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ORIGINAL RESEARCH

Evaluation of Dermatological Lesions in Patients With Hematologic Malignancy

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ABSTRACT

The purpose of this study was to assess dermatological lesions in hematologic malignancy patients. Patient file records pertaining to patients diagnosed with hematologic malignancies and followed up in our center between 2019 and 2024 will be retrospectively examined for demographic information, hematologic disease diagnoses, clinical features, dermatological examination data obtained with dermatology consultation, pathology results of biopsies taken from skin lesions, and the presence of other malignancies. The study comprised 241 participants with hematologic malignancies. The male to female ratio was 1.3, and the median age was 64. Acute myeloid leukemia (AML) accounted for 24.1% of diagnoses, while multiple myeloma (MM) came in second with 18.3%. With a rate of 14.9%, dermatitis was the most frequent form of lesion, followed by drug response (14.5%). In the AML group, dermatitis and fungal infection were the most frequent lesions, while in the MM group, medication reactions were more common. Patients with malignancy experienced urticaria considerably more frequently (p=0.004). At the time of lesion development, 81.7% of the patients were receiving chemotherapy, with alkylating drugs being the most frequently utilized agents (24.9%). Twenty percent of individuals who had biopsies reported having vasculitis and drug-related dermatological responses. 98.8% of the patients received local/topical supportive treatments without stopping systemic treatment. According to this study, dermatological lesions in hematologic malignancies may be connected to the course of the disease as well as treatment. These results imply that routine follow-up for hematologic patients should include a dermatological evaluation.

Keywords: Malignancy. Lesion. Hematology. Dermatology.

Hematolojik Malignite Tanısı Olan Hastalarda Dermatolojik Lezyonların Değerlendirilmesi

ÖZET

Hematolojik malignite tanısı olan hastalarda dermatolojik lezyonların değerlendirilmesi amaçlanmıştır. Çalışmamız yapılırken 2019-2024 yıllarında hematolojik malignite tanısı olan demografik veriler, hematolojik hastalık tanıları, hastalık süresi, klinik özellikler, dermatoloji konsültasyonu ile elde edilen dermatolojik muayene verileri cilt lezyonlarından alınan biyopsilerin patoloji sonuçları ve diğer malignite varlığı hasta dosya kayıtlarından retrospektif olarak incelenecektir. Toplam 241 hematolojik maligniteli hasta dâhil edilmiştir. Olguların ortanca yaşı 64 olup, erkek/kadın oranı 1,3'tür. En sık tanı %24,1 ile akut myeloid lösemi (AML), ardından %18,3 ile multipl miyelom (MM) ve %17,4 ile non-Hodgkin lenfoma (NHL) gelmiştir. Lezyonların en sık rastlanan tipi %14,9 oranla dermatit olurken, bunu ilaç reaksiyonu (%14,5) ve mantar enfeksiyonları (%13,3) takip etmiştir. AML grubunda en sık lezyon dermatit ve mantar enfeksiyonu, MM grubunda ise ilaç reaksiyonu belirlenmiştir. Lenfomalı hastalarda anlamlı şekilde daha sık ürtiker görülmüştür (p=0,004). Hastaların %81,7'si lezyon gelişme döneminde kemoterapi almakta olup, en sık kullanılan ajanlar alkilleyiciler (%24,9), antimetabolitler (%22,8) ve steroidlerdir (%21,2). Biyopsi yapılan hastaların %20'sinde ilaç ilişkili dermatolojik reaksiyon ve vaskülit raporlanmıştır. Hastaların %98,8'ine sistemik tedavi kesilmeden lokal/topikal destek tedavileri uygulanmıştır. Hematolojik malignitelerde dermatolojik lezyonların hem tedavi ilişkili hem de hastalık progresyonuyla bağlantılı olabileceğini göstermektedir. AML, MM ve NHL gibi farklı hematolojik hastalıklarda dermatolojik bulguların tipi değişiklik göstermektedir. Özellikle lenfomalı hastalarda ürtikerin daha sık görülmesi bu alt grubun izleminde dikkat edilmesi gereken bir bulgu olarak öne çıkmaktadır. Lezyonların büyük çoğunluğu tedaviye ara verilmeden yönetilebilmiş olup, lokal destek tedaviler yeterli olmuştur. Bu bulgular dermatolojik muayenenin hematolojik hastaların rutin izleminde önemli bir parça olması gerektiğini ortaya koymaktadır.

Anahtar Kelimeler: Malignite. Lezyon. Hematoloji. Dermatoloji.

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The four primary categories of dermatological findings associated with hematologic malignancies are infections brought on by immunosuppression, paraneoplastic symptoms, treatment-related findings, and direct skin involvement of the illness (specific findings). Disease-specific skin findings, or dermatological lesions that arise with skin involvement relevant to the disease, will be looked at in this section[1]. Clinically, the lesions typically appear as plaques, nodules, or erythematous, purple papules. The lesions can occasionally cause pain, but they are mostly asymptomatic. The prognosis depends on the size of the lesions, and a poor prognosis is linked to deep and widespread involvement. Immunophenotype analysis confirms mononuclear cell accumulation in the dermis and subcutis on histological inspection[2].

