HbA1c  $\geq 6.5\%$  or random blood glucose  $\geq 200$  mg/dl.<sup>14</sup>

In this patient, the diagnosis of diabetes mellitus was made based on the results of the patient's random blood glucose examination 451 mg/dl and HbA1c 12.3%.

The initial management of the patient with SIDM is lifestyle education emphasizing diet, exercise, and weight loss. Nevertheless, insulin can be the best initial therapy for SIDM if blood glucose

reveals above the normal value.<sup>15</sup> Based on the patient, following the theory, with the results of sugar levels, this patient is given insulin drip four units/hour. The insulin dose is gradually decreased and stopped, along with decreasing the patient's blood glucose. After several days of hospitalization, the patient's blood glucose examination results were 123 mg/dl and blood glucose 2-hours postprandial 140 mg/dl.

## CONCLUSION

Steroid use is still the main therapy for PV. Although, steroid use risks metabolic complications, such as diabetes mellitus. Therefore, regular monitoring is needed when the patient receives steroid therapy to prevent complications due to steroid use.

## ETHICS IN PUBLICATION

The patient approved clinical finding documentation and publication.

## AUTHORS CONTRIBUTION

All authors have contributed from patient examination, treatment, follow-up medication, reference finding, manuscript preparation, and publication.

## CONFLICT OF INTEREST

None.

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