Title
Lichenoid eruption in a child receiving growth hormone for dwarfism

Journal
Dermatology Online Journal, 28(1)

Author
Alhameedy, Meshal M

Publication Date
2022

DOI
10.5070/D328157061

Lichenoid eruption in a child receiving growth hormone for dwarfism

Meshal M Alhameedy MBBS MD

Affiliations: Department of Dermatology, King Fahd Specialist Hospital, Buraydah, Qassim, Saudi Arabia

Corresponding Author: Meshal M Alhameedy, King Abdullah Road, An Naziyah, Buraydah 52366, Qassim, Saudi Arabia, Tel: 966-563324270, Email: Meshal.alhameedy@gmail.com

Abstract

A wide variety of medications have been associated with lichenoid drug eruption. They present similarly or even identically to idiopathic lichen planus, both clinically and histologically. Lichenoid eruption has been associated with recombinant human growth hormone intake in two previous patients. Herein, we describe a young boy who developed a lichenoid eruption following growth hormone injection for dwarfism.

Keywords: children, dermoscopy, eruption, growth, hormone, lichen, lichenoid, planus

Introduction

Lichen planus-like or lichenoid drug eruption may arise from a wide range of medications and chemicals, with a clinical presentation and pathological findings similar, or even identical to idiopathic lichen planus. Lichenoid eruption has been associated with recombinant human growth hormone intake in two previous patients [1,2]. Common medications and chemicals known to trigger lichenoid eruption include angiotensin converting enzyme inhibitors, diuretics, beta-blockers, anti-malarial agents, TNF inhibitors, terbinafine, atorvastatin, metals (gold and mercury), and others (imatinib, pembrolizumab, and nivolumab), [3-5]. There are no clear or distinct clinical or histologic features that reliably distinguish lichenoid drug eruption from idiopathic lichen planus. A few clinical and pathological clues can help in differentiating idiopathic lichen planus from lichenoid drug eruption (**Table 1**), [6].

Case Synopsis

A 9-year-old boy of nonconsanguineous parents had been treated with somatotropin injections (growth hormone, Norditropin NordiFlex®) daily due to dwarfism for two years. Within three months of starting somatotropin injections, asymptomatic linear-reticulated hyperkeratotic violaceus papules and plaques developed, distributed symmetrically over both extensor forearms (**Figure 1**) and legs. Dermoscopic examination showed a central whitish scar-like area (Wickham striae-like) with peripheral patchy globular pigmentation (**Figure 2**). Examination of the mucosa (ocular, oral, and genital), hair, nails, teeth, palms, and soles were

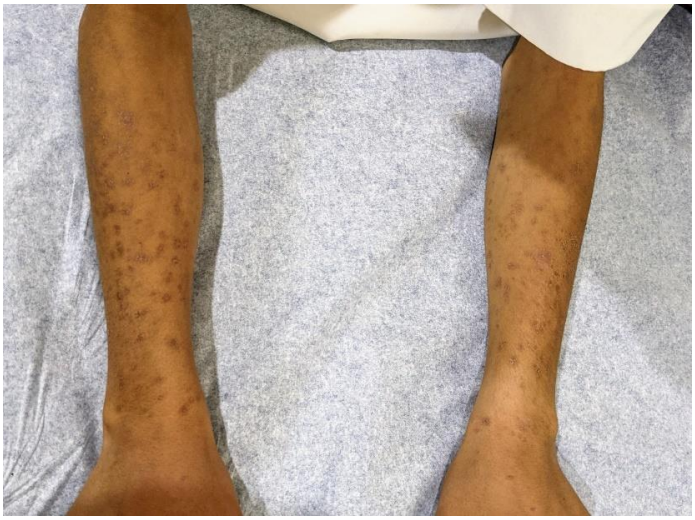

Figure 1. *Violaceus hyperpigmented scaly papules and plaques arranged in linear patterns over the extensor aspect of both arms.*

