Alopecia caused by isoniazid

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ABSTRACT

Drug-induced alopecia is a known clinical entity and mainly seen with anti-mitotic drug therapy. Alopecia during anti-tuberculosis therapy is very uncommon and previously observed with isoniazid, thiacetazone, and ethionamide. Present communication describes an additional case of isoniazid-induced alopecia in a 10-year-old male child, which was reversible after isoniazid withdrawal. Possible mechanisms of drug-induced alopecia are also briefly discussed.

Key words: Alopecia, drugs, isoniazid

INTRODUCTION

Alopecia is not an uncommon condition observed in clinical practice. A wide range of conditions can cause alopecia that includes medical disorders, nutritional deficiencies, physical agents, infections, drugs, etc. Drugs are one of the important causes of alopecia and among them anti-mitotic agents are routinely known to be associated with this. Other drugs in rare circumstances can also produce alopecia that includes a variety of drugs. Drug-induced alopecia is usually reversible after the withdrawal of the offending drug. Alopecia due to anti-tuberculosis drugs is very uncommon and has been reported with only isoniazid, thiacetazone, and ethionamide. The present communication describes a 10-year-old male child who developed alopecia during anti-tuberculosis therapy that was reversible only after withdrawal of isoniazid. The literature on drug-induced alopecia is also briefly discussed.

CASE REPORT

A 10 year old male child diagnosed to be having pulmonary tuberculosis was started on anti-tuberculosis chemotherapy containing isoniazid, rifampicin, ethambutol, and pyrazinamide according to the body weight daily. Patient improved clinically with the above therapy. However, he started complaining of fall of scalp hairs after 2-3 weeks that became more evident after 3-4 weeks. There was no itching or pain over the affected area of the scalp. On examination, there was alopecia affecting the frontal portion of scalp. Hairs were tapered with broken roots; however, there were no signs of inflammation, redness, scaling, etc. Patient was further investigated to rule out underlying medical illnesses. There were no signs of nutritional deficiencies, skin diseases, gonadal or hormonal disorders clinically. The subsequent work-up included blood for human immunodeficiency virus testing, thyroid profile, skin scrapings of the affected area for fungus, histological examination, and collagen profile (anti-nuclear antibody testing, lupus erythematosus cell and rheumatoid arthritis testing). All these investigations were unremarkable. Routine blood biochemistry was also normal. A thorough clinical history this time also did not reveal any intake of drugs including

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over-the-counter medications or herbal remedies apart from prescribed anti-tuberculosis therapy in recent or remote past. A possibility of drug-induced alopecia was considered. Since the anti-tuberculosis drug regimen the patient was receiving was not having thiacetazone or ethionamide, the possibility of isoniazid-induced alopecia was considered as only these three drugs are mentioned in literature to cause alopecia. The patient was reassured, isoniazid was withdrawn, and other drugs were continued in usual doses. The hair regrowth was observed after 3 weeks of isoniazid withdrawal with complete recovery after 6 weeks. The subsequent treatment period was uneventful. The patient was cured from pulmonary tuberculosis after 6 months of anti-tuberculosis chemotherapy. The long-term follow-up was also uneventful for next 5 years.

DISCUSSION

Alopecia can be divided into two broad types: Cicatricial (scarring) and non-cicatricial (non-scarring). In the former, a group of rare disorders (lupus erythematosus, lichen planus, graft vs host disease, scleroderma, dermatomyositis, sarcoidosis, malignancy, etc.) destroys the hair follicles to replace it with scar tissue and cause permanent hair loss. In non-cicatricial alopecia, the underlying cause is usually the drugs apart from androgenic alopecia. It is non-scarring type of alopecia that is reversible upon discontinuation of the offending agent. Although large number of drugs can interfere the hair cycle to produce alopecia, only few drugs routinely cause hair loss that includes anti-mitotic agents. There are reports of drug-induced alopecia associated with anti-coagulants, anti-hyperlipidemic drugs, tricyclic anti-depressants, anti-thyroid drugs, oral contraceptives, cimetidine, some anti-tuberculosis drugs, etc.

According to the phase of hair follicle cycle interfered by drugs, the alopecia can be of two types that is anagen effluvium and telogen effluvium. In anagen effluvium, there is abrupt cessation of active anagen stage (growth phase) with shedding of hairs within days or weeks. This is often dose related, almost always reversible, and usually seen with cytotoxic chemotherapy. In telogen effluvium, the hair loss may be a consequence of drug therapy or events such as severe illness or toxic insults such as child birth, fever, hemorrhage, etc. Since the telogen stage (resting phase) is affected, it becomes evident 2-4 months after the exposure to initiating cause. In our case, the alopecia was anagen effluvium type.

Alopecia during anti-tuberculosis therapy is very uncommon and is only reported with isoniazid, thiacetazone, and ethionamide previously. Fitz Gerald et al. described isoniazid-induced alopecia in 5 Canadian-born white people in 1996 while treating 141 tuberculosis patients. Three among five cases were HIV seropositive. In all cases, the condition was reversible following isoniazid withdrawal, considering isoniazid to be the offending drug and HIV infection as a possible aggravating factor. The next report on isoniazid-induced alopecia was reported by Sharma et al. in a 32-year-old woman who developed generalized lichenoid eruptions apart from diffuse loss of scalp hair of anagen effluvium type. The patient required oral prednisolone therapy in this case and complete recovery was observed following isoniazid withdrawal.

