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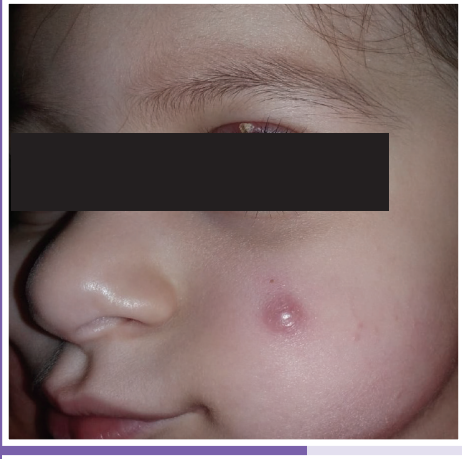

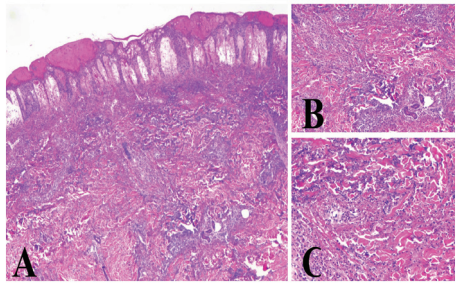

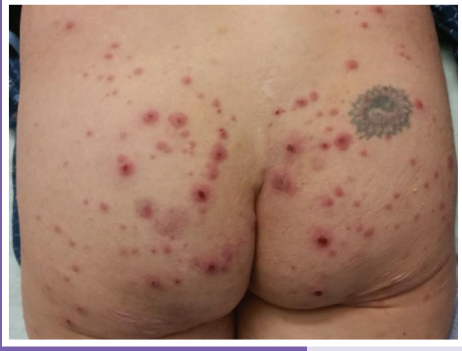

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I:Introduction

II:Methods

III:Results

IV:Conclusions

References

the appendices

FIGURE LEGENDS

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Mareledwane NG. A randomized, open-label, comparative study of oral doxycycline 100 mg vs. 5% topical benzoyl peroxide in the treatment of mild to moderate acne vulgaris. Int J Dermatol 2006; 45: 1438-1439. PMID: 17184250

Doger FK, Dikicioglu E, Ergin F, Unal E, Sendur N, Uslu M. Nature of cell kinetics in psoriatic epidermis. J Cutan Pathol 2007; 34: 257-263. PMID: 17302610

Book: - Monsel G, Delaunay P, Chosidow O. Arthropods. In: Griffiths C, Barker J, Bleiker T, Chalmers R, Creamer D, editors. Rook's Textbook of Dermatology, 9th ed. Singapore: Blackwell Science; 2016. p. 32-34.

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CONTENTS

ORIGINAL ARTICLE

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Evaluation of Serological Test Results of Other Sexually Transmitted Diseases in Patients with Anogenital Warts

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ABSTRACT

Background: Anogenital warts (AGW) are a highly infectious disease caused by the human papilloma virus (HPV). HPV infection is the most common sexually transmitted viral infection in the world.

Materials and Methods: In our study we aimed to determine coexistence of other sexually transmitted diseases in patients with AGW. Our study is a retrospective cross-sectional study, and the files of all cases diagnosed with AGW in Ankara City Hospital between December 2020-December 2021 were examined.

Results: Of the 1,111 patients 858 were male and 213 were female patients. The mean age was 32.69 years. Hepatitis B surface antigen positivity in 2.4% of the cases, human immunodeficiency virus (HIV) antibody positivity in 2.9% of the cases, hepatitis C virus antibody positivity in 1.1% of the cases, Venereal Disease Research Laboratory-rapid plasma reagin positivity in 0.6% of the cases were detected. While 3 of 32 HIV-positive cases were newly diagnosed cases, 29 were already under treatment. We think that this situation may be related to the fact that our hospital is a tertiary referral hospital in Ankara (the capital city of Turkey). Other tests routinely performed in patients with AGW in our clinic enabled the diagnosis of 3 HIV-positive cases and the treatment of 7 asymptomatic syphilis cases.

Conclusion: We recommend that all cases with AGW should be evaluated in terms of other sexually transmitted diseases.

Keywords: Anogenital warts, Serological test, Sexually transmitted infections, Human papilloma virus, Hepatitis, HIV, Syphilis

Introduction

Human papilloma virus (HPV) infection is the most common sexually transmitted viral infection in the world. HPV in the anogenital area can be the trigger of malignant lesions as well as can cause benign lesions such as anogenital warts. Four distinct subtypes of anogenital warts have been defined: condyloma acuminata (spiky warts), flat/macular lesions, papular and keratotic lesions [1]. Clinical symptoms include itching, burning, dysuria and bleeding. HPV 6 and 11 are the most common infections but oncogenic types such as HPV 16 and 18 can also prevail in some cases. Although the frequency of anogenital warts is not known completely, its annual incidence was calculated as 160-289 per 100 thousand in a systematic review [1]. It can be conceived that the risk of another sexually transmitted disease may increase in a patient with a sexually transmitted disease [2]. Our aim in this study is to evaluate the demographic characteristics and serological test results of patients with anogenital warts.