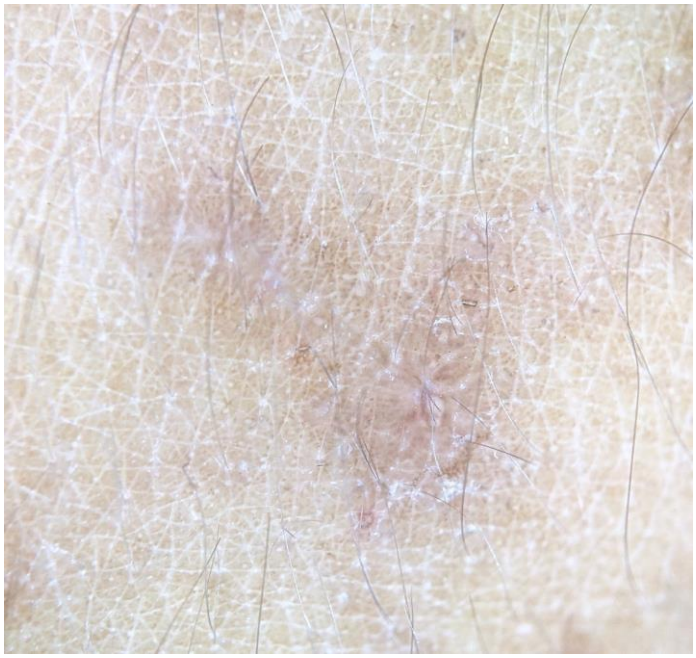

Figure 2. *Dermatoscopic examination shows a central whitish scar-like area (Wickham striae-like) with peripheral patchy globular pigmentation.*

unremarkable. No family history of a similar condition was reported. No other possible associations or triggers have been identified, e.g., trauma, infections, neoplasms, and family history of autoimmune diseases. Topical corticosteroids and topical calcineurin inhibitors were used for the last 6 months with no significant improvement.

Histopathological examination revealed hyperkeratosis, hypergranulosis, acanthosis, and a band-like lichenoid infiltrate involving the papillary dermis and extending to the deep periadnexal and perivascular plexus (**Figure 3**). Laboratory evaluation, including complete blood count, chemistry, hepatitis virus B and C, and HIV serology, erythrocyte sedimentation rate, C-reactive protein, and urine analysis were within normal limits. Based on the clinical presentation and pathology findings, a presumptive diagnosis of a lichenoid drug eruption in association with recombinant human growth hormone intake (Norditropin NordiFlex®) was made.

Since growth hormone intake is essential for the child's growth and could not be stopped, a trial of narrowband UVB phototherapy (three sessions per week) with topical corticosteroids (mometasone furoate cream 0.1%) twice per day) was started with regular follow-ups. At four months follow-up, he showed an almost complete resolution of skin lesions with only postinflammatory hyperpigmentation (**Figure 4**).

Case Discussion

Herein, we describe a young boy with cutaneous presentation overlapping between idiopathic lichen planus and lichenoid drug eruption as linear-reticulated, violaceus papules and plaques distributed symmetrically over extensor surfaces of the upper and lower extremities. In addition, the lesions were asymptomatic with no involvement of the mucosa, nails, or hair. Dermatoscopic evaluation was similar to idiopathic lichen planus, with central whitish lines resembling Wickham striae, which usually represent hypergranulosis pathologically. Histopathologically, features of idiopathic lichen planus (hyperkeratosis, hypergranulosis, band-like lichenoid infiltrate with interface dermatitis, apoptotic keratinocytes, and pigment incontinence) were evident. On the other hand, superficial and deep lymphohistiocytic infiltrate involving both the

