CASE REPORT

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Successful alopecia universalis treatment with the combination of cyclosporine and oral corticosteroid: a case report

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ABSTRACT

Background: Alopecia universalis is an autoimmune condition on hair follicles with the characteristics of ovoid or round-shaped hair loss (focal) that develops into multiple hair losses and is the most severe form of alopecia. The pathogenesis of alopecia universalis is unclear. However, the most accepted hypothesis is based on the immunologic factor, especially T-cell mediated autoimmune process.

Case: A 19-year-old male Indonesian complained of hair loss all over his body. Efflorescence of the whole body showed an alopecia patch. The Severity of Alopecia Tool (SALT) score showed 100%. Skin dermoscopy indicated yellow dots. The patient was given 8 mg of intraoral methylprednisolone every 8 hours and 100 mg of intraoral cyclosporine every 12 hours for four weeks and slowly tapering off. The patient experienced acneiform eruption and was topically treated with 2% sulfur lotion every 12 hours. After 51 days of observation, an improvement was found in terminal hair growth on the head, eyelashes, and eyebrows, visible growth of vellus hair on the body, and a SALT score of 40%.

Conclusion: Alopecia universalis is rare and can cause significant damage and psychological pressure to the affected individuals. Treatment with corticosteroid and cyclosporine resulted in good therapy response.

Keywords: Alopecia, alopecia universalis, alopecia areata, SALT.
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INTRODUCTION

Alopecia universalis and totalis is the severe clinical form of alopecia areata.[1] Alopecia areata is an autoimmune disease of the hair follicles, marked by ovoid or round-shaped hair loss (focal), and can develop into multiple hair losses.[2–4] Around 5% of alopecia areata cases develop into alopecia totalis, marked by the total hair loss on the scalp.[5] Meanwhile, around 1-2% of alopecia areata cases can develop into alopecia universalis, marked by the total hair loss on the scalp and body.[2,5]

Alopecia areata occurs in all populations in the world.[6] The prevalence in the US is around 0.1%.[7] Meanwhile, the prevalence for alopecia totalis and alopecia universalis is around 0.08%.[8] Based on the visit data of the cosmeceutical polyclinic of Sanglah General Hospital from January 2018 to March 2022, there were 14 alopecia areata cases and two alopecia universalis cases.[9] In general, alopecia areata can affect males and females with similar proportions.[6] However, several studies showed that the male gender predominates in adults.[6]

The cause of alopecia universalis is still not known for certain. Persistent alopecia universalis causes significant damage and psychological pressure to the affected individuals.[10,11] Other than that, there has not been any therapy that can provide maximum results. The pathogenesis of alopecia universalis is unclear. However, the most accepted hypothesis is based on an immunological factor, especially T-cell mediated autoimmune process. Therefore, oral cyclosporine therapy has been widely used with different response levels for each individual.[12,13] However, systemic corticosteroids are also said to support hair regrowth in alopecia areata by utilizing immunosuppressive effects.[13]

The following reported a case of alopecia universalis in a male patient who was given a combination therapy of oral cyclosporine and systemic corticosteroid. This case was reported because alopecia universalis rarely occurs, thus becoming a challenge for clinicians to establish a diagnosis and provide treatment.

CASE DESCRIPTION

A 19-year-old male Balinese visited the Dermatology and Venereology Outpatient Clinic of Sanglah General Hospital with the main complaint of hair loss all over his body. It appeared suddenly, started with itchiness, followed by hair loss. The hair loss started from the lower extremities' region, then rapidly developed within two weeks into hair loss throughout the body. The patient said that previous hair growth was normal. He had no habit of pulling hair. The patient had no history of nail damage, patches on numb skin, red patches on the skin, and redness on the face when exposed to the sun. The patient also had a history of sneezing in the morning, especially during cold weather

or dusty air, which he experienced at three years old. He also had a history of dry skin since childhood and often felt itchy.

He never used traditional oil on his head and body. He visited a dermatology and venerology specialist within the last year and was given 10 mg of cetirizine tablet every 24 hours and 0.5% of topical betamethasone cream every 12 hours. The patient reported that the complaint showed no improvement during treatment. He had no history of systemic diseases such as thyroid, cardiovascular, malignancy, or drug allergy.

