Original Article

Spectrum of cutaneous infections in patients of leukemia

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Abstract

Background Cutaneous infections are common in patients of leukemia due to immunosuppression caused by the disease itself and its therapy.

Objectives This study was aimed to analyze the incidence, types and clinical presentations of various cutaneous infections in different types of leukemias in this part of the world.

Patients and methods This observational, descriptive and cross sectional study was carried out in department of dermatology, King Edward Medical College & Mayo Hospital, Lahore. Two hundred and fifty diagnosed patients of leukemia were enrolled from pediatrics, oncology, dermatology and medical units of Mayo Hospital, Lahore. Detailed dermatological examination was performed and the cases having any skin infection were further investigated. The incidence and morphological patterns of various cutaneous infections in leukemia were analyzed.

Results Out of the 250 enrolled patients, cutaneous infections were present in 177 (71%) patients. Out of these 177 patients, 101(57%) were male while 76(43%) were female. The age ranged from 2-76 years. Infections of skin were more common in acute as compared to chronic leukemias ($p < 0.01$). Candidiasis was the commonest infection (72%) seen, while bacterial, viral and dermatophytic infections were present in 31%, 35% and 12% of the patients, respectively. Scabies was found in 12%. More than half of the patients (54%) had two or three types of concomitant infections. Bacterial infections were more frequent in myelogenous leukemias ($p < 0.001$), while candidal and dermatophytic infections were more common in lymphocytic leukemias ($p<0.001$ and < 0.05, respectively). Dissemination, higher grade of severity and atypical morphology was frequently seen with these infections.

Conclusions The incidence of cutaneous infections in leukemic patients is very high and these are more common in acute as compared to chronic leukemia. Candidiasis is the commonest infection. Bacterial infections are more frequent in myelogenous leukemias, whereas superficial fungal infections are more in lymphocytic leukemias. Infections with higher degree of severity, dissemination and atypical morphology are common.

Key words
Leukemia, cutaneous infections.

Introduction

Cutaneous manifestations of leukemia are divided into specific and nonspecific. Specific lesions are due to metastatic infiltration of neoplastic cells in the skin but these cells are not present in the nonspecific lesions.[1] Nonspecific (non-metastatic) dermatologic manifestations are more frequent than the specific ones and infections form the bulk of such manifestations.[2] Severe scabies and

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bacterial, viral, and fungal infections are very common in immunosuppression, and patients of leukemia are especially vulnerable to these infections.[3,4]

In addition to the higher incidence, the infections in these patients also have atypical morphology. These are usually of severe degree, disseminated, recurrent and with unusual presentations. Infection is the leading cause of death in patients with leukemia.[5] The diversity in types and morphology of cutaneous infections in these patients often pose a significant diagnostic challenge. Familiarity with the clinical spectrum of these infections is necessary for prompt clinical evaluation and aggressive therapy to alleviate morbidity and mortality associated with these immunosuppressed patients.

This study was carried out to analyze the incidence, types and clinical presentations of various cutaneous infections in different types of leukemias in this part of the world.

Patients and methods

This observational, descriptive and cross sectional study was planned and conducted in dermatology department, King Edward Medical College/Mayo Hospital, Lahore. Cases with established diagnosis of any type of leukemia were included. The patients were enrolled from pediatrics, oncology, dermatology and medical units of Mayo Hospital, Lahore. Two hundred and fifty patients of either sex and any age, fresh as well as on therapy, were registered for the study.

Relevant findings of history, general physical and systemic examination of each patient were recorded on a predesigned pro forma. A thorough dermatological examination, including skin, mucosae and adenexa was carried out. Suspected cases of cutaneous infections were further worked up. Detailed clinical features of all the cutaneous lesions in every patient were recorded. Diagnosis of cutaneous infections was established by clinical features and relevant investigations like scraping, smear, culture, histopathology, etc. All the data collected was tabulated and analyzed in a database.

Statistical analysis

All categorical variables were described as percentages and the only continuous variable, the age, as mean +/-SD (standard deviation). Odds ratios were calculated for risk of various infections in different groups of leukemia. Chi-square statistics was applied to test the significance of differences between categorical variables. Statistical significance was defined as $p < 0.05$.

