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CHRONIC HEPATITIS C VIRUS;

DERMATOLOGICAL MANIFESTATIONS OF INTERFERON PLUS RIBAVIRIN THERAPY IN PATIENTS

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ABSTRACT: Objective: To determine the frequency and pattern of dermatological manifestations in patients receiving interferon and ribavarin for hepatitis C. **Patients & Methods:** The study was conducted in the Dermatology out patients department (OPD) of Dow University Hospital Karachi from April –November 2013.Patients diagnosed with hepatitis C who received interferon a(3 MIU subcutaneously thrice weekly) plus ribavirin (1200 mg daily for 24 weeks).Detailed history and dermatological examination including mucous membrane,hair and nails was performed initially and then monthly for six months and findings were recorded. **Results:** A total of 109 patients were included in the study.Frequency of various skin diseases in these patients werepruritis 44(40.36%), transient alopecia 14(12.84%),generalized morbiliform rash in 22 (20.18%),photosensitivity in 8(7.33%), secondary hyperpigmentation in 17(15.59%) patients.Lichen Planus was observed in 6 (5.50%) patients while brittle nails were seen in 5 (4.58%), glossitis in 4(3.66%),chelitis in 8(7.33%)and generalized exfoliating dermatitis in 9(8.25%) patients.Apthous ulceration was observed in 7 (6.42%) patients. **Conclusions:** HCV and its treatment with interferon plus ribavirin is associated with significant dermatological complications. Physicians should be aware of these side effects and patients should be counseled before starting treatment.

Key words: Hepatitis C, interferon a, ribavirin, dermatological manifestations.

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INTRODUCTION

Hepatitis C is a major health problem globally with an estimated 170 million people affected worldwide[1].Current recommendations for the treatment of chronic hepatitis C virus (HCV) infection requires the use of interferon plus ribavirin[2]. Treatment with the combination of these two agents has been associated with various side effects including dermatological manifestations in 13-23% of HCV patients[3].

Frequently reported side effects are cutaneous necrosis, purpura secondary to mixed cryoglobulinemia, porphyria cutaneatarda, psoriasis, pruritis, lichen planus, vitiligo, alopecia and injection site reactions[4-6]. As both HCV infection and therapy with interferon and ribavirin are associated with cutaneous manifestations, it may be difficult to differentiate between HCV related and therapy related skin changes. Most of these side effects are usually mild however, severe reactions can occur on rare occasions. Health care professionals should be aware of these side effects and its effect on treatment outcomes.

The objective of the present study was to determine the frequency and pattern of dermatological manifestations in patients receiving interferon a and ribavarin for the treatment of hepatitis C.

PATIENTS & METHODS

This cross sectional study was conducted in the Dermatology out patients department (OPD) of Dow University Hospital Karachi, a tertiary care university based hospital from April-November 2013. Patients diagnosed with hepatitis C virus (HCV) infection who received Interferon a plus ribavirin were observed during the study period for dermatological manifestations. Detail history was taken and complete physical examination was performed including skin, mucous membranes, hair and nails before starting treatment and then monthly till the completion of treatment.

Laboratory investigations included complete blood count, erythrocyte sedimentation rate, bilirubin, ALT, AST and alkaline phosphatase at baseline and then monthly. HCV was diagnosed on detection of serum HCV-RNA by polymerase chain reaction. INF was given in a dose of 3 MIU s/c three times per week with 1200 mg of ribavirin daily for six months.

Data was analyzed on Statistical Package for Social Sciences (SPSS), version 13.0. Continuous variables are presented as Mean± SD. Categorical variables like gender and various dermatological manifestations are presented in the form of frequency and percentage.

RESULTS

A total of one hundred and nine (51 male, 58 female) patients were enrolled in the study. The age of participants ranged from 20-76 years (Mean age 40.73±10.72). Distribution of age and gender is given in Table I.

A gr group	Male n (%)	Female n (%)	Overall n(%)
20-30	10 (45.5%)	12 (54.4%)	22 (100%)
31-40	18 (43.9%)	23 (56.0%)	41 (100%)
41-50	17 (54.8%)	14 (45.1%)	31 (100%)
51-60	3 (33.3%)	6 (66.6%)	9 (100%)
>60	3 (60%)	2 (40%)	5 (100%)

Table-I. Distribution of patients by gender and age

The frequency of various skin problems identified in these patients is shown in Table II. Pruritis was the most common side effect observed in 44(40.36 %) patients. It was generalized and usually started in the first month of treatment. Hyperpigmentation was seen in 17 (15.59%) patients out of which 5 patients had oral, 7 had nail involvement while 5 patients experienced generalized pigmentation. Frequency of various other skin problems in these patients were transient alopecia 14(12.8%), generalized morbiliform rash in 22(20.18%), photosensitivity in 8(7.33%) patients. Lichen Planus was observed in 6 (5.50%) patients while brittle nails were seen in 5(4.58%), glossitis in 4(3.66%), chelitis in 8(7.33%)and generalized exfoliating dermatitis in 9(6.73%) patients.Apthous ulceration was observed in 7(6.42%) patients.