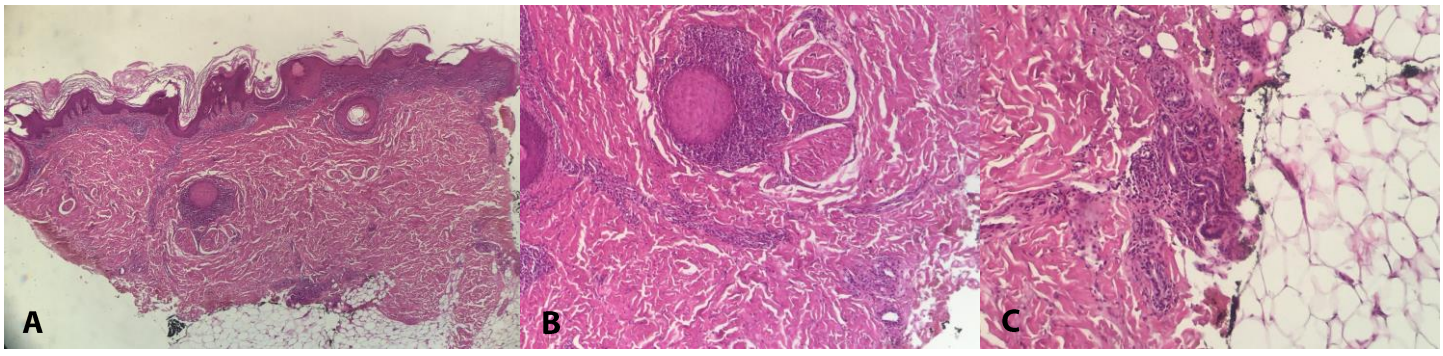

Figure 3. *Hyperkeratosis, hypergranulosis, and acanthosis, a band-like lichenoid infiltrate involving the papillary dermis and extending to the deep periadnexal and perivascular plexus. H&E,* ***A)*** *4×; B,* ***C)*** *40×.*

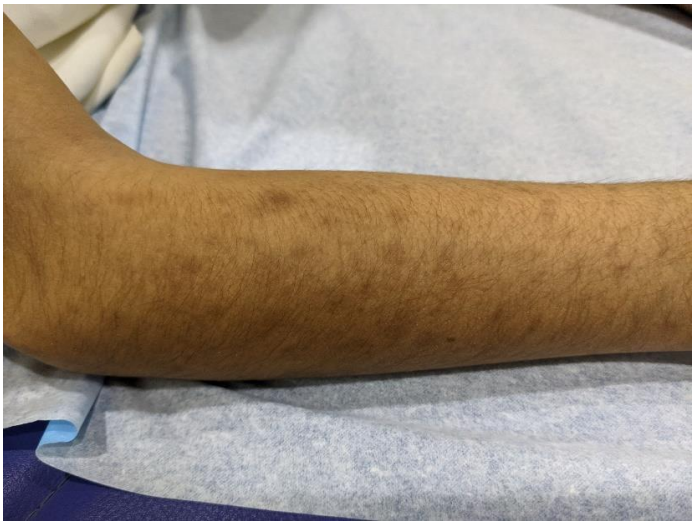

Figure 4. *At four months follow-up, an almost complete resolution of skin lesions with only postinflammatory hyperpigmentation.*

periadnexal (hair follicles and sweat glands) and perivascular plexus were suggestive of lichenoid drug eruption.

Lichenoid drug eruption, also known as drug-induced lichen planus, are often clinically and histologically identical to idiopathic lichen planus. Certain medications (**Table 2**) have also been implicated in oral and photodistributed variants of lichenoid drug eruption [7]. Although lichenoid drug eruption is morphologically similar to classic idiopathic lichen planus, the eruptions tend to be more polymorphic, lack Wickham striae, and show more pronounced desquamation with psoriasiform or eczematous morphology (**Table 1**), [6]. Lichenoid drug eruption usually arises several months or even years after the exposure to the offending medication. The underlying basis for this delay remains unclear but is likely to be influenced by multiple variables, including the dose, medication class, drug-drug interactions, and other host factors [8]. Lichenoid drug eruption typically resolves within weeks-to-months of withdrawing the offending agent, although resolution can be seen sooner or even while the patient remains exposed to the medication [7,9].