Materials and Methods

Our study is a retrospective cross-sectional study, and all cases diagnosed with anogenital warts in Ankara City Hospital between December 2020-December 2021, following the approval of the Ankara City Hospital Non-interventional Clinical Research Ethics

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Committee (decision number: E1-21-2214, date: 15.12.2021), were examined. Demographic data of patients, hepatitis B surface antigen (HBsAg), HBs antibody (anti-HBs), hepatitis C virus antibody (anti-HCV), human immunodeficiency virus antibody (anti-HIV), Venereal Disease Research Laboratory (VDRL), rapid plasma reagin (RPR) test results were obtained from patient files.

Statistical Analysis

While evaluating the findings obtained in the study, SPSS (Statistical Package for the Social Sciences) Statistics 24.0 program was used for statistical analysis. Chi-square test, Fisher's Exact chi-square test, Fisher-Freeman-Halton Exact chi-square test were used to compare the qualitative data besides the descriptive statistical methods of the study data. Significance was evaluated at the $p<0.05$ level.

Results

The total number of cases was 1,128 and 17 cases with deficiency of data were excluded from the study. In our study, there were 1,111 cases, 858 males and 213 females, aged between 18 and 76. The mean age was 32.69 years and 77.3% (n=859) of the cases were under the age of 40, and 22.7% (n=252) were over the age of 40. It was observed that the female cases in our study were mostly under the age of 25 (38.5% of all female cases), while the male cases were mostly between the ages of 26-35 (42.5% of all male cases). HBsAg positivity in 2.4% (n=27) of the cases, anti-HBs positivity (n=565) in 50.9%, anti-HIV positivity (n=32) in 2.9%, anti-HCV positivity (n=12) in 1.1%, VDRL-RPR positivity (n=7) in 0.6% were detected (Table 1). Treponema pallidum hemagglutination (TPHA) tests were also performed in 7 positive VDRL-RPR cases, and TPHA was found positive in all of them. When all cases were examined there was no statistically significant difference between male and female cases in terms of HBsAg, anti-HCV and anti-HIV positivity. The incidence of HBsAg positivity among age groups is significantly higher in the patient groups aged 46-55 and over 55 years of age compared to the patient groups aged under 25 years old. The incidence of anti-HBs positivity in the patient group over 55 years of age is significantly higher than in the 36-45 age group. The incidence of anti-HCV positivity in the 46-55 age group is significantly higher than the age groups under 25, 26-35 years and 36-45 years old. When the rates of anti-HIV positivity among age groups were evaluated, it was found that the 36-45 age group was significantly higher than the other age groups ($p<0.05$) (Table 2).

Discussion

Genital warts are a common health problem especially in urbanized societies. In a meta-analysis conducted with female sex workers in China, it was found to be the most common sexually transmitted disease with a rate of 27% [3]. Because of the oncogenic nature of HPV, it is a problem that should be considered in terms of public health. Due to the potential to be a carrier of sexually transmitted diseases such as HIV, hepatitis B, hepatitis C and syphilis, it is possible to transmit other diseases as well as genital warts [4]. There are few recent studies in the literature evaluating the relationship between anogenital warts and other sexually transmitted diseases [2,4,5,6]. When the studies in the last 15 years are examined, one of the most comprehensive studies is the retrospective cohort study of Sturgiss et al. [5] with 1,015 patients with a diagnosis of newly diagnosed anogenital warts. Our study is the study with the highest number of cases in the literature as far as we have examined.

80.8% of our cases were male and 19.2% were female. When we examine other studies in the literature, the male/female ratio was found to be 88.3/11.7% in the study of Ünal et al. [6] and 88.8/11.2% in the study of Mueller et al. [2]. It was observed that the distribution of men and women was similar to the literature. The reason for this distribution may be that risky sexual behaviors are more common in men and some women apply to gynecology clinics. The mean age in our study was 32.69 years. The mean age was 36.3 years in

Table 1. Distributions of study parameters

		n	%
HbSag	Negative	1,084	97.6
	Positive	27	2.4
Anti-HBs	Negative	546	49.1
	Positive	565	50.9
Anti-HCV	Negative	1,099	98.9
	Positive	12	1.1
Anti-HIV	Negative	1,079	97.1
	Positive	32	2.9
VDRL-RPR	Negative	1,104	99.4
	Positive	7	0.6

HbSag: Hepatitis B surface antigen, Anti-Hbs: Hepatitis B surface antibody, Anti-HCV: Hepatitis C virus antibody, Anti-HIV: Human immunodeficiency virus antibody, VDRL: Venereal Disease Research Laboratory, RPR: Rapid plasma reagin