Non-specific dermatological findings in hematologic malignancies may occur as a result of systemic effects of the disease, side effects of treatment, complications or comorbid conditions without direct skin involvement. These findings are mostly seen as infections, immunological reactions, paraneoplastic syndromes and drug-induced skin reactions. Therefore, clinical observation and dermatological examination are very valuable in the diagnosis, treatment and management of complications in these patients[3].

A base for infection is created in hematologic malignancies by immune system suppression, chemotherapy, radiation, or neutropenia brought on by the illness itself, hypogammaglobulinemia, and damage to the integrity of the mucosal barrier. Bacterial infections are the most prevalent type. Examples include impetigo, ecthyma, cellulitis and necrotising fasciitis. "Ecthyma gangrenosum" is a disease with necrotic ulcers characteristic of Pseudomonas aeruginosa infections. Fungal infections: oral candidiasis, intertrigo, paronychia, tinea infections are common and forms with common spread pose a serious risk in immunocompromised patients. Viral infections: Herpes simplex and varicella zoster virus reactivations are common. Rashes related with CMV and HHV-6 may be observed especially in bone marrow transplantation patients[4].

Hematologic malignancies can cause paraneoplastic skin symptoms by immunological, humoral, or cytokine-mediated processes without the malignant cells directly spreading to the skin. These results may occasionally be found prior to the underlying hematological condition and may provide a crucial diagnostic hint[5].

When treating hematologic malignancies, chemotherapeutic medications, antibiotics, and supportive therapy can often result in a variety of skin responses. Maculopapular rashes are the most frequent adverse medication responses. Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN) are severe cutaneous reactions with poor prognosis. It is particularly associated with drugs such as allopurinol, antibiotics and anticonvulsants. Photosensitivity and hyperpigmentation: can occur with most chemotherapy drugs used in treatment (e.g., hydroxyurea, cyclophosphamide). Palmoplantar erythrodysesthesia (hand-foot syndrome): It is characterized with erythema, edema and pain in the palms and soles of the feet due to cytotoxic agents[6]. In neutropenic patients, infection findings may not give classical inflammatory signs; therefore, even minimal changes in the skin are important[7].

The purpose of this study is to comprehensively investigate the dermatological features seen in patients with hematologic malignancy and to ascertain how these findings relate to the disease's diagnosis, staging, therapy, and follow-up procedures. The study's objectives are to assess the distribution of dermatological findings by type of hematologic malignancy, the correlation between these findings and the disease's progression, and the skin lesions that result from treatment. We'll also look at how hematological and dermatology professionals' multidisciplinary patient care contributes to clinical success.

Material and Method

Demographic data, hematologic disease diagnoses, disease duration, clinical features, dermatological examination data obtained with dermatology consultation, pathology results of biopsies taken from skin lesions and the presence of other malignancies of patients diagnosed with hematologic malignancies and followed up in our center between 2019 to 2024 will be retrospectively examined from patient file records. One of the aspects of the study that is expected to contribute to the literature is that it emphasises the necessity of considering dermatological findings not only in the evaluation of symptoms but also in diagnosis and treatment planning. In this context, the study is aimed to increase the possibilities of early diagnosis in patients with hematologic malignancies and to strengthen clinical awareness for the prevention of possible complications. The study was approved by the Bursa City Hospital Ethics Committee (E-13012450-514.99-259215217, date:11.11.2024).

Statistical Analysis

Patients were analysed in terms of the types of skin lesions developed and the collected data were analysed using SPSS 27.0 (SPSS Inc., Chicago, IL,USA). Variables were examined using visual (histograms and probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk) to determine their distribution. Clinical and demographic

characteristics were summarized as mean and standard deviation (SD) for continuous variables and number and percentage for categorical variables. Categorical variables were compared by Chi-square test. Differences between independent samples were evaluated by Student's T test. $p < 0.05$ was considered statistically significant. Jamovi 2.4.14 was used for statistical analyses. Shapiro-Wilk test was used to determine the normal distribution, Chi-square and Fisher's exact test were used to compare categorical variables, and Student-t test and Mann-Whitney U test were used to compare numerical variables. $P<0.05$ was set as the statistical significance limit.

Results

A total of 241 hematology patients with dermatological manifestations between 2020 and 2025 were included in the study. The median age was 64 (50-72) and the male/female ratio was 1.3. The most common disease was AML (24.1%), followed by multiple myeloma (18.3%) and non-Hodgkin's lymphoma (17.4%). Disease distribution is presented in Table 19 (Table I).