The mechanism by which recombinant human growth hormone can induce lichen planus is unknown. However, growth hormone may induce immunologically mediated diseases like lichen planus through increasing thymocyte migratory responses and intrathymic traffic of developing T cells [10]. Recombinant human growth hormone therapy has been associated with lichenoid drug eruption in two pediatric patients. First, a 9-year-old boy treated with recombinant human growth hormone for dwarfism developed classic lichen

Table 1. *Comparison between idiopathic lichen planus and lichenoid drug eruption [6].*

	Idiopathic lichen planus	Lichenoid eruption
Clinical	Involve wrists, flexor forearms, presacral area, lower legs, genitalia Shiny, flat-topped, polygonal, violaceous papules (+) Mucosal involvement (+) Wickham striae	Generalized and symmetric or photodistributed Eczematous, psoriasiform or pityriasis rosea-like (-) Mucosal involvement (-) Wickham striae
Pathological	(-) Parakeratosis (-) Eosinophilic and/or plasma cell infiltrates (-) Deep perivascular infiltrate	(+) Parakeratosis (+) Eosinophilic and/or plasma cell infiltrates (+) Deep perivascular infiltrate

Table 2. *Drug culprits and their associated lichenoid manifestation [5].*

Drug culprit	Lichenoid manifestation
Angiotensin-converting enzyme inhibitors, antimalarials, b-blockers, gold, lithium; mercury amalgam, methyldopa, penicillamine, quinidine, sulfonylureas, thiazide diuretics, tumor necrosis factorea, or tyrosine kinase inhibitors	Classic cutaneous lichenoid drug eruption
Angiotensin-converting enzyme inhibitors, allopurinol, anticonvulsants, antiretrovirals, gold, ketoconazole, or nonsteroidal anti-inflammatory drugs.	Cutaneous and oral lichen planus
Carbamazepine, chlorpromazine, diltiazem, ethambutol, quinidine, quinine, tetracyclines, and thiazide diuretics	Photodistributed lichenoid drug eruption

Table 3. *A Comparison between our patient and the two previously reported patients of RHGH-induced lichenoid eruption [1-2].*

	Our patient	Case one [1]	Case two [2]
Clinical	A nine-year-old Saudi boy, treated with somatotropin injections (Norditropin NordiFlex®) daily due to dwarfism for two years Within three months of starting somatotropin injections, linear-reticulated hyperkeratotic violaceus papules and plaques, distributed symmetrically over both extensor forearms and legs No mucosal or extracutaneous involvement	A nine-year-old boy, treated with weekly intramuscular injections of human recombinant growth hormone (hrGH) for dwarfism Within few days of starting injections, three brownish pruritic papules on the neck developed. At one month follow up, lesions rapidly spread over the trunk, extremities, and glans penis Mouth, nails, and scalp were not involved	A nine-year-old girl diagnosed with Turner syndrome, Recombinant Human Growth Hormone (RHGH) therapy is given for the treatment of short stature Within two months of starting injections, numerous pruritic scaly papules were observed on the palms and soles. In addition, numerous interlacing white keratotic lines were noted involving labial and buccal mucosa
Histopathological	Hyperkeratosis, hypergranulosis, acanthosis, and a band-like lichenoid infiltrate involving the papillary dermis and extending to the deep periadnexal and perivascular plexus No eosinophils or plasma cell infiltrate	Orthokeratotic hyperkeratosis, hypergranulosis and liquefaction degeneration of the basal cell layer. A band-like lymphocytic and histiocytic infiltration was observed in the upper dermis Few eosinophils were identified	Biopsy from oral mucosa showed band-like inflammatory cell infiltrate, mainly of lymphocytes at the connective tissue junction
Treatment and outcome	nbUVB therapy with topical corticosteroids (Mometasone furoate cream 0.1%) shows a significant improvement without the need to discontinue or change the medication At four months follow-up, he shows an almost complete resolution of skin lesions with only postinflammatory hyperpigmentation	Potent topical steroid was prescribed: however, the lesions were resistant to therapy During the course of hrGH treatment, no apparent regression of the lesions was seen. Some pinpoint discrete papules enlarged or coalesced into flat-topped, violaceous papules or small plaques with central depression	Clobetasol propionate 0,05% cream for palmoplantar lesions and dexamethasone mouthwash for oral lesions three times a day After one month of treatment, the palmoplantar lesions completely disappeared whereas the oral lesions remained present The oral lesions remained stable until the patient discontinued the use of RHGH and the oral lesions completely disappeared