Results

Cutaneous infections were present among 71% (177) of the 250 enrolled cases of different types of leukemia (**Table 1**). Out of these 177 patients, 101 (57%) were male and 76 (43%) were female with male to female ratio of 1.3:1. Eighty-three (47%) were children (<12 years) with mean age of 7.3 years (SD +/- 2.2) and the rest 94 (53%) were adults (>12 years) with mean age of 40.9 years (SD +/- 13.9). Overall age ranged from 2-76 years (**Table 2**).

Type of leukemia	*Total patients*	*Patients with infections No. (%)*
AML	77	56 (73)
ALL	118	91 (77)
CML	42	23 (55)
CLL	13	7 (54)
Total	250	177 (71)

Table 1 Cutaneous infections in leukemia
AML: acute myelogenous leukemia, ALL: acute lymphoblastic leukemia, CML: chronic myeloid leukemia, CLL: Chronic lymphocytic leukemia,

Table 2 Demographic data

Parameters	*AML (n = 56) No. (%)*	*ALL (n = 91) No. (%)*	*CML (n = 23) No. (%)*	*CLL (n = 7) No. (%)*	*Total (n = 177) No. (%)*
Age					
<12 Yrs. (%)	14 (25)	66 (73)	3 (13)	0 (0)	83 (47)
> 12 Yrs. (%)	42 (75)	25 (27)	20 (87)	7 (100)	94 (53)
Sex					
Male (%)	31 (55)	57 (63)	9 (39)	4 (57)	101 (57)
Female (%)	25 (45)	34 (37)	14 (61)	3 (43)	76 (43)
M:F	1.22:1	1.68:1	1:1.55	1.33:1	1.32:1

AML: Acute myelogenous leukemia, ALL: Acute lymphoblastic leukemia, CML: chronic myeloid leukemia, CLL: Chronic lymphocytic leukemia

Table 3 Types of cutaneous infections in different leukemias

Type of infection	*AML (n = 56) No. (%)*	*ALL (n = 91) No. (%)*	*CML (n = 23) No. (%)*	*CLL (n = 7) No. (%)*	*Total (n = 177) No. (%)*
Bacterial	23 (41)	17 (19)	14 (64)	1 (14)	55 (31)
Viral	22 (39)	31 (34)	7 (30)	2 (29)	62 (35)
Superficial fungal infections	32(57)	82(90)	11(48)	7(100)	132(75)
Candidal	32 (57)	77 (85)	11 (48)	7 (100)	127 (72)
Dermatophytic	4 (7)	14 (15)	1 (4)	2 (29)	21(12)
Pityriasis versicolor	0(0)	3(3)	2(9)	1(14)	6(3)
Scabies	8 (14)	9 (10)	5(22)	0 (0)	22 (12)

AML: Acute myelogenous leukemia, ALL: Acute lymphoblastic leukemia, CML: chronic myeloid leukemia, CLL: Chronic lymphocytic leukemia

Cutaneous infections were more common in acute leukemias (AML + ALL = 75%) as compared to chronic leukemias (CML + CLL = 55%) and the difference is statistically significant (p<0.01). The odds ratio for risk of infection for acute leukemia is 1.263 and for chronic leukemia is 0.496 (**Figure 1**). Superficial fungal infections (candidiasis, dermatophytosis or pityriasis versicolor) were present in 132 (75%) of the 177 patients of leukemia with cutaneous infections. Among this group candidiasis

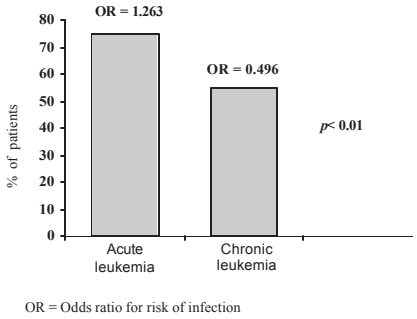

Figure 1 Cutaneous infections: acute vs. chronic leukemias (n=250)