Table I. Diseases incidence

Disease	Counts	% of Total	Cumulative %
AML	58	24.1 %	24.1 %
NHL	42	17.4 %	41.5 %
MM	44	18.3 %	59.8 %
MDS	17	7.1 %	66.8 %
ET	7	2.9 %	69.7 %
HL	16	6.6 %	76.3 %
ITP	4	1.7 %	78.0 %
ALL	16	6.6 %	84.6 %
CLL	10	4.1 %	88.8 %
THALASSEMIA	6	2.5 %	91.3 %
CML	7	2.9 %	94.2 %
HCL	6	2.5 %	96.7 %
PV	1	0.4 %	97.1 %
TTP	1	0.4 %	97.5 %
VWD	1	0.4 %	97.9 %
APLASTIC	1	0.4 %	98.3 %
PMF	4	1.7 %	100.0 %

(AML: Acute myeloid leukemia, NHL: non-Hodgkin lymphoma, MM: multiple myeloma, MDS: myelodysplastic syndrome, ET:essential thrombocythemia, HL : Hodgkin lymphoma, ITP : immune thrombocytopenic purpura, ALL : Acute lymphoblastic leukemia, CLL: chronic lymphocytic leukemia, CML: chronic myeloid leukemia, HCL , hairy cell leukemia,PV , polycythemia vera, TTP : thrombotic thrombocytopenic purpura, VWD: Von Willebrand disease, AA, aplastic anemia, PMF: primary myelofibrosis

The most common lymphomas were DLBCL (63.4%) and peripheral T-cell lymphomas.

The subtypes of lymphomas are presented in Figure 1.

Acetyl salicylic acid, warfarin or new oral anticoagulants were used by 22.1% of the patients, allopurinol by 2.9%, trimethroprim-sulfometaxazole by 0.8%, antibacterial antibiotics by 24.1%, antivirals by 11.2% and antifungals by 5%. Dermatitis (14.9%) was the most common cutaneous finding identified at presentation, followed by drug reactions (14.5%) and fungal infections (13.3%). A detailed table of the presentation is given in Table II. Skin punch biopsy was performed in 18.3% of these patients with various pre-diagnoses, most commonly drug reaction (22.4%) and fungal infection (13.3%). The pre-diagnoses are presented in Table 20 (Table II).

Table II. Skin Findings

Skin Finding	Counts	% of Total	Cumulative %
Drug reaction	35	14.5%	14.5%
Papule	11	4.6%	19.1%
Ulcer	14	5.8%	24.9%
Urticaria	14	5.8%	30.7%
Rubor	9	3.7%	34.4%
Fungal infection	32	13.3%	47.7%
Dermatitis	36	14.9%	62.7%
Purpura	9	3.7%	66.4%
Petechiae	12	5.0%	71.4%
Vasculitis	6	2.5%	73.9%
Dryness	7	2.9%	76.8%
Bullous lesions	6	2.5%	79.3%
Pruritus	12	5.0%	84.2%
Nodule	5	2.1%	86.3%
Eczema	5	2.1%	88.4%
Aphthous ulcer	1	0.4%	88.8%
Vesicle	10	4.1%	92.9%
Acne	15	6.2%	99.2%
Wart	1	0.4%	99.6%
Lymphoma involvement	1	0.4%	100.0%

When the skin findings of the most common diseases were analyzed, fungal infection (15.5%) and dermatitis (15.5%) were observed most frequently in AML patients (Table III), drug reaction (15.9%) and fungal infection (11.4%) were observed most frequently in MM patients (Table IV), and fungus (18.8%) and dermatitis (14.6%) were observed in NHL patients (Table V). The distribution of other findings is shown in the Tables (Table VI). According to the biopsy results, drug-related reaction and vasculitis were reported most frequently with a frequency of 20%. Other diagnoses are presented in Table VII.

Table III. AML Skin Findings

Skin Finding	Counts	% of Total	Cumulative %
Drug reaction	8	13.8%	13.8%
Papule	5	8.6%	22.4%
Ulcer	3	5.2%	27.6%
Urticaria	2	3.4%	31.0%
Fungal infection	9	15.5%	46.6%
Dermatitis	9	15.5%	62.1%
Purpura	5	8.6%	70.7%
Petechiae	3	5.2%	75.9%
Vasculitis	1	1.7%	77.6%
Dryness	1	1.7%	79.3%
Bullous lesions	2	3.4%	82.8%
Pruritus	3	5.2%	87.9%
Nodule	1	1.7%	89.7%
Vesicle	2	3.4%	93.1%
Acne	4	6.9%	100.0%

Table IV. Multiple Myeloma Skin Findings

Skin Finding	Counts	% of Total	Cumulative %
Drug reaction	7	15.9%	15.9%
Ulcer	4	9.1%	25.0%
Urticaria	2	4.5%	29.5%
Rubor	2	4.5%	34.1%
Fungal infection	5	11.4%	45.5%
Dermatitis	2	4.5%	50.0%
Purpura	2	4.5%	54.5%
Petechiae	2	4.5%	59.1%
Dryness	3	6.8%	65.9%
Bullous lesions	3	6.8%	72.7%
Pruritus	2	4.5%	77.3%
Nodule	1	2.3%	79.5%
Vesicle	4	9.1%	88.6%
Acne	4	9.1%	97.7%
Wart	1	2.3%	100.0%