Table 2. Evaluations according to age

		<25	26-35	36-45	46-55	>55	
		n (%)	n (%)	n (%)	n (%)	n (%)	p-value
HbSag	Negative	296 (99.7%)	445 (99.6%)	227 (95.4%)	82 (89.1%)	34 (91.9%)	[1]0.000*
	Positive	1 (0.3%)	2 (0.4%)	11 (4.6%)	10 (10.9%)	3 (8.1%)	
Anti-Hbs	Negative	12 (4%)	219 (49%)	211 (88.7%)	78 (84.8%)	26 (70.3%)	[2]0.017*
	Positive	285 (96%)	228 (51%)	27 (11.3%)	14 (15.2%)	11 (29.7%)	
Anti-HCV	Negative	297 (100%)	446 (99.8%)	236 (99.2%)	84 (91.3%)	36 (97.3%)	[1]0.000*
	Positive	0 (0%)	1 (0.2%)	2 (0.8%)	8 (8.7%)	1 (2.7%)	
Anti-HIV	Negative	292 (98.3%)	435 (97.3%)	223 (93.7%)	92 (100%)	37 (100%)	[1]0.010*
	Positive	5 (1.7%)	12 (2.7%)	15 (6.3%)	0 (0%)	0 (0%)	

[1]Fisher-Freeman-Halton Exact test, [2]Chi-square test, *p<0.05, HbSag: Hepatitis B surface antigen, Anti-Hbs: Hepatitis B surface antibody, Anti-HCV: Hepatitis C virus antibody, Anti-HIV: Human immunodeficiency virus antibody

the study of Mueller et al. [2], 33.7 years in the study of Aktaş et al. [4] and 34.9 years in the study of Ünal et al [6]. When evaluated from this point of view, it was observed that the mean age of our patients was close to the mean age of the patients in the literature. It was observed that most of the cases (77.3%) were under the age of 40. While the incidence of anogenital warts is highest in women under the age of 25, it was observed that anogenital warts in men are concentrated in the age range of 26-35 years. In total, it was observed that the most cases were between the ages of 26-35. In the study of Mueller et al. [2], similar to our study, the majority of the cases were found to be between the ages of 26-35.

As a result of different samples in our country, the frequency of HbsAg was found to be between 0.8-5.7% [7]. In our study, HBsAg positivity was observed at a rate of 2.4%. The frequency of HBsAg was found to be 2.6% in the study of Mueller et al. [2] and 3.2% in the study of Ünal et al. [6]. The low incidence of HBsAg in our study, particularly among patients under the age of 25 (0.3%), may be related to the vaccination program initiated in children in our country since 2001 [7]. It has been observed that the frequency of HBsAg is similar both in the general population and in other studies conducted. In our study, the frequency of anti-HBs was found to be 50.9%. In a country-wide viral hepatitis prevalence study conducted between the years 2008 and 2011, anti-HBs positivity was found to be 32% [8]. The higher incidence of anti-HBs in our study may be related to increase in the general immunity of the population against hepatitis B through vaccination studies in the last 10 years [7,8]. The prevalence of hepatitis C in our country varies between 1-1.9% [9]. In our study, anti HCV positivity was found to be 1.1% and it was found at a frequency similar to the studies conducted with the general population in our country. When we examined the literature, the HCV seroprevalence was found to be 1% in the study conducted with sex workers [3]. While anti HCV positivity was found in 1 (0.9%) case in the study of Aktaş et al. [4], no anti HCV positive case was found in the study of Ünal et al. [6]. In the study of Sturgiss et al. [5], the frequency of HCV was found to be 5.6%. This case was explained by the fact that only the patient group with risk factors were tested for hepatitis C in the study of Sturgiss et al. [5]. In our study, it is both surprising and satisfying that hepatitis B and C did not increase in people with anogenital warts when we consider all patients without division according to age groups, which is a risky population in terms of sexually transmitted diseases.

Studies on the frequency of VDRL-RPR and anti-HIV in our country are few. In a broad-series study conducted with blood donors, RPR positivity was found to be 0.2% and anti-HIV seropositivity was approximately 0.001% in 2002 [10]. In our study, anti-HIV and VDRL-RPR positivity were found to be higher than the normal population. Considering the studies on anogenital warts; Aktaş et al. [4], Sturgiss et al. [5] and Ünal et al. [6] did not find any HIV positive cases in their studies. In our study, the rate of HIV positive cases was 2.9%, which was detected to be significantly higher compared to both the general population and other studies. While 3 of 32 HIV-positive cases were newly diagnosed cases, 29 were already under treatment. We think that this situation may be related to the fact that our hospital is a tertiary referral hospital in Ankara (the capital city of Turkey) and it is a hospital where HIV-positive patients apply for HIV treatment frequently. In our study, VDRL-RPR positivity was found in 7 cases. It was observed that TPHA was also requested from these cases and TPHA was positive in all of them. Physical examination of these cases revealed no signs of syphilis. While VDRL-TPHA positivity was observed at a rate of 3.1% in the study of Ünal et al. [6], no VDRL positivity was found in the study of Aktaş et al. [4] and the study of Sturgiss et al. [5]. Interestingly, in the study of Mueller et al. [2], syphilis was reported as the most common sexually transmitted infection with a rate of 11.9% in asymptomatic AGV patients, however, no explanation has been given for this situation [2]. Our cases were also asymptomatic, and the required test for AGV have allowed these cases to receive treatment for syphilis.

