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Case Report

PHENYTOIN INDUCED ALOPECIA AND LUPUS: A CASE REPORT

***N. S. Neki**
Department of Medicine, Government Medical College, Amritsar (India)
**Author for Correspondence*

ABSTRACT
Drugs are capable of producing a wide spectrum of hair loss, ranging from barely detectable shedding to irreversible baldness. Drug-induced alopecia is usually described as a diffuse non-scarring alopecia which is reversible upon withdrawal of the drug. Usually (antimitotic agents) cause hair loss while many drugs. Hair loss is reported secondary to some anticonvulsant agents. Other drugs like anti hypertensives, salicylates or nonsteroidal analgesics, anticoagulants and antithyroids, oral contraceptives, cimetidine, retinoids, amphetamines, bromocriptine and levodopa and some hypocholesterolaemic and few psychotropics may cause alopecia. Some anticonvulsants like phenytoin rarely can cause alopecia. Diagnosis of drug-induced alopecia remains difficult. The only way to confirm it is to see if an improvement occurs after cessation of the suspected drug.

***Keywords**: Phenytoin, Alopecia, Lupus*

INTRODUCTION
Drug induced hair loss may vary from minor shedding to permanent baldness and may become reversible on stoppage of the offending agent. Various drugs include chemo-therapeutics, anti-convulsants, anti-hypertensives, NSAIDs, anticoagulants, anti-thyroids, cimetidin, oral contraceptives, amphetamines, bromocriptin, levodopa, cholesterol lowering agents and few psychotropics. These drugs cause an autoimmune response thereby producing symptoms resembling systemic lupus erythematosus. Phenytoin, an anticonvulsant, very rarely causes alopecia and lupus. Diagnosis is made by significant response on withdrawl of offending drug.

CASES
A 28 years old male presented with history of generalised tonic clonic seizures on phenytoin 300 mg/day since last 2 years with well controlled seizure activity. Then patient noticed increased hair loss on combing and following shampoo since 3-4 months which gradually progressed to present as a patch over scalp. On examination patch was smooth and well circumscribed and measuring about 3 x 4 cm and for which dermatological opinion was taken to be diagnosed as alopecia areata (Figure-1). Patient was assured and prescribed medication like flucinoloneacetonide cream 0.2% twice a day and minoxidil 5% solution application. After 15 days patient presented with increased hair loss despite continued medication. At this time suspicion of drug induced alopecia was considered and patient was subjected to anti nuclear antibody (ANA), anti double stranded DNA (anti ds DNA), and anti histone antibody. Patient was positive for ANA and anti histone antibody and negative for anti ds DNA. Thus a diagnosis of drug induced alopecia areata was confirmed. Then phenytoin was gradually tapered off and started phenobarbitone 90 mg/day. The alopecia improved gradually after discontinuation of phenytoin.

DISCUSSION
Drug-induced lupus erythematosus (DIL or DILE) is an autoimmune disorder (similar to systemic lupus erythematosus [SLE] caused by chronic use of certain drugs. These drugs cause an autoimmune response producing symptoms similar to those of SLE.

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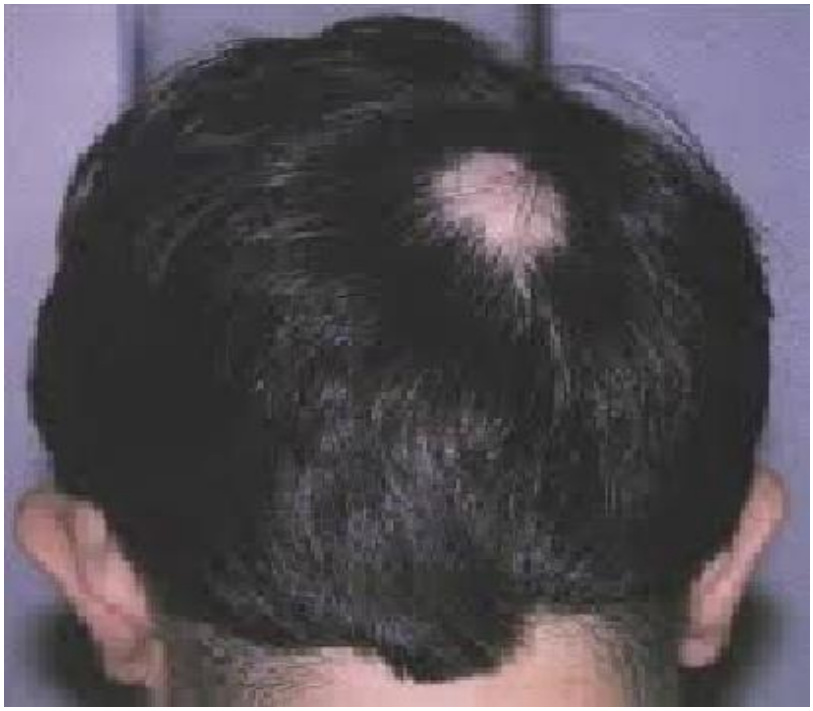