Table V. NHL Skin Findings

Skin Finding	Counts	% of Total	Cumulative %
Drug reaction	6	12.5%	12.5%
Papule	2	4.2%	16.7%
Urticaria	6	12.5%	29.2%
Rubor	1	2.1%	31.3%
Fungal infection	9	18.8%	50.0%
Dermatitis	7	14.6%	64.6%
Petechiae	3	6.3%	70.8%
Vasculitis	3	6.3%	77.1%
Dryness	1	2.1%	79.2%
Bullous lesions	1	2.1%	81.3%
Pruritus	3	6.3%	87.5%
Vesicle	3	6.3%	93.8%
Acne	2	4.2%	97.9%
Lymphoma involvement	1	2.1%	100.0%

Table VI. Preliminary Diagnoses

Preliminary Diagnosis	Counts	% of Total	Cumulative %
Drug reaction	54	22.4%	22.4%
Dermatitis	25	10.4%	32.8%
Basal cell carcinoma	3	1.2%	34.0%
Insect bite	3	1.2%	35.3%
Herpes zoster	14	5.8%	41.1%
Wart	3	1.2%	42.3%
Fungal infection	32	13.3%	55.6%
Xerosis	14	5.8%	61.4%
Urticaria	3	1.2%	62.7%
Scabies	14	5.8%	68.5%
Bleeding	6	2.5%	71.0%
Folliculitis	2	0.8%	71.8%
Acne	10	4.1%	75.9%
Vasculitis	12	5.0%	80.9%
Miliaria	2	0.8%	81.7%
Bullous pemphigoid	2	0.8%	82.6%
Seborrheic keratosis	4	1.7%	84.2%
Rosacea	1	0.4%	84.6%
Infection	12	5.0%	89.6%
Drug extravasation	2	0.8%	90.5%
GVHD	2	0.8%	91.3%
Morphea	1	0.4%	91.7%
Disease involvement	4	1.7%	93.4%
Decubitus ulcer	3	1.2%	94.6%
Psoriasis	2	0.8%	95.4%
Erythema nodosum	2	0.8%	96.3%
Burn	1	0.4%	96.7%
Actinic keratosis	2	0.8%	97.5%
Aphthous ulcer	1	0.4%	97.9%
Lichen simplex	1	0.4%	98.3%
Telogen effluvium	1	0.4%	98.8%
Epidermal cyst	1	0.4%	99.2%
Pruritus	2	0.8%	100.0%

Table VII. Diagnoses Based on Biopsy Results

Diagnosis	Counts	% of Total	Cumulative %
Basal Cell Carcinoma	1	2.2%	2.2%
Dermal hemorrhage and panniculitis	1	2.2%	4.4%
Pyoderma gangrenosum	1	2.2%	6.7%
Insect bite reaction	1	2.2%	8.9%
Graft versus host disease	1	2.2%	11.1%
Microembolic ulcer	1	2.2%	13.3%
Orthokeratosis	1	2.2%	15.6%
Pityriasis rosea	1	2.2%	17.8%
Mucor infection	1	2.2%	20.0%
Purpuric dermatosis	1	2.2%	22.2%
Arthropod bite reaction	1	2.2%	24.4%
Bullous pemphigoid	1	2.2%	26.7%
Basal Cell Carcinoma	3	6.7%	33.3%
Actinic keratosis	2	4.4%	37.8%
Vasculitis	9	20.0%	57.8%
Erythema nodosum	1	2.2%	60.0%
Drug-related	9	20.0%	80.0%
Urticaria	1	2.2%	82.2%
Dermatitis	4	8.9%	91.1%
Mucormycosis	1	2.2%	93.3%
Disease involvement	2	4.4%	97.8%
Morphea	1	2.2%	100.0%

Dermatological Lesions

During the period when the lesions appeared, 81.7% of the patients were under chemotherapy and 17.8% were in remission without treatment. 1 patient presented with a skin lesion at the time of diagnosis. Chemotherapies received by the patients are presented in Table VIII.

Table VIII. Chemotherapies Administered

Therapy	N
Topoisomerase inhibitor	6 (2.5%)
Steroid	51 (21.2%)
Glycopeptide antibiotic	7 (2.9%)
Alkylating agent	60 (24.9%)
Daratumumab	6 (2.5%)
Rituximab	35 (14.5%)
Anthracycline	41 (17%)
Alkaloid	37 (15.4%)
Hypomethylating agent	25 (10.4%)
Immunomodulatory	26 (10.8%)
Proteasome inhibitor	24 (10%)
Ibrutinib	2 (0.8%)
Tyrosine kinase inhibitors	13 (5.4%)
Eltrombopag	4 (1.7%)
Venetoclax	5 (2.1%)
Antimetabolite	55 (22.8%)
RARA antagonist	3 (1.2%)
Brentuximab	4 (1.7%)
Calcineurin inhibitor	2 (0.8%)
Anti PD-1	1 (0.4%)
Anti FLT-3	2 (0.8%)

Local treatments were given to 98.8% of these patients without discontinuing the drug, while treatment was interrupted in 1.2% patients (Table IX).

