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"Unmasking the Beast": A Retrospective Analysis of Clinical and Histopathological Features of Hypopigmented Mycosis Fungoides

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Abstract

Background: Mycosis fungoides (MF) is the commonest type of cutaneous T-cell lymphoma. It typically has a chronic progressive course. In classic MF, there is infiltration of the skin with T lymphocytes, clinically manifest as erythematous or pigmented skin patches, mainly over covered body sites, which then progress in to infiltrative plaques and finally to tumors. Hypopigmented mycosis fungoides is observed in patients with pigmented skin, and it is categorized under patch stage of MF. However, compared to classic MF, expert observation has not reveled any progression beyond patch stage, any internal organ involvement or abnormal investigations results, compared to classic MF, even among those presenting with several years of hypopigmented mycosis fungoides. Research on hypopigmented Mycosis fungoides is lacking except for few case reports and few case series.

Methods: This is a descriptive study, which was conducted on patients who were diagnosed with hypopigmented mycosis fungoides.

Results: 90% of the patients were females and the mean age of the patients was 29.9 years. The patients had long duration of skin lesions and most of the time the correct diagnosis was missed. However, none of the patients had any internal organ involvement or abnormal investigation results, even among those presenting with several years of the disease. Zero deaths were observed during the studied period. On the other hand, revealing the diagnosis has made the patients anxious and, has significantly affected their quality of life. Most of the patients (90%) were treated with PUVA, with variable response.

Conclusion: Hypopigmented mycosis fungoides is categorized under cutaneous T cell lymphoma. However, as the disease shows very benign, nature, is it justified to classify and manage hypopigmented mycosis fungoides as same as classic MF?

Further discussions needed regarding classification of hypopigmented mycosis fungoides. Similarly, more clinical research should be conducted in a view of identifying an effective treatment for hypopigmented mycosis fungoides.

Keywords: Hypopigmented mycosis fungoides, Cutaneous T cell lymphoma, MF- Mycosis Fungoides

Introduction

Mycosis fungoides (MF) is a type of cutaneous T cell lymphoma. It has three sequential stages; patch stage, plaque stage and tumor stage. Characteristically, patients with classic mycosis fungoides progress from patch stage to plaque stage and finally to tumor stage over the years.

Hypopigmented mycosis fungoides is observed in patients with pigmented skin, including children [1]. It is common in Asians and exceedingly rare in Caucasians [2,3]. Clinically, the lesions show generalized hypopigmentation or even depigmentation, without much epidermal changes such as scaling (Figure 1). Although hypopigmented mycosis fungoides is categorized under patch stage of MF, it does not progress beyond patch stage. Furthermore, compared to classic MF, there is no organ such as lymph nodes or liver involvement. Also, unlike in classic MF, hypopigmented mycosis fungoides does not cause any haematological abnormalities [4].

Although hypopigmented mycosis fungoides has histological features of typical MF5, immunohistochemical features are different and needed further evaluation. To date, no definition or criteria published to evaluate hypopigmented mycosis fungoides [5]. Most importantly, a clinicopathological correlation is essential to make the accurate diagnosis.

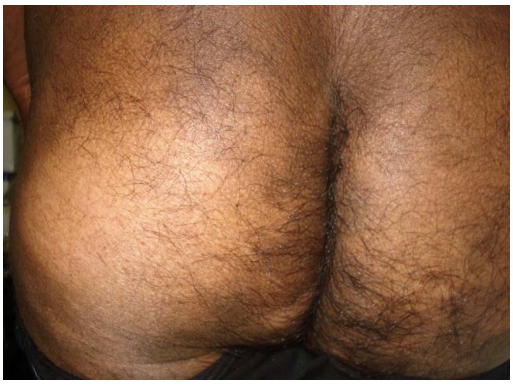

Figure 1: Typical lesions of Hypopigmented Mycosis Fungoides.

Research on hypopigmented mycosis fungoides is lacking except for few case reports and few case series [6]. This may due to disease prevalence in pigmented skin and is not common in countries where large studies are conducted.

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Rarity of this entity could be due to lack of awareness and also due to misdiagnosis, especially in the early stages, since it may mimic a variety of common cutaneous conditions such as pityriasis versicolor, progressive macular hypomelanosis, post inflammatory hypopigmentation, leprosy or even vitiligo. As hypopigmented lesions are common in our patients with dark skin, awareness regarding this disease should be adequately increased. Hypopigmented Mycosis fungoides should be included in the differential diagnosis of any persistent hypopigmented patch, especially if the lesion is on a covered body site.

Several reviews and guidelines on the management of classic MF have been published, but neither EORTIC consensus nor other guidelines has focused on either diagnosis or management of hypopigmented mycosis fungoides [7,8].