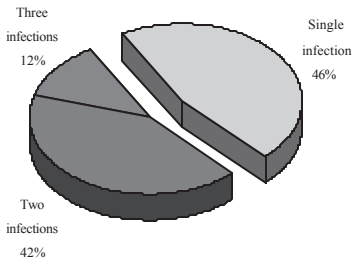

Figure 2 Concomitant cutaneous infections (n=177)

Figure 3 Concomitant infections, candidiasis and herpes simplex

Figure 4 Severe folliculitis with scarring alopecia

Figure 5 Kaposi's varicelliform eruption

Figure 6 Disseminated dermatophytosis

Figure 7 Generalized pityriasis versicolor

(cutaneous or mucocutaneous) was the most prevalent, being present in 72% of the cases, whereas 12% had dermatophytosis and only 3% had pityriasis versicolor. Bacterial and viral infections were also common and affected 31% and 35% of the cases

Table 4 Type of infections - myelogenous vs. lymphocytic leukemias

Type of infection	Myelogenous leukemia (AML + CML) (n = 79)			Lymphocytic leukemia (ALL + CLL) (n=98)			*p* value
	No.	%	Odds Ratios	No.	%	Odds ratios	
Bacterial	37	47	1.954	18	18	0.499	<0.001
Viral	29	37	1.076	33	34	0.942	0.674
Superficial fungal infections	43	54	0.407	89	91	3.371	<0.001
Candidal	43	54	0.516	84	86	2.107	<0.001
Dermatophytic	5	6	0.502	16	16	1.449	<0.05
Pityriasis versicolor	2	3		4	4		
Scabies	13	17	1.138	9	9	0.712	0.145

Table 5 Types of bacterial, viral and dermatophytic

Infections	*No. of patients*	*%*
Bacterial infections (n = 55)		
Furuncles	18	33
Impetigo	12	22
Folliculitis	8	15
Pyoderma	8	15
Cellulitis	6	11
Carbuncle	3	5
Viral infections (n = 62)		
Herpes simplex	21	34
Herpes zoster	14	23
Varicella	9	15
Verruca vulgaris	8	13
Verruca plana	6	10
Molluscum contagiosum	4	6
Dermatophytic infections (n = 21)		
Tinea corporis	8	38
Tinea unguium	7	33
Tinea cruris	5	24
Tinea capitis	4	19
Tinea pedis	4	19
Tinea faciei	4	19

respectively. Scabies was seen in only 12% of the patients (**Table 3**). More than half of the patients (54%) had multiple types of infections (bacterial, viral, superficial fungal, scabies, etc.). Out of these 42% had two and 12% had three types of concomitant infections (**Figures 2** and **3**). Frequencies of various infections in myelogenous vs. lymphocytic leukemias are summarized in **Table 4** along with the statistical analysis showing odds ratios for risk of infection and p value for each group. Bacterial infections were more frequent in myelogenous as compared to lymphocytic leukemias and the difference was highly significant ($p<0.001$). Conversely, superficial fungal infections (as a group) were more common in lymphocytic leukemias, again with a highly significant difference ($p<0.001$). And within this group, candidiasis and dermatophytic infections individually were also significantly more in lymphocytic leukemia with p value of <0.001 and <0.05 respectively, whereas statistical difference was not calculated for pityriasis versicolor due to small sample size. The difference in two groups of leukemias is not statistically significant for viral infections and scabies (value of p is 0.674 and 0.145, respectively).

Among the bacterial infections furunculosis and impetigo were more common, however, folliculitis, nonspecific pyoderma, cellulitis and carbuncles were also seen (**Table 5**). In most of the patients they were very severe, widespread and involved multiple areas of the skin (**Figure 4**). Herpes simplex and herpes zoster were common viral infections seen (**Table 5**). In herpes simplex severe local disease was frequent and hemorrhagic and necrotic lesions were seen in some