The patient is the second child of three siblings. Both siblings had no similar complaints. The patient's mother was reported to have a history of asthma. There was no history of systemic diseases in the family, such as thyroid disorder and malignancy. Regarding social history, the patient is a student who has dropped out of school since he suffered from this disease. He was embarrassed to face his school friends, so he dropped out. Currently, the patient helps his parents sell drinks at home. Vital signs and general status were within normal limits. Dermatological status on all body locations showed efflorescence of alopecia patches (Figure 1a-j). The Severity of Alopecia Tool (SALT) score showed 100%.

Based on history taking and physical examination, the differential diagnosis for the patient was alopecia universalis and trichotillomania. Scalp dermoscopy revealed yellow dots (Figure 2a-2b). The adjunctive examination was also carried out to determine the underlying disease, such as thyroid disease and anemia. TSH examination showed 0.45 IU/ml (0.27-4.2 IU/ml) and ferritin level was 58.31 ng/ml (6-67 ng/ml). Complete blood count, liver function, and kidney function were within normal limits.

Based on history taking, physical examination, and adjunctive examination, the patient was diagnosed with alopecia universalis. The patient was given the treatment of 8 mg of oral methylprednisolone tablet every 8 hours and 100 mg of intraoral cyclosporine tablet every 12 hours. The patient was also given counseling, information, and education concerning disease course, how to use the medicine, side effects, and routine follow-up.

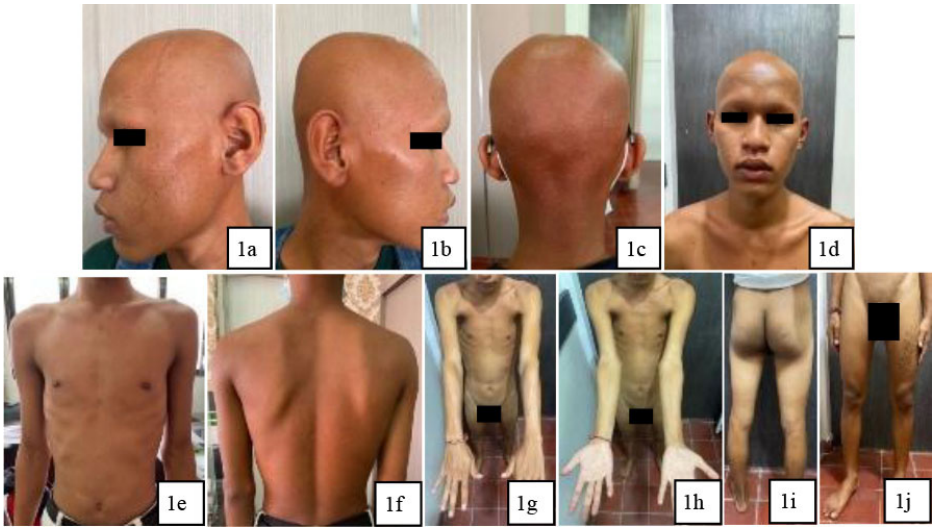

Figure 1a-1j. Clinical appearance of the patient. No hair growth throughout the body.

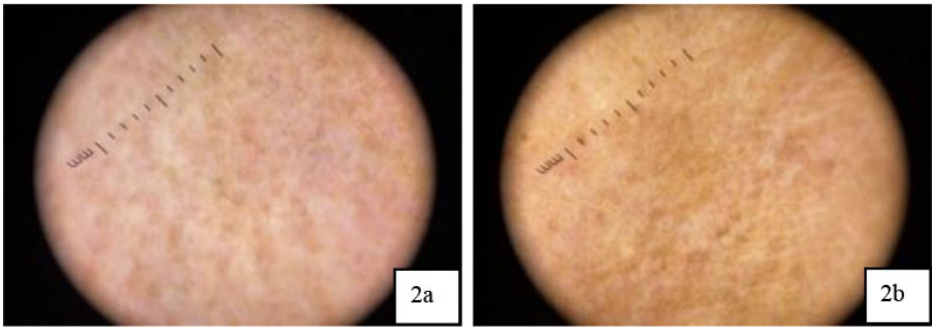

Figure 2a-2b. Scalp dermoscopy showed yellow dots.