Since hypopigmented mycosis fungoides is more prevalent in people with pigmented skin, especially Asians, it is necessary to have statistically analyzed data regarding the disease. This will aid diagnosis and management of the disease at local setup as well as development of guidelines for management of the disease in the future.

The aim of this retrospective analysis to have Sri Lankan data on the disease, as it is not uncommon in our patients, and to identify the clinical and histopathological features of hypopigmented mycosis fungoides. Furthermore, findings from this study may helpful in development of local guidelines for management of the disease.

Methodology

This was a descriptive study, conducted in patients who were diagnosed with Hypopigmented Mycosis fungoides, IA and 1B Stages, who has had the disease for more than 3 years at the time study. The study commenced on 1st March 2016.The study was conducted at dermatology clinic, National Hospital of Sri Lanka. All the patients with hypopigmented mycosis fungoides IA and 1B Stages, who has had the disease for three or more years were included in the study.

All the patients with hypopigmented mycosis fungoides who meet inclusion criteria were taken in to the study. Power calculation couldn't be applied to calculate the sample size, since there are no published studies on the topic.

Data was collected using an interviewer-administered questionnaire, clinic records, histology reports and investigation results. Data was entered using Statistical Package for Social Sciences (SPSS). The analysis was carried out using the SPSS 17th version. The charts were made using Spreadsheet application Software (MS. Excel).

Results

All the patients with hypopigmented mycosis fungoides for three years or more were included in the study.

Twenty-one patients with hypopigmented mycosis fungoides were following up in the clinic. The Out of 21 patients, 18 (85%) were females (Figure 2). Out of three males, two were 25-year-old and the other was 39 years. Mostly of the patients were young and 11(52.3%) were between 20- 39 age group. The mean age of the patients was 29.9 years (Figure 3).

Most of the patients had a delay in diagnosis of the disease (Figure 4). Out of 21 patients, nine patients (42.8%) had the lesion for more than 10 years. The longest duration of skin lesions before the diagnosis was 20 years, in a 38-year-old lady, who was treated as pityriasis versicolar.

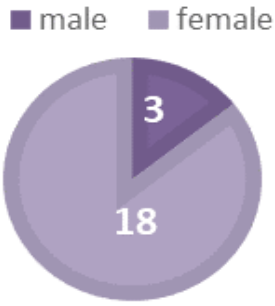

Figure 2: Gender distribution of the patients.

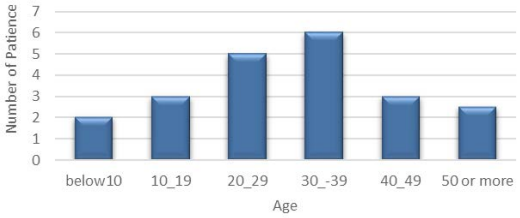

Figure 3: Age distribution of the patients.

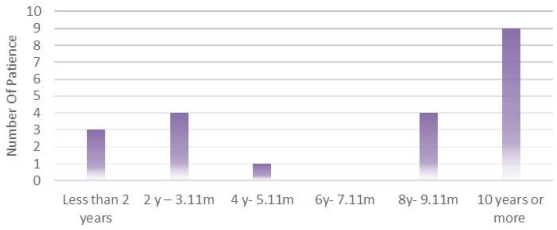

Figure 4: Duration of symptoms.

The patients presented directly to dermatology clinics with their skin lesions were diagnosed as hypopigmented mycosis fungoides and confirmed by skin biopsy. There were four patients who directly presented to dermatology units. One of them had skin lesions for 3 months, the second one for 6 months, and other two had skin lesions for 8 years and 10 years respectively, though both of them were neglecting their skin lesions.

However, most of the others have gone to general practitioners, and unfortunately, they were misdiagnosed. The most common misdiagnosis was pityriasis versicolar (67%), two patients were diagnosed as pityriasis lichenoides chronica (PLC), and another two patients were misdiagnosed as dermatitis and one patient as vitiligo (Figure 5).

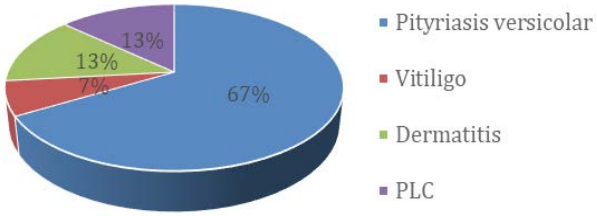

Figure 5: Previous diagnosis.

Out of 21 patients, two patients were previously treated by a doctor, but unaware of their diagnosis and no records available on diagnosis or treatment. Most of the patients were treated with antifungal creams, steroid creams or combinations before the diagnosis of hypopigmented mycosis fungoides (Figure 6).

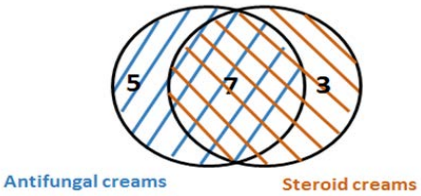

Figure 6: Previous Treatment.