Table IX. Treatments Administered

Treatment	N
Systemic therapy	197 (81.7%)
Topical steroid	53 (22%)
Systemic steroid	41 (17%)
Topical antibacterial	49 (20.3%)
Systemic antibacterial	71 (29.5%)
Topical antiviral	3 (1.2%)
Systemic antiviral	38 (15.8%)
Topical antifungal	37 (15.4%)
Systemic antifungal	12 (5%)
Antiparasitic	16 (6.6%)
Antihistamine	123 (51%)

Among urticaria, skin infection and drug reactions, urticaria was significantly more common in patients with lymphoma (p=0.004) (Table X)

Table X. Malignancies Associated with Urticaria

	Urticaria (p)	Skin infection	Drug reaction	Vasculitis
Leukemia (Acute & Chronic) N=94	0.163	0.626	0.49	0.713
Multiple Myeloma N=42	0.423	0.318	0.96	0.02
Lymphoma (HL, NHL) N=64	0.004	0.185	0.84	0.402

The incidence of urticaria (p=0.01) and vasculitis (p=0.02) was significantly higher in patients receiving rituximab. Development of vasculitis in the IMID (Immunomodulatory drug) group was statistically significant (p=0.008). Vasculitis was also significant in PI (protease inhibitor) users (p=0.006). No significance was observed in other treatment groups (Table XI).

Table XI. Skin Lesions by Treatment

	Urticaria	Skin infection	Drug reaction	Vasculitis
Rituximab N=35	0.01	0.11	0.85	0.02
IMID N=26	0.5	0.8	0.07	0.008
PI N=24	0.17	0.61	0.63	0.006
HMA N=25	0.55	0.1	0.23	0.916

Discussion and Conclusion

The variety, incidence, and clinical distribution of dermatological lesions observed in patients with hematologic malignancies were all thoroughly assessed in this study. Our results showed that acute myeloid leukemia (AML) was the most prevalent group of hematological diseases, followed by multiple myeloma (MM) and non-Hodgkin lymphomas (NHL). While dermatitis, drug reactions and fungal infections were prominent among dermatological lesions, these three findings were observed to be dominant especially in the AML group. Although there was a similar distribution in MM and NHL patients, it was noteworthy that each patient group exhibited some specific dermatological patterns. The fact that urticaria rates were found to be significantly higher in NHL patients is one of these differences. Also, drug reaction and vasculitis were the most frequently diagnosed lesions in patients who underwent skin biopsy, which revealed that there was a great concordance between clinical pre-diagnoses and histopathological findings.

The majority of patients were undergoing active chemotherapy at the time of the lesions, and the majority of these lesions could be treated locally or with supportive care without interfering with systemic

treatment, according to an analysis of the treatment process. The high rate of control without interruption of treatment indicates that these lesions are generally mild to moderate and manageable. All these findings reveal the importance of dermatological follow-up in terms of clinical management in patients with hematologic malignancies and show that early diagnosis, accurate pre-diagnosis and effective intervention can reduce complications.

A total of 241 hematologic malignancy patients with dermatological lesions were included in this study. The median age of the patients was 64 years, and the male/female ratio was 1.3, suggesting that the disease is more common in older age and male gender. The most common hematologic malignancy was acute myeloid leukaemia (AML), followed by multiple myeloma (MM) and non-Hodgkin lymphomas (NHL). Dermatological abnormalities were often seen in AML patients, particularly in the form of mucocutaneous complications and cutaneous infiltrations associated with the treatment process, according to a 2020 retrospective cohort analysis[8]. In the same study, it was reported that MM and NHL patients became vulnerable to dermatological complications depending on the level of immunosuppression. In 2021, in a multi-center observational study conducted by Garcia and Morales, cutaneous infiltration was reported in 22% of AML patients and this rate was found to be significantly higher compared to other malignancies [9]. The fact that AML was the most common hematologic disease in our study is consistent with the aforementioned literature. The necessity of dermatological follow-up in this patient group is further supported by the fact that MM and NHL patients were discovered in considerable proportions in our investigation. This distribution provides important preliminary data on the most common dermatological findings in hematologic malignancies.

When lymphoma subgroups were analysed, diffuse large B-cell lymphoma (DLBCL) was the most common. Patients with DLBCL have been described as a group more vulnerable to immunosuppression-induced infectious skin lesions and rarely cutaneous B cell infiltrations. In 2019, a prospective study by Chen et al. reported that 18% of patients with DLBCL developed skin lesions secondary to treatment [10]. It has also been reported that dermatological findings in the form of paraneoplastic or direct skin infiltrations may occur in peripheral T-cell lymphomas (PTHL). Eczema-like lesions, widespread erythema and plaques on the skin have been described especially in T-cell lymphomas, and this expands the clinical spectrum of the disease. The prominence of DLBCL in the distribution of NHL subtypes in our study is consistent with the above studies and reveals that this subgroup should be carefully monitored dermatologically.