Study Limitations

One of the aims of our study is to evaluate the necessity of screening for other sexually transmitted diseases of anogenital warts cases. Our study had limitations such as the cases were not evaluated in terms of herpes virus infection, other sexually transmitted diseases such as *Neisseria gonorrhoea* and *Chlamydia*. In our study, no case with more than one sexually transmitted coinfection was detected. The total number of cases with sexually transmitted co-infection was 78, which was 7% of all cases. Even though the prevalence of hepatitis did not increase compared to the general population in our study, when we analyzed it according to age groups, it was found that the incidence of hepatitis B and C was significantly higher in the 46-55 age group compared to other age groups, and it was also higher in this age group than in the general population. Other tests routinely requested from patients with anogenital warts in our clinic enabled the diagnosis of 3 HIV-positive cases and the treatment of 7 asymptomatic syphilis cases.

Conclusion

We recommend that all cases with anogenital warts should be evaluated in terms of other sexually transmitted diseases.

Ethics

Ethics Committee Approval: Our study was approved by the Ankara City Hospital Non-interventional Clinical Research Ethics Committee (decision number: E1-21-2214, date: 15.12.2021).

Informed Consent: Retrospective cross-sectional study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: F.E., Design: F.E., Data Collection or Processing: F.E., A.Y.İ., Analysis or Interpretation: F.E., A.Y.İ., Literature Search: F.E., A.Y.İ., Writing: F.E.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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ORIGINAL ARTICLE

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The Analysis of the Patients Who Have Received Phototherapy During the COVID-19 Pandemic

Defne Özkoca, Tuğba Kevser Üstünbaş Uzunçakmak, Zekayi Kutlubay

Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Dermatology and Venereology, Istanbul, Turkey

ABSTRACT

Background: The coronavirus pandemic has lead to major changes in our daily practices. Due to the increased risk of transmission in the waiting areas, all of the non-emergency patients have been requested to stay home during the peak periods of the pandemic which lead to the cancellation of phototherapy sessions during the peak period. The aim of this study is to evaluate the demographics of, diagnoses of and the phototherapy modalities used in the patients who have received phototherapy during the first year of the coronavirus pandemic; and to evaluate if they have contracted coronavirus during their treatment.

Materials and Methods: This is a retrospective study performed in the phototherapy unit of Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Clinic of Dermatology.

Results: A total of 137 patients were included in this study. Most common diagnoses to receive phototherapy were psoriasis vulgaris, mycosis fungoides and morphea. The most treatment modality to be used during the pandemic was narrowband ultraviolet-B. Only nine of the patients were diagnosed with coronavirus during phototherapy sessions, all had a benign disease course.

Conclusion: The risk of disease transmission due to phototherapy sessions is quite low. On the contrary, relapse risk is high if the treatment is stopped. We suggest that phototherapy modalities should be continued in necessary patients during this period given that the protective precautions can be applied in the phototherapy units.

Keywords: COVID-19, Demographics, Pandemic, Phototherapy

Introduction

The new coronavirus pandemic has started in central China in 2019 and soon spread to the entire world. Similar to other specialties, dermatology outpatient services have also been shifted to emergency-only and dermatologists worked in the coronavirus inpatient services. Due to the increased risk of transmission in the waiting areas, all of the non-emergency patients have been requested to stay home during the peak periods of the pandemic. Phototherapy sessions have first been cancelled during the peak period. Thereafter with the decline in the case numbers, the patients in whom the benefit of phototherapy outweighed the risk of coronavirus were rescheduled with long intervals and appropriate personal protective equipment use [1,2,3]. The aim of this study is to evaluate the demographics of, diagnoses of and the phototherapy modalities used in the patients who have received phototherapy during the first year of the coronavirus pandemic; and to evaluate if they have contracted coronavirus during their treatment.

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Materials and Methods

This is a retrospective study in which patients who have received any modality of phototherapy in Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Dermatology and Venerology, between 11 March 2020 and 31 March 2021 were included. The gender, age (years), dermatological diagnosis, phototherapy modality used [narrow band (ultraviolet-B), (ultraviolet-A)-1, psoralen plus UVA (PUVA) or local PUVA] were noted from the patient files. During treatment, each patient was questioned for the presence of signs and sypmtoms of coronavirus; and if present they have been tested with nasal swab polymerase chain reaction.

The approval of Istanbul Univeristy-Cerrahpasa, Cerrahpasa Faculty of Medicine Ethics Committee was taken before initiating the study (approval number: 103633, date: 02.06.2021).