Regarding the distribution of the lesions, eleven (52.38%) patients had lesions on both double covered areas such as breasts and buttocks and photo-protected skin (according to their clothing habits). One patient had lesions only on her breasts and another one had lesions only over buttocks. Two patients had lesions over covered skin without having lesions on double- covered areas. Both had lesions on their backs. Two patients had lesions over photo-protected skin and exposed areas of forearms. Four patients had lesions in generalized distribution including double-covered areas, covered areas and exposed body sites including face. None of the patients had lesions on their distal limbs (Figures 7-9).

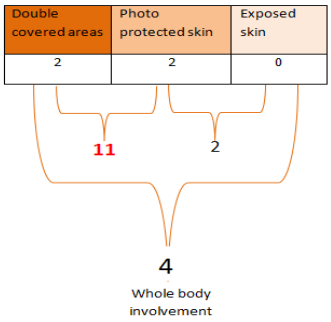

Figure 7: Number of patients in different patterns of distribution of the lesions.

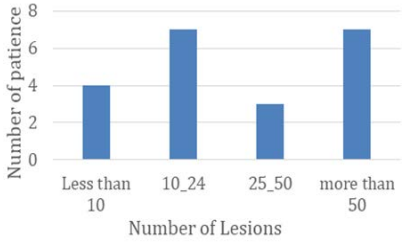

Figure 8: Number of lesions.

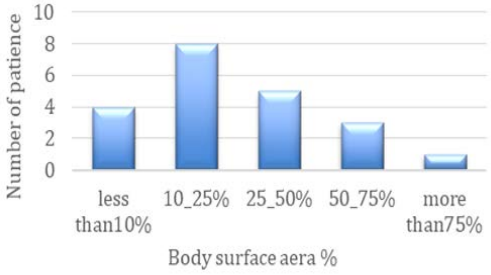

Figure 9: Body surface area of the lesions.

Regarding the sizes and the number of lesions, two patients had unilesional hypopigmented mycosis fungoides. One patient had the lesion over her back and the other one had the lesion over the buttock.

Seven patients (33.3%) had 10-25 lesions also another seven (33.3%) of patients had large number of small lesions, sometimes hundreds. Most of the patients had combination sizes of lesions. No one had lesions smaller than diameter of 1cm.

Nine patients (42.8%) had only medium sized (1 cm-5 cm) lesions. Four patients (19%) had very large lesions of more than 10 cm size. Most of the patients (61%) had 10%-50% of body surface area involvement.

All the patients have undergone skin biopsies (Figure 10) 100% of biopsies showed predominant epidermotropihism and atypical, hyper convoluted lymphocytes both in epidermis and dermis. Other prominent histological features were atypical lymphocytes arranged like a band along the papillary dermis (71%) and Pautrier's microabcess (8%). All the patients have undergone skin biopsies (Figure 10) 100% of biopsies showed predominant epidermotropihism and atypical, hyper convoluted lymphocytes both in epidermis and dermis. Other prominent histological features were atypical lymphocytes arranged like a band along the papillary dermis (71%) and Pautrier's microabcess (8%).

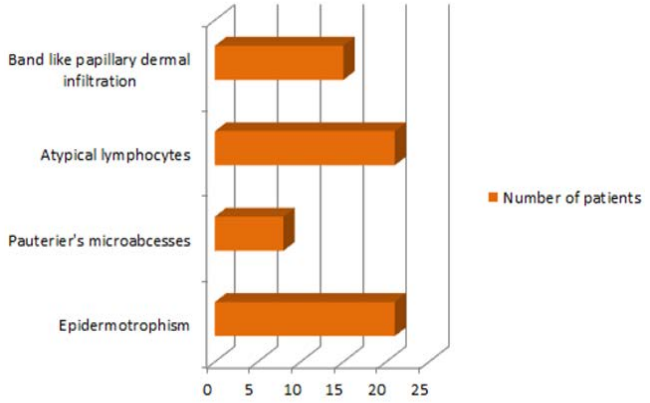

Figure 10: Histology of skin biopsies.

Full blood count, ESR and Ultrasound scan done in all the patients and did not show any abnormalities (Table 1). Initial treatment was PUVA for 19 patients and two children were given UVB. Out of 19 patients, 15 patients have completed initial 36 cycles.

Full Blood Count (FBC)	None of the patients had abnormal results
Erythrocyte Sedimentation Rate (ESR)	All the patients had normal ESR according to age and gender
Abdominal Ultrasound scan	None of the patients had abnormal ultrasound findings

Table 1: Basic investigation results of the patients

Among 15 patients, who completed PUVA, only 11(73.3%) got complete clearance of the lesions and other four patients had partial clearance of the lesions. The patients with partial clearance were given UVB according to the expert opinion. Ten patients have undergone PUVA more than one year at the time of the study. Recurrences were common during the first year. Out of ten patients, five (50%) have experienced recurrences during the first year following PUVA (Figure 11).