patients. One case presented as Kaposi's varicelliform eruption (**Figure 5**). Extensive necrosis and ulceration along with involvement of greater number of adjacent dermatomes was a common finding in herpes zoster. Generalized cutaneous dissemination was also seen in four cases. One patient with CML had bilateral herpes zoster. In most of the patients of viral warts and molluscum contagiosum, the lesions were numerous and persistent and sometimes with atypical morphology. Almost all the clinical types of dermatophytic infections were seen but tinea corporis and tinea unguium were most common (**Table 5**). Multiple lesions and widespread local dissemination was frequent (**Figure 6**). Nine cases had dermatophytic infection on multiple sites of the body. Generalized pityriasis versicolor was present in one patient of CML (**Figure 7**). Majority of the patients had oral candidiasis, however, vaginal involvement, intertrigo, paronychia and onychia were also frequent. Extensive local disease along with involvement of more than one site was common. Scabies in most of the patients was very severe and often secondarily infected. Two cases of crusted (norwegian) type were also seen.

Discussion

Immunosuppression in leukemia results from the depletion of immunocompetent cells, primarily due to premature/abnormal leukocytes of the lineage involved[6] and secondarily from the marrow failure due to the infiltration by these malignant leukocytes. It is further aggravated by the cytotoxic therapy. In this background, primary cutaneous infections and systemic infections with secondary skin involvement are common complications.[7-9] The incidence of various cutaneous infections in our patients was 71% (**Table 1**). Moreover, 54% of the patients had more than one type of infections (**Figure 2**). In addition to immunosuppression, poor hygiene, limited diagnostic facilities, inadequate isolation and exposure to nosocomial infections may be the contributory factors for this high incidence in our setting.

Cutaneous and mucocutaneous candidiasis was the commonest infection (72%) encountered in this study (**Table 3**). This is in agreement with the previous reports regarding immunosuppressed patients in the literature.[7,10,11] This is due to the fact that the medical conditions that cause defects in cell-mediated immunity or neutropenia, and chronic immunosuppressive therapy can predispose the patients to candidal infection.[12] Although less serious than systemic candidiasis, mucocutaneous candidiasis is a common complication observed in immunosuppressed patients.[13,14]

In acute leukemias the production of immature cells is very high as compared to chronic leukemias. This increased load of neoplastic cells causes greater degree of marrow infiltration at the expense of normal hemopoietic elements including leukoctytes.[15] The resulting greater overall immunosuppression in acute leukemias may be responsible for the statistically significant difference between the frequencies of cutaneous infections in acute (75%) vs. chronic (55%) leukemias (**Figure 1**). In disorders of phagocytosis, bacterial infections are characteristically more common.[16] The significantly high incidence

of bacterial infections found in myelogenous leukemias as compared to lymphocytic leukemias in our study (**Table 4**) may be due to defective phagocytic defence function in leukemias of myeloid series. Fungal and viral infections are predominant in conditions with deficient cell-mediated immunity.[11] The greater impairment of cellular immunity in lymphocytic leukemias may have given rise to significantly higher incidence of candidiasis and dermatophytic infections in lymphocytic leukemias than the myelogeneous ones (**Table 4**). The lack of statistically significant difference regarding viral infections, among the two groups in this study, can not however be explained on such basis.

In immunocompromised patients the classic clinical findings are distorted. There are unusual presentations of common infections or infections with atypical and opportunistic pathogens. In leukemia, infections are usually of severe degree, disseminated and with atypical presentation & protracted course. They are acute and fulminant or chronic and recurrent, with only partial response to conventional treatment.[2,3,4,17-24] Similar morphological profile of various infections was encountered in this study as well, e.g. widespread and severe bacterial and fungal infections, disseminated and necrotic herpes simplex and zoster, Kaposi's varicelliform eruption, bilateral herpes zoster, generalized and atypical viral warts and molluscum contagiosum, crusted scabies, etc.

In conclusion, the incidence of various cutaneous infections in leukemic patients is very high and they are more common in acute leukemia as compared to chronic leukemia. Candidiasis is the commonest infection. Bacterial infections are more frequent in myelogenous leukemias, whereas superficial fungal infections are more in lymphocytic leukemias. Infections with higher degree of severity, dissemination and atypical morphology are common.

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