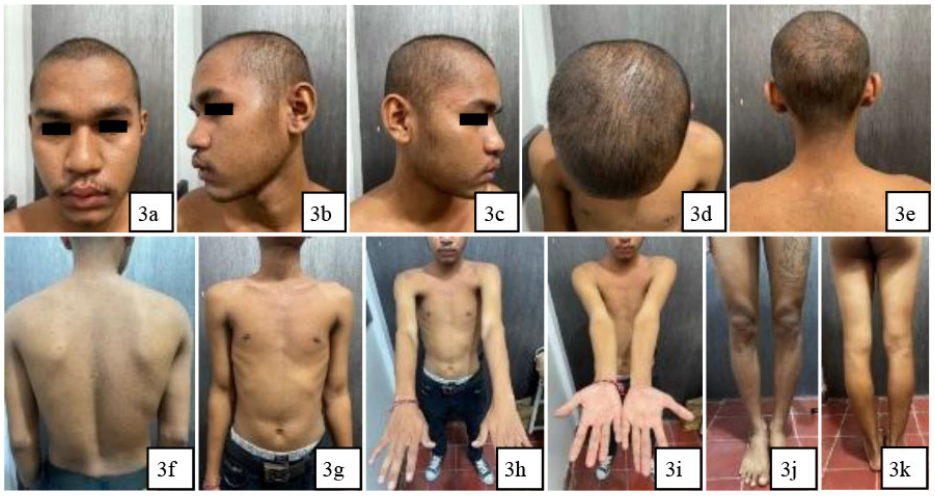

Figure 3. The scalp and eyebrow region showed black hair growth with 0.8 cm in length (**a-e**). Anterior and posterior thoracoabdominal regions showed vellus hair growth (**f-g**). Superior and inferior right and left extremities regions did not show signs of hair growth (**h-k**).

Day 28 observation showed an acne-like lesion on the body for a week. On the scalp, the anterior and posterior thoracoabdominal region showed efflorescence of skin-colored oval or round, well-defined multiple papules with a diameter of 0.3-0.5 cm, discretely spread, and without comedones. The Severity of

Alopecia Tool (SALT) score showed 91%. According to dermoscopy, the scalp and eyebrow regions showed blackish yellow vellus hair growth. The patient experienced alopecia universalis accompanied by acneiform eruptions. The patient was given 8 mg of intraoral methylprednisolone every 12 hours (tapering off), 100 mg of intraoral cyclosporine tablet every 12 hours, and 2% topical sulfur lotion every 12 hours on papules.

Day 51 observation indicated more hair growth on the eyebrows, head, and body. The patient had no complaint of hair loss. He still felt acnes, albeit reduced. The patient did not feel nauseous or had an increase in appetite. He had no problem eating, drinking, or urinating. Vital signs and general status were within normal limits. The alopecia location showed black hair growth measuring 0.8 cm long (Figure 3a-e). The anterior and posterior thoracoabdominal regions showed yellowish vellus hair growth (Figure 3f-g). However, no hair growth was found in the regions of the superior and inferior right and left extremities (Figure 3h-k). The scalp and anterior and posterior thoracoabdominal region showed an efflorescence of skin-colored ovoid-round well-defined multiple papules measuring 0.3-0.5 cm in diameter, discretely spread, and without comedones. The severity of Alopecia Tool (SALT) score was 40%. Dermoscopy on the scalp and eyebrows showed black terminal hair growth. The diagnosis was alopecia universalis follow-up (improved) and acneiform eruptions. Treatment was continued with 4 mg of intraoral methylprednisolone every 12 hours (tapering off), 100 mg of intraoral cyclosporine tablet every 12 hours, and 2% topical sulfur lotion every 12 hours on papules.

DISCUSSION

Alopecia areata is a common autoimmune disease of the hair. Around 5% of alopecia areata patients can experience whole scalp hair loss (alopecia areata totalis), and 1%-2% of alopecia areata patients can experience whole body hair loss (alopecia areata universalis).[2,5] This case reported a 19-year-old male patient who complained of a sudden onset of hair loss for three years. The patient stated that hair loss first occurred in the legs and rapidly developed into whole body hair loss within two weeks. There was no family history of similar complaints.