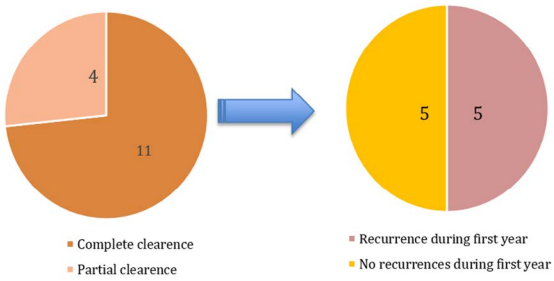

Figure 11: Response to PUVA treatment.

All the patients participated in the study have had asymptomatic lesions and they lead otherwise normal life despite of their disease. During the time of data collection, the patients were gathered to have focus group discussions to assess their concerns. Most of the patients, even young females have not much bothered about their skin lesions until the diagnosis of hypopigmented mycosis fungoides made. However, after the diagnosis, many patients searched on web regarding their diagnosis and almost all of them became significantly anxious about their problem as the disease is categorized under skin cancers.

Discussion

Majority of patients presenting with hypopigmented mycosis fungoides were females. It may be due to true female predominance or clothing patterns of female as their UV exposure is less. Sometimes, it may be purely due to higher attention to skin among females.

As hypopigmented mycosis fungoides mimics a variety of common dermatological diseases, misdiagnosis was common and usually the proper diagnosis was delayed. However, even with the delay of diagnosis for years, it has not shown less favorable prognosis in view of morbidity and mortality.

Distribution of hypopigmented mycosis fungoides showed some similarity to classic MF, majority (52%) of patient had lesions on both double covered areas and photo protected skin. However, only two patients had lesions exclusively on double covered skin.

General and systemic examinations of the patients were normal. Lymph node involvement or hepatomegaly was not detected in any patient, even who had extensive cutaneous involvement. Histopathology was similar to classic MF, epidermotropihism and atypical lymphocytosis were most significant histological features. Histological features were similar to those published cases of hypopigmented mycosis fungoides.

Twelve patients were undergoing immunophenotyping. In contrast to classic MF, immunohistochemical studies showed CD8+ predominance, though there were CD4 cells as well. Basic investigations were normal in all the patients.

Expected 5-year survival rate is 73%-89% in IB stage of classic MF [7,8], but the prognosis of hypopigmented mycosis fungoides appears to be excellent with lack of progression beyond stage IB [6]. Furthermore, hypopigmented mycosis fungoides has excellent mortality rates [9-11].

To date hypopigmented mycosis fungoides is categorized under cutaneous T cell lymphoma, a "skin cancer" in simple language, which creates high anxiety in both the patient and the treating dermatologist. As the disease shows very benign, innocent nature, is it justified to classify and manage Hypopigmented Mycosis fungoides as same as classic MF or should it be considered as a separate category?

In this era of easy access to information through the web, patients often read up on their diagnosis, and available data when mycosis fungoides is searched, can lead to unnecessary fear and anxiety, especially if the patient is in pediatric age group Though the experts tend to reassure them, there is no proven evidence for the benign nature of the disease, except for observation and experience. Patients in this study clearly mentioned that, awareness of the diagnosis, has adversely affected patients' quality of life, as the disease is categorized under skin cancers.

It should be also highlighted that; the patients were treated with traditional phototherapy though the clinical response was variable and the recurrence rates were high. Furthermore, PUVA has its own side effects including long-term risk of skin cancers. As PUVA cannot be repeated with frequent recurrences, UVB, which has fewer side effects, would be a good option for treatment of hypopigmented mycosis fungoides. Also, whether any another treatment will be effective for hypopigmented mycosis fungoides, should be studies in near future.

Conclusions

Majority displayed a diagnosis delay with frequent misdiagnoses. Distribution of hypopigmented mycosis fungoides lesions was commonly on double covered and photo protected body sites.

Hypopigmented mycosis fungoides did not show lymph nodes, liver or systemic involvement. Histological pattern of hypopigmented mycosis fungoides is similar to classic MF, but immunohistochemistry is different with predominant CD8+ cell recruitment. Hypopigmented mycosis fungoides responds to PUVA, but recurrences are common. Hypopigmented mycosis fungoides has an excellent prognosis without progression beyond stage 1B.

Therefore, there is an urgent requirement to conduct larger scale studies to have statistically analyzed data on hypopigmented mycosis fungoides to assess the disease prognosis the management of the disease. Depending on different clinical features and prognosis, classification of hypopigmented mycosis fungoides should be revised and should consider independently from classic MF.

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