planus-like presentation both clinically and pathologically, even though few eosinophils were identified [1]. Second, a 9-year-old girl diagnosed with Turner syndrome (TS) received recombinant human growth hormone for short stature and developed cutaneous (pruritic scaly papules over hands and feet) and mucosal (white keratotic lines over buccal and labial mucosa) lichen planus, which showed classic histopathological findings of lichenoid drug eruption [2]. A comparison between our patient and the two previously reported patients of RHGH-induced lichenoid eruption are shown in **Table 3**.

Conclusion

We describe a young boy who developed overlapping features of idiopathic lichen planus and lichenoid drug eruption three months following somatotropin injections (growth hormone) for dwarfism. He showed a significant improvement with combination narrowband UVB phototherapy and topical corticosteroid without the need to discontinue or change the medication. Although a causal relationship cannot be established. Further attention to recombinant human growth hormone-associated cutaneous eruptions is warranted. One must also consider the full composition of the

preparation as it is possible that other excipients besides the actual growth hormone could be the culprit.

Potential conflicts of interest

The author declares no conflicts of interest.

References

1. Oono T, Arata J. Childhood lichen planus in a patient receiving growth hormone for dwarfism. *Dermatology*. 1996;192:87-8. [PMID: 8832965].
2. Soares MQ, Mendonca EF. Lichen planus-like drug reaction associated with recombinant human growth hormone therapy in a child patient with Turner syndrome. *Dermatol Online J*. 2016;22:13030/qt4k61f5jn. [PMID: 27136634].
3. Halevy S, Shai A. Lichenoid drug eruptions. *J Am Acad Dermatol*. 1993;29:249-55. [PMID: 8335745].
4. Forouzan P, Riahi RR, Cohen PR. Atorvastatin-induced Lichenoid Drug Eruption: A Case Report and Review of Statin-associated Cutaneous Adverse Events. *Cureus*. 2020;12: e7155. [PMID: 32257699].
5. Cohen PR, Erickson CP, Calame A. Terbinafine-induced lichenoid drug eruption: case report and review of terbinafine-associated cutaneous adverse events. *Dermatol Online J*. 2020;26:13030/qt9jh9p0xp. [PMID: 32898398].
6. Shiohara T, Mizukawa Y. Lichen Planus and Lichenoid Dermatoses. In: Dermatology. Bolognia J, Schaffer J, Cerroni L, editors. 4th ed. Elsevier Limited;2017. p. 188-207.
7. Tziotzios C, Lee JYW, Brier T, et al. Lichen planus and lichenoid dermatoses: Clinical overview and molecular basis. *J Am Acad Dermatol*. 2018;79:789-804. [PMID: 30318136].
8. Asarch A, Gottlieb AB, Lee J, et al. Lichen planus-like eruptions: an emerging side effect of tumor necrosis factor-alpha antagonists. *J Am Acad Dermatol*. 2009;61:104-11. [PMID: 19539844].
9. Seehafer JR, Rogers RS 3rd, Fleming CR, Dickson ER. Lichen planus-like lesions caused by penicillamine in primary biliary cirrhosis. *Arch Dermatol*. 1981;117:140-2. [PMID: 6452095].
10. Smaniotto S, Martins-Neto AA, Dardenne M, Savino W. Growth hormone is a modulator of lymphocyte migration. *Neuroimmunomodulation*. 2011;18:309-13. [PMID: 21952682].