Gupta et al. reported another case of isoniazid-induced alopecia in a 30-year-old female. Hair regrowth was observed after 2 months of stopping isoniazid. In our case, the patient was not receiving thiacetazone and ethionamide; hence, isoniazid was the culprit drug for alopecia as the patient improved following isoniazid withdrawal. Furthermore, there was nothing to suggest any other cause for alopecia on thorough work up of the case. This case recorded a score of 6 on the Naranjo probability scale, incriminating the drug as a probable cause for the reaction.

Isoniazid is an important drug among first-line anti-tuberculosis therapy. This is very effective and well tolerated most of the time. The common adverse drug reactions reported with this drug are fever, skin rash, peripheral neuritis, jaundice, etc., Hematological reactions, vasculitis, arthritic symptoms, convulsions, and other neurotoxic reactions including mental abnormalities are occasionally seen with this drug. Alopecia due to isoniazid is very uncommon and has not been addressed in standard text books.

Although exact mechanism of drug-induced alopecia is not clear, cytotoxic drugs act by inhibiting mitosis in the hair papilla leading to narrowing of the hair shaft with subsequent hair fracture or complete failure of hair formation. These drugs may produce broken shafts and anagen shedding in some follicles and premature catagen, followed by telogen shedding in others. Molecular mechanisms of chemotherapy-induced alopecia is also linked to p53 activity. Over expression of bcl2 (potent apoptosis inhibitor protein) in follicular keratinocytes...
is also associated with accelerated spontaneous and cyclophosphamide-induced hair follicle regression (catagen) process.\[14\] Drug-induced alopecia by non-cytotoxic drugs is not well addressed in previous reports (including those associated with isoniazid) and literature. Certain drugs such as danazol, metyrapone, and anabolic steroids may cause alopecia by androgenic activity. Another mechanism could be estrogen receptor antagonism as seen with tamoxifen.\[17\] Although exact mechanism of isoniazid-induced alopecia is still not clear, a possible androgen mechanism could possibly exist as alteration in estrogen-androgen metabolism has been associated with isoniazid.\[15\] The possibility is further supported by the fact that the pattern of alopecia in our case was mimicking androgenic type (affecting the frontal region of the scalp in male).

Although rare, a possibility of alopecia caused by isoniazid may be considered and the treating physician should be aware of it. This event should be recognized early as this may be a cause of poor compliance in some patients.

REFERENCES

1. Tosi A, Misciali C, Piraccini BM, Peluso AM, Bardazzi F. Drug-induced hair loss and hair growth. Incidence, management and avoidance. Drug Saf 1994;10:310-7.
2. FitzGerald JM, Turner MT, Dean S, Elwood RK. Alopecia—side effect of antituberculosis drugs. Lancet 1996;347:472.
3. Gupta DK, Kumar R, Kumar V, Aggarwal AK. Diffuse toxic alopecia due to thiacetazone. Indian J Chest Dis Allied Sci 1983;25:74-5.
4. Arshad N, Jain RC, Verma K. Ethionamide induced alopecia. Indian J Tub 1984;31:373-4.
5. Rongioletti F, Christana K. Cicatricial (scarring) alopecias: An overview of pathogenesis, classification, diagnosis, and treatment. Am J Clin Dermatol 2012;13:247-60.
6. Llau ME, Viraben R, Montastruc JL. Drug-induced alopecia: Review of the literature. Therapie 1993;50:145-50.
7. Lee A, Thomson J. Drug-induced skin reactions. Adverse Drug Reactions. 2nd ed. United Kingdom: Pharmaceutical Press; 2006. p. 147.
8. Tengetrand M, Star K, van Puijenbroek EP, Hill R. Alopecia in association with lamotrigine use: An analysis of individual case safety reports in a global database. Drug Saf 2010;33:653-8.
9. Barth JH, Dawber PR. Drug induced hair loss. BMJ 1989;298:675.
10. Sharma PK, Gautam RK, Bhardwaj M, Kar HK. Isonicotinic acid hydrazide induced anagen effluvium and associated lichenoid eruption. J Dermatol 2001;28:737-41.
11. Gupta KB, Kumar V, Vishvkarma S, Shandily R. Isoniazid-induced alopecia. Lung India 2011;28:60-1.
12. Petri WA Jr. Chemotherapy of tuberculosis, mycobacterium avium complex disease and leprosy. In: Brunton LL, Lazo JS, Parker KL, editors. Goodman and Gilman’s The Pharmacological Basis of Therapeutics. New York: McGraw-Hill; 2011. p. 1556-7.
13. Botchkarev VA. Molecular mechanisms of chemotherapy-induced hair loss. J Invest Dermatol Symp Proc 2003;8:72-5.
14. Müller-Röver S, Rossiter H, Paus R, Handjiski B, Peters EM, Murphy JE, et al. Overexpression of Bcl-2 protects from ultraviolet B-induced apoptosis but promotes hair follicle regression and chemotherapy-induced alopecia. Am J Pathol 2000;156:1395-405.
15. Dixit R, George J, Sharma AK, Chhabra N, Jangir SK, Mishra V. Ethionamide induced gynecomastia. J Pharmacol Pharmacother 2012;3:196-9.

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