Results

A total of 137 patients were included in this study. Of these 137 patients 54 (39.4%) were male and 83 (60.6%) were female. The mean age of all patients was 42.7 years; the mean age of female patients was 44.6 years and of male patients was 42.7 years. The diagnoses of the patients were as follows: psoriasis vulgaris (43), mycosis fungoides (22), morphea (15), pruritus/prurigo nodularis (11), palmoplantar eczema (10), palmoplantar pustulosis (4), vitiligo (4), granuloma annulare (4), atopic dermatitis (3), perforating collagenosis (3), lichen planus (3), scleroderma (3), photodermatosis (2), macular amiloidosis (2), pityriasis lichenoides et varioliformis acuta (2), palmoplantar psoriasis (2), lichen amiloidosis (1), lichen sclerosis (1), lichen simplex chronicus (1) and urticaria pigmentosa (1). Figure 1 demonstrates the distribution of the patients who have received phototherapy during this period. Of theses 137 patients, 94 (68.6%) received narrowband UVB, 20 (14.6%) received UVA-1, 15 (11%) received local PUVA and 8 (5.8%) received systemic PUVA. Figure 2 demonstrates the distribution of the treatment modalities used.

Nine (6.6%) of the patients have been diagnosed with the coronavirus infection during phototherapy treatment. The mean age of these patients was 44.8; 5 were female and 7 were male. Of these patients, 7 were receiving narrowband UVB, 1 was receiving PUVA and 1 was receiving local PUVA; mycosis fungoides (3), psoriasis vulgaris (2), morphea (1), macular amiloidosis (1), and perforating collagenosis (1). None of these patients were hospitalized in the inpatient services or the intensive care units. They have been tested negative afterwards and had no sequela.

Discussion

The rising case numbers in the coronavirus pandemic has led to the closure of the outpatient services in our clinic similar to the world in order to overcome the transmission risks along with the national lock-down that was implemented by the government [1,2,3]. During the lock-down period, home-phototherapy modalities have been implemented in centers [4], however, none of our patients could use this modality due to financial reasons. After a decline in the case numbers, and the removal of the lock-down measures by the government, we started to provide phototherapy treatment with the necessary protective measures to our patients when the benefit outweighed the risk. This study includes the data of our clinic during the lockdown, immediately after the lockdown and the period in which the health services were shifted back to the pre-pandemic era, which is referred to as the "normalisation period".

The majority of our patient population was composed of psoriasis, mycosis fungoides and morphea patients. Since 49% of the patients

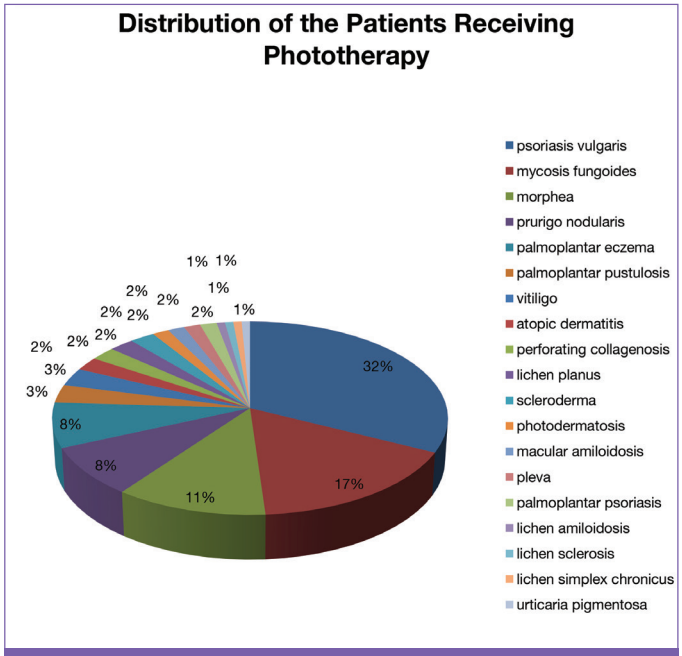

Figure 1. Distribution of the patients who received phototherapy

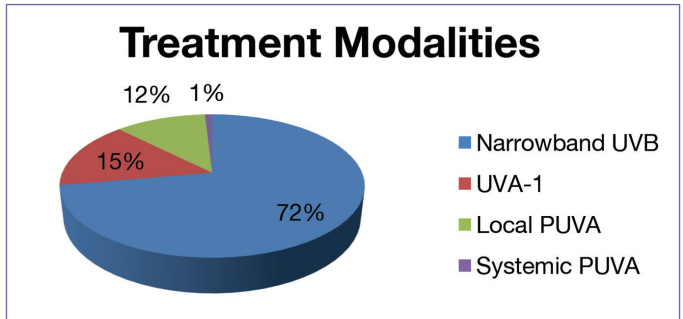

Figure 2. Treatment modalities used

UVB: Ultraviolet-B, UVA-1: Ultraviolet A-1, PUVA: Psoralen plus UVA

had either psoriasis or mycosis fungoides, the most common treatment modality used was narrowband UVB in our patient population. Nine of our patients have contracted coronavirus during this period; however, the source of contraction (if it is hospital acquired or community acquired) is unknown. None of the patients had a severe disease course or required hospitalisation.