The pathogenesis of alopecia areata is highly affected by auto-active CD8 cytotoxic T-cells (affected hair follicles and nails) and by immune response affected by interferon-γ (comprises of interferon-γ and other chemokines induced by interferon-γ). Several risk factors include autoimmune conditions (atopy, vitiligo, lichen planus, morphea, Hashimoto thyroiditis, pernicious anemia, diabetes mellitus), genetic (related to HLA-A1, HLA-B62, HLA-DQ1, HLA-DQ3, and non-HLA molecules such as major histocompatibility complex class I chain-related gene A). It is also related to mood disorders such as stress, depression, anxiety, post-acute disease, drugs, systemic diseases, hormones, and nutrition deficiency.[4,10,14] Several studies found the existence of CD8+ cytotoxic T-cells subset NKG2D+ (natural-killer group 2 member D-positive) in inflammatory infiltrates of alopecia areata and an increase of 2 NKG2D ligands in hair follicles. Other types of cells, such as natural killer cells, may also play a role in alopecia areata as alopecia areata regulator.[14]

One of the risk factors of alopecia areata is atopic condition. Around 10% to 60% of patients with atopic diseases such as asthma, atopic dermatitis, and rhinitis allergy were reported to have alopecia areata. Patients with atopic history had a 24% risk of developing totalis and alopecia universalis.[7] Meanwhile, Sung *et al.* concluded that patients with a history of atopic in the respiratory tract, such as rhinitis allergy, had a higher risk of developing alopecia areata than asthma patients.[15]

The relationship of both can be associated with immunology potential mediated by T-cells that are targeted against hair follicle autoantigen.[3,7] Atopic diseases occur because of the Th2 cytokine pathway, including IL-4, IL-5, IL-13, and IL-31. Meanwhile, alopecia areata patients showed an increase in plasma circulation and Th1 cytokine lesions, such as interferon-γ and IL-2, and an increase in IL-3 and IL-7, which showed that the pathogenesis of autoinflammation is multifactorial.[16] Furthermore, alopecia areata and atopic disease have a Th2 cytokine pattern with an increase in IgE level, antibodies, mast cells, and eosinophils. Th2/IL-4 cells can stimulate the production of IL-5.[1] In this case, the patient had a history of rhinitis allergy from when he was three years old. The patient's mother also had a history of asthma. This patient's atopic history can be a risk factor for alopecia universalis. The patient also said he dropped out of school because he was embarrassed about his condition. This can cause stress that can aggravate the patient's condition.

Possible adjunctive examinations to help diagnose are dermoscopy, blood tests, and biopsy. Dermoscopy examination will show several variations that show the degree of severity of the disease. In general, alopecia areata will show black dots, yellow dots, exclamation mark hairs, broken hairs, and cadaver hair (the rest of the hair shaft is visible as a black dot in the follicular ostia). Black dots and exclamation mark hairs are specific findings that show disease course, while yellow dots can be associated with disease severity. Yellow dots show keratinous plugs and empty hair follicles that swell and are filled with sebum and keratin. Dermoscopy usually shows a point or whitish-yellow to yellow-pinkish polycystic with various sizes and uniform colors.[14,17–20] Bains *et al.* stated that yellow dots are always found in alopecia universalis and alopecia totalis.[21] Patch-type alopecia areata will show more broken hairs.[21,22]

Meanwhile, trichotillomania will show a dermoscopy result of reduced hair thickness, shortened vellus hair, broken hair with different shaft lengths, rounded hair, trichoptilosis, and rare yellow dots.[23] This case only included dermoscopy and laboratory tests. Skin dermoscopy showed yellow dots. Thyroid hormone and ferritin tests were within normal limits. From history taking, physical examination, and adjunctive examinations, the patient was diagnosed with alopecia universalis.

Based on American National Alopecia Areata Foundation, the degree of severity of alopecia areata is classified into S1 (<25% of scalp involvement), S2 (26% to 50%), S3 (51% to 75%), S4 (76% to 99%), and S5 (100%, alopecia totalis and alopecia

universalis).[24] Meanwhile, there is a scoring system using the Severity of Alopecia Tool score that divides the head area into four parts, i.e., a vertex that consists of 40% of the scalp area, 18% of the right scalp, 18% of the left scalp, and 24% of the posterior scalp.[25] In this case, the degree of severity based on the American National Alopecia Areata Foundation was included in S5 because hair loss was found in all scalp. Meanwhile, the Severity of Alopecia Tool score was 100%.