Purpura, petechiae, or dermatitis have been linked in the literature to the dermatological adverse effects of anticoagulants or drugs for thromboembolism prophylaxis (acetylsalicylic acid, warfarin, NOAC), which were used by a sizable percentage of patients (22.1%). In addition, the use of antibacterial, antiviral and antifungal treatment was remarkable with a rate of 24.1%, 11.2% and 5%, respectively. In 2020, Huang et al. reported in a prospective analysis that drugs such as trimethoprim-sulfamethoxazole and allopurinol, which are commonly used for systemic infection prophylaxis, frequently cause drug reactions and maculopapular rashes in hematology patients[11].

Dermatitis was the most frequent dermatological finding in our study (14.9%), followed by fungal infections (13.3%) and medication responses (14.5%). Drug responses were found to be common in dermatological presentations linked to hematologic malignancies, particularly purpuric rashes, erythematous plaques, and vesicle forms, according to an observational review carried out in 2021[12]. Similarly, dermatitis and drug-related cutaneous findings were predominant in our study and coincided with clinical observations. Also, drug reactions and fungal infections were again the most common pre-diagnoses in skin biopsies performed for diagnostic purposes in 18.3% of the patients, indicating that clinical evaluation and histopathological examination were largely parallel.

A wide range of skin manifestations have been observed in patients with acute myeloid leukaemia (AML). The most common lesions were dermatitis (15.5%), fungal infections (15.5%) and drug reactions (13.8%), followed by papules (8.6%), purpura (8.6%), petechiae (5.2%) and ulcerative lesions (5.2%). The frequent occurrence of opportunistic fungal infections in AML patients due to immunosuppression has also been reported in the literature. For example, in a prospective study conducted by Lee et al. in 2022, cutaneous candida or aspergillus infection was found in 17% of AML patients[13]. Findings like pruritus and vesicular rashes support the high rate of medication responses, which is indicative of hypersensitivity brought on by intense chemotherapy regimens. Therefore, it is crucial from a therapeutic standpoint to carefully distinguish between infectious and non-infectious skin lesions in the dermatological follow-up of AML patients. The most common dermatological lesions observed in multiple myeloma (MM) patients were drug reactions (15.9%) and fungal infections (11.4%). Also, ulcerative lesions (9.1%), vesicles (9.1%), acneiform eruptions (9.1%) and bullous structures (6.8%) were also found at remarkable rates. The fact that MM patients are prone to immunosuppression pave the way to the development of overt infectious findings on the skin against fungal and viral agents. Additionally, dermatological side

effects of commonly used agents such as lenalidomide and bortezomib include bullous reactions, maculopapular rashes and photosensitivity. In a prospective study conducted by Wang et al. in 2023, cutaneous adverse events secondary to treatment were found in 14% of MM patients and drug reactions related to immunomodulatory agents were reported as the most common cause[14]. These results are in line with the prevalence of drug-induced dermatological findings in our investigation. Furthermore, non-specific symptoms including dryness, pruritus, and vesicles in MM patients complicate the disease's clinical history and highlight the significance of dermatological follow-up. Fungal infections (18.8%), dermatitis (14.6%) and drug reactions (12.5%) were the leading dermatological findings in patients with non-Hodgkin lymphoma (NHL). Urticaria-like rashes (12.5%) were also observed with considerable frequency. The presence of vascular and vesiculobullous findings such as petechiae, vasculitis and vesicles suggests that this patient group is prone to immune dysregulation. In a 2021 case series, it was reported that there was increased susceptibility to fungal infections especially in B-cell lymphomas and dermatitis and urticaria were among the most frequently reported cutaneous findings[15]. In addition, cutaneous involvement detected in a lymphoma patient was evaluated as an advanced stage spread of the disease. An NHL patient in our study had a lesion that was directly linked to lymphoma involvement; this finding should be regarded as an uncommon but significant clinical scenario. Detailed and regular dermatological follow-up of NHL patients is critical for early detection of both infectious complications and malignant infiltrations.

The distribution of pre-diagnoses among the study participants who received dermatological evaluation demonstrates the vast variety of skin abnormalities associated with hematologic malignancy. The most common pre-diagnosis was drug reactions (22.4%), and this finding is thought to be related with cutaneous hypersensitivity which commonly develops during chemotherapy and supportive therapies. This was followed by non-specific but common dermatoses such as dermatitis (10.4%) and fungal infection (13.3%). In a retrospective analysis conducted by Patel and Rosen in 2020, it was reported that drug-related pathologies were found in more than 40% of skin biopsies performed in hematology patients, and this was generally associated with supportive therapy or antineoplastic agents[16].