Dragan et al. [5] have also reported their phototherapy patient population of 36 patients, during the pandemic. The most common diagnoses that have received phototherapy during this period in their clinic were psoriasis, vitiligo and mycosis fungoides. They did not report on the modality that has been used. Only one of their patients have been diagnosed with the coronavirus [5].

Spigariolo and Piccinno [6] reported the patients who have recieved phototherapy during the lockdown period. They had a total of 92 patients who have been receiving phototherapy before March 3, 2020. This number declined to a total of 9 with the lockdown period: 3 mycosis fungoides, 2 psoriasis, 2 pitriasis rubra pilaris and 2 eczema. Narrowband UVB was used in 6 of these patients, whereas PUVA was used in 3. They selected their patients based on age, comorbidities, transportation method and disease severity [6].

Costa et al. [7] have surveyed the patients who have been receiving phototherapy right before the pandemic. Of their 86 patients, only 19% wished to continue their therapy. Ninety-five percent of the patients who have stopped attending the phototherapy sessions, either by their own wish or on medical recommendation, had relapse of their disease [7].

Conclusion

In alliance with the previous literature, our patient population also revealed that the risk of disease transmission due to phototherapy sessions is quite low. On the contrary, relapse risk is high if the treatment is stopped. Therefore, we suggest that phototherapy modalities should be continued in necessary patients during this period given that the protective precautions can be applied in the phototherapy units.

Ethics

Ethics Committee Approval: The approval of Istanbul Univeristy-Cerrahpasa, Cerrahpasa Faculty of Medicine Ethics Committee was taken before initiating the study (approval number: 103633, date: 02.06.2021).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.Ö., T.K.Ü.U., Z.K., Concept: D.Ö., T.K.Ü.U., Z.K., Design: D.Ö., T.K.Ü.U., Z.K., Data Collection or Processing: D.Ö., T.K.Ü.U., Analysis or Interpretation: D.Ö., Literature Search: D.Ö., Writing: D.Ö., T.K.Ü.U.

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CASE REPORT

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Syringotropic Mycosis Fungoides, an Unusual Variant with Distinctive Features

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ABSTRACT

Syringotropic mycosis fungoides (SMF) is a rare variant of mycosis fungoides (MF). It is characterised by infiltration of ecrine glands by neoplastic lymphocytes. Clinical lesions are frequently seen as solitary, punctate erythematous papules, plaques, and nodules. Pruritus, alopecia, anhydrosis, superficial erosions and ulcers) can also seen in SMF. Histopathologically SMF is characterised by hyperplastic eccrine glands and ducts infiltrated by atypical lymphocytes and syringometaplasia, Here we present a case with SMF, to draw attention about this rare form of MF.

Keywords: Syringotropic, Mycosis fungoides, Folliculotropism

Introduction

Syringotropic mycosis fungoides (SMF) is a rare variant of mycosis fungoides (MF), and it is characterised by infiltration of eccrine glands by neoplastic lymphocytes. According to the current guidelines, SMF is classified in the group of adnexotropic MF with folliculotropic MF (FMF) [1,2].

Clinical lesions are frequently seen as solitary, punctate erythematous papules, plaques, and nodules [1,2]. Pruritus, alopecia, anhydrosis, superficial erosions and ulcers can also be seen in SMF. Colour and shape of the skin lesions may vary; they can be round, circular or irregular in shape, and red, dark red or they can be dark brown in color [1,2,3,4,5,6].

SMF was first identified by Sarkany in 1969 [1,4]. SMF has a predilection for extremities and palm and soles [3,4,7]. Histopathology is the gold standard for diagnosis of MF and STMF. Histopathologically SMF is characterised by hyperplastic eccrine glands and ducts infiltrated by atypical lymphocytes and syringometaplasia [1,3,7]. Although clinically similar to FMF, SMF is less aggressive and has a better prognosis [3,5,6,8].

Here we present a case with SMF, in order to draw attention to this rare form of MF.

Case Report

Eighty-three-year-old man presented with a 1 year history of skin lesions and severe pruritus. First lesion appeared on the arm, followd by legs and abdomen. He did not apply to dermatologist before but he took non-spesific treatment for pruritus. Dermatological examination showed diffuse kserosis, erythematous plaques on abdomen and back, erythematous plaques and nodular lesions on lower extremity with a small ulceration. There was also hair loss on arms and legs (Figure 1A-D). There was no lympadenopathy or hepatosplenomegaly at physical examination. Routine biochemistry was normal. Viral serology was negative for hepatitis B, C and human immunodeficiency virus. Excisional biopsy was taken from the lesions on arm, trunk and legs. Histopathological examination