Intralesional corticosteroid therapy is an effective alternative, especially for patients with mild alopecia areata. Meanwhile, a systemic steroid is suitable for alopecia universalis.[13,14] Oral corticosteroid given for six weeks is often enough to trigger hair regrowth. However, the growing hair will immediately be lost when therapy is halted.[26] The use of systemic corticosteroids is still controversial because of its side effects, such as striae, acneiform eruptions, obesity, cataract, and hypertension.[27] The dose used varies, from an initial 20-40 mg of prednisone per day, tapered down to 5 mg per day within several weeks, to a pulse therapies regime, which is administering short-term high dose oral prednisolone (100-300 mg) or intravenous methylprednisolone (250 mg).[14] Ahu *et al*. used oral steroids and found that 7 (46.7%) of patients showed total recovery, and 5 (33.3%) showed regrowth in the lesion region and positive light pull. Three (20%) of these patients did not respond to treatment.[13]

Cyclosporine can reduce the activity of the immune system by inhibiting the activity of T-cells specifically. Histopathology examination showed a reduction in immune system cells, including T-cells, helper-inducer T-cells (CD4), suppressor/cytotoxic T-cells (CD8), and Langerhans cells from hair follicles during cyclosporine therapy. The most acceptable pathogenesis for alopecia areata is based on immunological factors, especially T-cell mediated autoimmune. Therefore, cyclosporin therapy has been widely used, especially on alopecia universalis.[12] Systemic cyclosporin with 4-5 mg/kg/day can benefit several patients with alopecia areata. The side effects of oral cyclosporine include serum transaminase increase, cholesterol increase, headache, dysesthesia, fatigue, diarrhea, gingival hyperplasia, flushing, and myalgia.[14]

The duration of alopecia is an important prognostic factor that may affect the response to treatment. Gurol *et al*. investigated 6 of 9 patients with fewer than four years duration who showed significant hair growth.[12] Cyclosporin can be combined with intraoral prednisone. This combination can be considered in patients with alopecia universalis accompanied by severe atopic dermatitis.[14] A study showed 46 alopecia universalis patients treated with the combination of cyclosporin and oral methylprednisolone and found three patients (6.5%) stopped their medicine because it did not show any effect. Out of the remaining 43 patients, 38 (88.4%) had a significant regrowth of hair, and five (11.6%) were considered failed in treatment. Nine (23.7%) had relapses during 12 months observation period. This study showed that the combination therapy of cyclosporine and methylprednisolone could be an effective medicine for alopecia universalis.[28] The treatment of alopecia universalis is more effective with cyclosporine and systemic corticosteroid (the most common therapy chosen is methylprednisolone) than monotherapy.[29] In this case, the patient was given combination therapy, i.e., 8 mg of methylprednisolone every 8 hours for four weeks, tapering off every two weeks, and 100 mg of cyclosporine every 12 hours. After four weeks of consuming systemic steroid medicine, the patient reported spots like acne. Acneiform eruptions suspected to be induced by drugs are often well-tolerated. The most important treatment step is identifying the causing drug and stopping treatment.[30,31] In this case, the patient was given 2% topical sulfur every 12 hours on acneiform eruption lesions. The patient did not find other side effects from steroids, such as striae, obesity, cataract, and hypertension. Side effects of kidney and liver dysfunction from cyclosporine could not be evaluated because the patient was scheduled for kidney and liver function tests after three months of treatment.

Patients with alopecia universalis are thought to be more resistant to treatment than alopecia areata.[32] The prognosis of this disease is poor if, in severe alopecia areata (alopecia totalis and alopecia universalis), there is a change in nails, atopic history, or other autoimmune diseases, long disease duration, and late treatment.[10] In this patient, the prognosis was poor because the chance for hair loss relapse in alopecia universalis is high.

CONCLUSION

A case of alopecia universalis in a 19-year-old male patient is reported. The diagnosis was based on history taking, physical, and adjunctive examination. History taking and physical examination showed hair loss throughout the body. Scalp dermoscopy showed yellow dots. The patient was given a combination therapy of methylprednisolone and cyclosporine. The Severity of Alopecia Tool (SALT) score was 100%. Fifty-one days of observation revealed terminal hair growth on the scalp, eyebrows, eyelashes, and vellus hair on the body. The prognosis of this patient was poor because alopecia universalis has a high relapse risk.

ETHICS IN PUBLICATION

The patient received informed consent and agreed to share his medical history and clinical image for publication.

CONFLICT OF INTEREST

The authors declared no conflict of interest regarding the publication of this article.

AUTHORS CONTRIBUTIONS

Author IGND contributes to patient treatment, manuscript preparation and submission. Author PSWT, PAYR, and PAM contribute to the literature review, patient examination and follow-up, manuscript preparation, and translation.

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