Most of these manifestations were however mild and did not require the discontinuation of treatment.

Cutaneous manifestations	Male n(%)	Female n(%)
Generalized pruritis	16 (14.67%)	28 (25.68%)
Morbiliform rash	12(11%)	10(9.17%)
Alopecia	4(3.6%)	10(9.17%)
Hiperpigmentation Oral Generalized Nail	 2(1.83%) 3(2.75%) 5(4.5%)	 3(2.75%) 2(1.83%) 2(1.83%)
Photosensitivity	5(4.5%)	3(2.75%)
Lichen planus	2(1.83%)	4(3.66%)
Brittle nails	3(2.75%)	2(1.83%)
Glossitis	2(1.83%)	2(1.83%)
Chelitis	2(1.83%)	6(5.50%)
Exfoliating dermatitis	7(6.4%)	2(1.83%)
Psoriasis	3(2.75%)	2(1.83%)
Urticaria	3(2.75%)	6(5.50%)
Aphthous ulcer	2(1.83%)	5(4.5%)
Trichomegaly	1(0.9%)	2(1.83%)
Synophyrs	2(1.83%)	2(1.83%)

Table-II. Frequency and type of skin manifestations in HCV patients receiving interferon & ribavirin

DISCUSSION

The present study demonstrates the frequency of various cutaneous manifestations of HCV treatment with INF and ribavirin. HCV and its treatment with this combination is associated with significant skin problems. Hair problems were commonly seen in our patients receiving INF, and included alopecia, thinning of hair, graying of hair as well as hypertrichosis of eyebrows. Evidence suggests that autoimmune alopecia maybe one of the cutaneous diseases associated with HCV[7]. Studies have also suggested that INF treatment can also cause hair loss affecting the whole body not just scalp[8,9]. Loss of hair and thinning in our patients started within the first month of treatment and was more common in females.Trichomegaly was observed in only few patients, a finding similar to other case reports[10,11].

Pigmentary disorders were observed in large number of patients and included generalized pigmentation as well as oral and nail pigmentation. Similar findings are reported earlier[11-13]. It has been postulated that IFN increases the expression of alpha melanocyte stimulating hormone (MSH) surface receptors which is responsible for this pigmentation. Most of these cases are reported in dark skin individuals as compared to Caucasians[14,15] and a high frequency of pigmentory disorders seen in our patients may also be due to the Fitzpatrick skin type IV and V in our population. Along with pigmentation graying of hair and discolouration of nail was seen in some patients.

Lichen Planus (LP) has been associated with chronic hepatitis C though the role of HCV in LP remains unclear[16,17]. Although the mechanism of disease induction by HCV is not clearly defined, various pathophysiological processes including replication in the oral mucosa, high rate of mutation in HCV and repeated immune activation has been implicated. In our study six patients developed LP during the treatment.Similar results has been reported in some studies[11,18] while others documented it as an incidental finding especially in HCV endemic areas[19].

Generalized morbiliform rash was seen in 22 patients while five patients developed Psoriasis. These rashes tend to be red, fine, petechial and most commonly seen on the arm and trunk. Mucous membranes were generally spared. The underlying mechanism of this rash is thought to be immunologic and is considered a cell mediated type IV hypersensitivity reaction[20].

A large number of patients in our study complained of pruritis. While pruritis is reported frequently in HCV infected individuals[21,22] it is difficult to ascertain HCV as a cause of pruritis, as it is a common symptom in a number of hepatic and non hepatic co morbidities in patients with HCV[6]. In our patients pruritis was generalized and started within one month of treatment. Similarly association with Psoriasis, urticaria and erythema multiforme (EM) was seen in our study however sufficient scientific evidence is lacking to establish a strong causal link with HCV treatment[23].

CONCLUSIONS

HCV and its treatment with IFN plus ribavirin is associated with significant dermatological complications. Physicians should be aware of these problems and effective management strategies will help in limiting the severity of these side effects. Patients should be counselled about these manifestations before starting treatment.

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Do not go where the path may lead, go instead where there is no path and leave a trail.

Ralph Waldo Emerson