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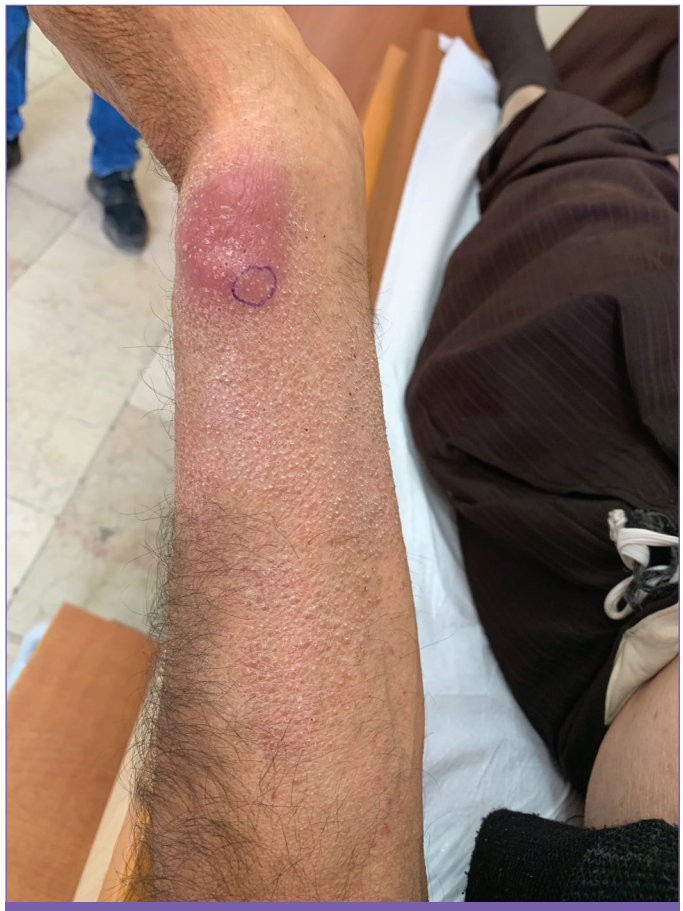