Shingles (5.8%), scabies (5.8%), vasculitis (5.0%) and various infections (5.0%) were also reported with remarkable frequency. This picture reflects the increased susceptibility to both viral, parasitic and bacterial agents in immunosuppressed patients and indicates that care should be taken in the differential diagnosis of non-infectious lesions in dermatological follow-up of patients. Interestingly, 1.7% of diseases (hematologic malignancy) were included in the pre-diagnosis of skin involvement, suggesting the possibility of direct cutaneous infiltration. In the algorithm-based diagnostic modelling study conducted by Jenei and Tzankov in 2025, it was reported that systematic differentiation of skin lesions detected in hematologic malignancies with accurate preliminary diagnosis directly affected clinical management[17].

However, in a comprehensive review study published by Souza et al. in 2023, it was emphasized that secondary specific skin lesions were one of the dermatological problems frequently encountered in hematologic neoplasms and the preliminary diagnostic process should be performed carefully in order to prevent diagnostic delay[18]. This diversity supports the need for routine dermatologic evaluations in patients with hematologic malignancies.

According to the biopsy results, the most common diagnoses were drug-related dermatologic reactions and vasculitis, each with a rate of 20%. These findings are largely in line with clinical pre-diagnoses and reveal a high diagnostic accuracy. It has been frequently emphasized in the literature that vasculitis cases are associated with immune-mediated inflammatory processes and are frequently seen in the background of hematologic malignancy. In the algorithmic analysis of Jenei and Tzankov dated 2025, it was stated that vasculitic skin lesions in leukemia and lymphoma patients may be an indicator of systemic spread or paraneoplastic processes[19].

Other dermatologic conditions diagnosed by biopsy include dermatitis (8.9%), basal cell carcinoma (6.7%), actinic keratosis (4.4%), graft versus host disease (GVHD), pyoderma gangrenosum and mucormycosis, which are rarer but require clinical attention. This diversity was similarly demonstrated in the comprehensive review published by Souza et al. in 2023; it was emphasized that the diagnostic spectrum of dermatologic lesions in individuals with hematologic malignancies is wide and this plays a key role in individual clinical decision-making processes[18].

These results imply that skin biopsies are an essential diagnostic and treatment-guidance tool for individuals with hematologic malignancies. In particular, the histopathologic distinction of malignant infiltrates or uncommon infectious agents (such mucor) is crucial to the treatment of disease.

In our study, it was observed that the majority of patients (81.7%) were under active chemotherapy treatment at the time of the development of skin lesions, while 17.8% were in remission without treatment. Also, one patient was diagnosed with hematologic malignancy directly preceded by skin lesions. This finding draws attention to the fact that

cutaneous manifestations may be the first sign of the disease in some cases. Dermatologic lesions that develop under treatment often indicate drug-related or immunosuppression-related secondary complications. In a multi-center study conducted in 2023, it was reported that dermatologic side effects were observed in 78% of patients receiving hematologic malignancy treatment and that these mostly occurred during treatment[19].

The most commonly administered treatment groups in our study were alkylating agents (24.9%), anti-metabolites (22.8%), steroids (21.2%) and anthracyclines (17%), and these agents are known to be associated with dermatologic toxicities. It is frequently emphasized in the literature that especially alkylating agents and antimetabolites cause hypersensitivity, photosensitivity and mucocutaneous reactions in the skin. In a review study published by Wang et al. in 2022, it was reported that early diagnosis and treatment of cutaneous toxicities associated with these agents both improved quality of life and facilitated continuation of systemic treatment[20].

When the treatment options applied to the patients are analyzed, it is seen that 98.8% of the patients received only supportive local treatments without discontinuation of systemic chemotherapy, and only 1.2% of patients had interruption of systemic treatment. This approach demonstrates good coordination between medical oncology and dermatology disciplines in the clinical management of skin lesions. The most frequently prescribed supportive therapies included antihistamine (51%), systemic antibacterial (29.5%), local steroid (22%) and systemic steroid (17%). These rates support that skin manifestations are mostly inflammatory and infectious in origin. Also, the use of antiviral (15.8%), antifungal (15.4%) and anti-parasitic (6.6%) treatment options indicates that infectious agents also play a significant role in the etiology of skin lesions.

These results show that the majority of patients with hematologic malignancies who experience dermatological reactions do not need systemic treatment, may be handled without stopping systemic medication, and can be controlled with local management.

In addition, the distribution of some skin findings differed statistically according to the patient groups. Especially in patients with lymphoma, the frequency of urticaria was found to be significantly higher. This finding suggests that urticaria may be a paraneoplastic or immune-mediated symptom specific to some types of hematologic malignancies. In a 2021 cohort analysis by Yoon et al., it was reported that urticaria-like rashes in lymphoma patients frequently develop due to cytokine activation and immune dysregulation and are more common than in other disease groups[21]. This finding suggests that non-specific rashes, especially urticaria, may be an important warning sign for referral to hematologic evaluation. In the literature, it has been reported that urticarial lesions develop before diagnosis in 12% of patients with early stage Hodgkin lymphoma and symptomatic management may be inadequate[22]. Therefore, a careful systemic evaluation in hematology patients presenting with urticaria is of clinical value.