Figure:1 Showing Patch of Alopecia

The most common drugs that cause DILE are hydralazine, procainamide, quinidine, isoniazid, diltiazem, and minocycline (Fritzler, 1994). In DILE, autoantibodies are thought to be generated by a mechanism other than molecular mimicry. The medications and other exposures implicated in DILE and flares of SLE produce autoantibodies more often than systemic autoimmune symptoms. The metabolites of the drug are subjected to oxidative metabolism and serve as a substrate for myeloperoxidase, which is activated in polymorphonuclear neutrophils. This interaction causes the formation of reactive metabolites that directly affect lymphocyte function in the thymus, disrupting central T-cell tolerance to the patient's own tissues and producing autoimmune T cells against them. Decreased T-cell methylation, an over expression of lymphocyte function–associated antigen (LFA-1) occurs. T cells with hypomethylated DNA become autoreactive and cause antibody formation. The genetic differences in an individual's P450 system cause drugs to be metabolized differently. This results in the generation of toxic metabolites that may facilitate autoimmunity.

Predisposing factors to the development of DILE include a slow drug-acetylator phenotype and advancing patient age. Slower acetylation may play a role in the greater predisposition for elderly persons to develop DILE (Grant *et al.*, 1990). These metabolites are created when leukocytes have been activated, meaning they are stimulated to produce a respiratory burst (Uetrecht *et al.*, 1988). Drugs may affect anagen follicles through 2 main different modalities: (i) by inducing an abrupt cessation of mitotic activity in rapidly dividing hair matrix cells (anagen effluvium) or (ii) by precipitating the follicles into premature rest (telogen effluvium). In anagen effluvium, hair loss usually occurs within days to weeks of drug administration, whereas in telogen effluvium, hair loss becomes evident 2 to 4 months after starting treatment (Tosti *et al.*, 1994).

Persons with drug-induced lupus erythematosus may have symptoms that affect the joints, heart, and lungs. Other symptoms associated with SLE, such as lupus nephritis and nervous system disease, are rare. Other include blurred vision, fever, general ill feeling (malaise), joint pain, joint swelling, loss of appetite, pleuritic chest pain, skin rash gets worse with sunlight and "Butterfly" rash across bridge of nose and cheeks and weight loss (Marzano *et al.*, 2011). Patients with DILE (unlike patients with SLE) typically

do not have features of mucosal ulcers, hair loss (alopecia), circular (discoid) plaques, photosensitivity (with the exception of thiazide-induced subacutelupuslike syndrome)
Compared with patients who have SLE, patients with DILE present with a higher prevalence of purpura, erythema nodosum (painful nodules, usually on the extremities), erythematous papules (typically on sun-exposed areas).
Tests that may be done include, antihistone antibody, antinuclear antibody (ANA) panel. A chest x-ray may show signs of pleuritis or pericarditis. An ECG may show involvement of the heart.CBC should be performed to evaluate for anemia, which is present in most patients with SLE but is rare in those with DILE. Blood urea nitrogen (BUN), creatinine, C3 and C4 levels should be measured. Complement levels are often reduced in persons with SLE, whereas they tend not to be reduced in persons with DILE.
Liver function tests can be performed to evaluate hepatic involvement. Urinalysis can be performed to evaluate for hematuria and proteinuria (Lowe *et al.,* 2011). Histologic examination reveals variable epidermal atrophy, basal vacuolar degeneration, apoptotic or dyskeratotic keratinocytes, and lymphocytic interface dermatitis.
Differential diagnoses include,discoid lupus erythematosus, neonatal lupus erythematosus, subacute cutaneous lupus erythematosus, systemic lupus erythematosus. Symptoms of drug-induced lupus erythematosus generally disappear days to weeks after medication use is discontinued. Non-steroidal anti-inflammatory drugs (NSAIDs) will quicken the healing process. Corticosteroids may be used if more severe symptoms of DIL are present.

Conclusion

Drug-induced lupus erythematosus (DIL or DILE) is an autoimmune disorder caused by chronic use of certain drugs. These drugs cause an autoimmune response (the body attacks its own cells) producing symptoms similar to those of SLE. The most common drugs that cause DILE are hydralazine, procainamide, quinidine, isoniazid, diltiazem, and minocycline. Most common in patients of slow drug-acetylator phenotype and advancing patient age. There is higher prevalence of the purpura, erythema nodosum and erythematous papules. NSAIDs and Corticosteroids are given as the treatment.

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