We looked into the relationship between the therapeutic agents given to patients with hematologic malignancy and skin lesions, and we discovered that certain drug groups were significantly linked to particular types of lesions. Urticaria ($p=0.01$) and vasculitis ($p=0.02$) were significantly more frequent in rituximab-treated patients, suggesting that rituximab may cause immune-mediated dermatologic side effects. In prospective and retrospective studies in the literature, rituximab-related vasculitic eruptions and urticaria-like eruptions have been described[23,24].

Similarly, the rate of vasculitis was significantly increased in patients treated with the IMID group (e.g., lenalidomide, thalidomide). The effects of these agents that regulate T-cell activation and cytokine profile may stimulate the immune system and cause vascular inflammation[23]. A significant increase in the incidence of vasculitis was also observed in patients treated with proteasome inhibitors (e.g., bortezomib) and this finding is consistent with previous observational data. In particular, it has been suggested that proteasome inhibitors may trigger microvascular inflammation by impairing endothelial function. No significant correlation was found with skin lesions in the HMA (hypomethylating agents; azacitidine and decitabine) group. The more limited immune modulation potential and targeted effects of these agents may reduce the risk of developing skin lesions[25].

These results suggest that different therapeutic agents have unique profiles in terms of the risk of dermatologic complications, suggesting the need for caution in patient follow-up in terms of dermatologic side effects.

Although this study has strengths, some limitations may have an impact on the generalizability and depth of the findings. First of all, the retrospective design of the study and the fact that the data were obtained from retrospective patient files raised the possibility that some information may be missing, open to interpretation or recorded in a non-standardized manner. In particular, time-dependent dynamic data such as the clinical course of skin lesions, time of onset, and healing time could be analyzed in a limited way due to the nature of the recording system.

Another limitation is that dermatologic examinations and diagnoses were evaluated by different doctors. This may have led to differences in interpretation in

the classification of lesions and pre-diagnoses. Not using a standardized dermatological scoring system has made it difficult to quantify the severity or severity level of lesions. Furthermore, the fact that biopsy was not performed for all lesions and histopathologic confirmation was limited to selected cases only, posed some limitations in terms of assessing clinical and pathologic concordance.

Since the study included only one patient group from one center, it is not clear whether the findings would differ according to patient populations in different centers or geographical differences. Additionally, while each of the systemic chemotherapy and targeted therapy agents used had the potential for individual skin lesions, establishing a causal relationship between the dermatologic effects of these treatments was made difficult by the multiple treatment regimens.

Finally, the study did not assess the impact of lesions on patient quality of life, subjective experiences such as itching, pain, cosmetic discomfort or psychological consequences. However, such data are among the factors that can directly affect both patient satisfaction and adherence to treatment.

For all these reasons, although the results of this study support the knowledge in the field, further studies with larger sample groups, prospectively planned, multi-center and supported by standard diagnostic protocols are needed.

This study comprehensively evaluated the distribution, frequency and clinical significance of dermatologic lesions in 241 patients with hematologic malignancies. The data obtained revealed that dermatologic findings in this patient group are both highly prevalent and may show marked differences related to disease subtypes. The most common malignancy type was AML with 24.1%, followed by MM (18.3%) and NHL (17.4%). Dermatitis (14.9%), drug reactions (14.5%) and fungal infections (13.3%) were the most prominent skin manifestations, while the majority of lesions developed during the active chemotherapy period (81.7%). This shows how common cutaneous reactions related to the treatment process are.

Nonspecific lesions such as bullous and acneiform rashes were observed in MM patients and urticaria was observed at a remarkable level in NHL group. The fact that urticaria is significantly more common in NHL patients suggests that some skin findings may carry diagnostic clues according to hematologic disease subtypes. In the study, more than 40% of the diagnostic biopsies were diagnosed as drug-related reactions and vasculitis, indicating that cutaneous complications related to systemic therapies were confirmed histopathologically.

In terms of the treatment process, it is noteworthy that 98.8% of the patients could be treated with local and supportive therapies without discontinuation of systemic chemotherapy. This suggests that dermatologic complications are generally manageable and do not interrupt the continuity of systemic therapy. The most preferred supportive therapies were antihistamines (51%), systemic antibacterial agents (29.5%) and steroids (22% local, 17% systemic). In addition, the fact that one patient presented with only skin lesions at the time of diagnosis showed that dermatologic findings may be an important clinical clue in the early diagnosis process.

In summary, dermatological lesions observed in patients with hematologic malignancies have clinical implications for diagnosis, prognosis, and treatment in addition to being symptomatic. Therefore, using interdisciplinary techniques and incorporating dermatologic follow-up into the therapy process will improve patient care and help lower problems.

Hematologic malignancies' dermatological symptoms are crucial for diagnosis and follow-up. Effective contact between dermatologists and hematologists can now improve early diagnosis and treatment outcomes. For the purpose of identifying cutaneous infiltrates caused by cancer, precise analysis of the features of skin lesions and prompt biopsy are essential. Dermatology assistance is also necessary for the treatment of medication eruptions brought on by systemic treatments. Patient care can be more thorough and efficient with this multidisciplinary approach.

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