Figure 1A. Nodular lesion on the arm

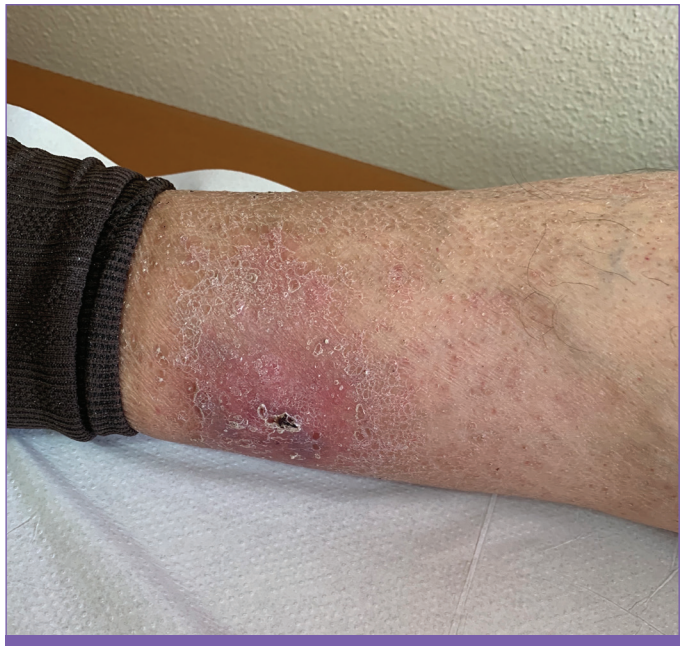

Figure 1B. Kserotik plaque lesion with ulceration

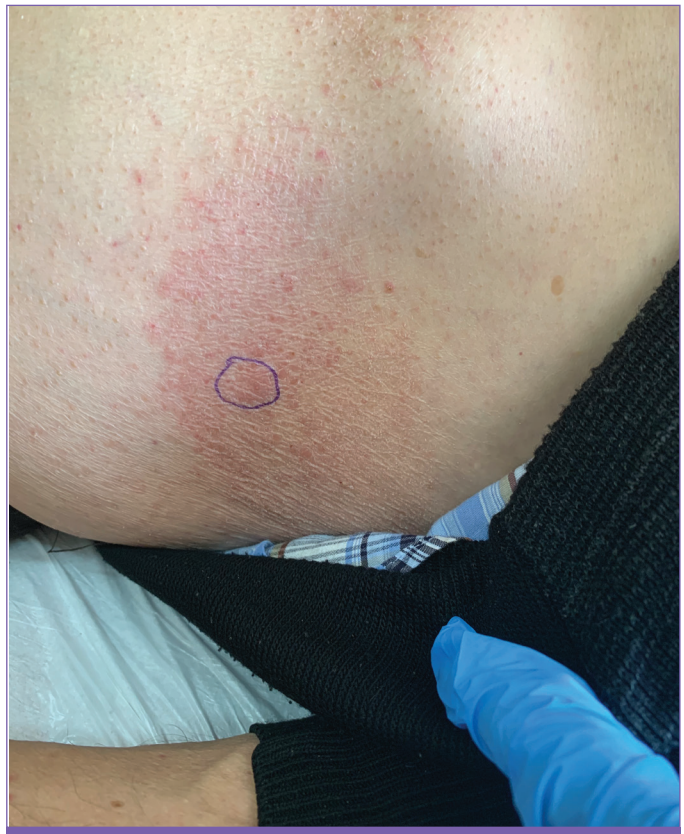

Figure 1C. Kserosis and erythematous plaque lesion on the abdomen

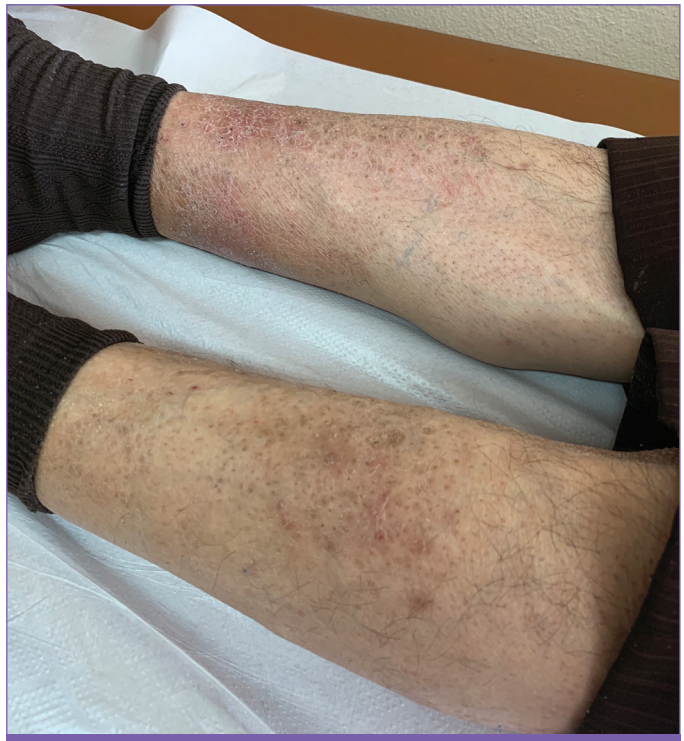

Figure 1D. Kserotic lesions and papular lesions

revealed lymphocyte, plasma cell, eosinophil and neutrophilic infiltration in the epidermis. There were lymphocytic infiltration involving eccrine glands, syringometaplasia, and granulomatous infiltration with two multi nuclear giant cells. Folliculotropism was present. Perifollicular and follicular lymphocytic infiltration were mostly positive for CD4, and CD7, and less predominantly positive for CD8 and CD20 (Figure 2A-H).

Informed consent was taken from the patient for possible case report publication. The patient was accepted as SMF. The patient didn't come to follow up and we couldn't treat the patient.

Discussion

MF is the most common type of cutaneous lymphoma, and it is classified in the group of cutaneous T-cell lymphomas (CTL), which is a heterogeneous group of extranodal non-Hodgkin lymphomas. MF compromises approximately about 50% of all CTLs [6,7]. MF has 3 well-known variants as solitary pagetoid reticulosis (Woringer-Kolopp), FMF, and granulomatous slack skin disease. Other than these variants, many other clinical and/or histopathologic forms have been described including the SMF [6,9]. Although there is a debate about SMF being a different entity or its a subtype of FMF, recent studies assumed SMF as a different entitiy with distinctive clinical and histopathological features [6,8].

Mostly seen lesions in SMF are papules, plaques and nodules [2]. Our patients had papules, plaques and nodular lesions. Ulceration is not a frequent finding in classical MF, but can be seen in SMF [4,10]. Alopecia on the lesions is a frequent finding in SMF [2,3,6]. Body hairs were lost on the skin overlying the lesions of our patient similar to the literature.

In SMF lesions are usually located usually on the extremities and palms and soles, whereas FMF usually affect head and neck regions [3,9]. Lesions were scattered on the abdomen, arms and legs in our patient, he had no involvement in palms and soles.

Solitary and localized lesions are more frequently seen in SMF than classical MF [6]. There were multiple lesions in our patient similar to the some previous reports [9].

Men are affected more than women [3,5,7,8]. Mean age of the patients was 50-55 years [7,8]. Our patient was male in accordance with the literature. He was at 83 years, with one of the oldest published case at 86-years-old patient from France [4].

Epidermotropic atypical lymphocytes can be seen in the majority of the cases [3,4,6]. Epidermotropism was found is our patient's specimens.

SMF histopathology consists of atypical lymphocytes surrounding eccrine coils. Syringometaplasia is a distinctive feature of SMF [3,4,6]. T lymphocytes can be CD2+, CD3+, and CD4+. In our case, lymphocytes were mostly positive for CD4 and CD7 and less predominantly positive for CD 8 and CD20. In the majority of the cases there are T-cell receptor gene rearrangements that are monoclonal [4]. Histopathologic differential diagnosis of SMF includes perniosis (no syringotropism

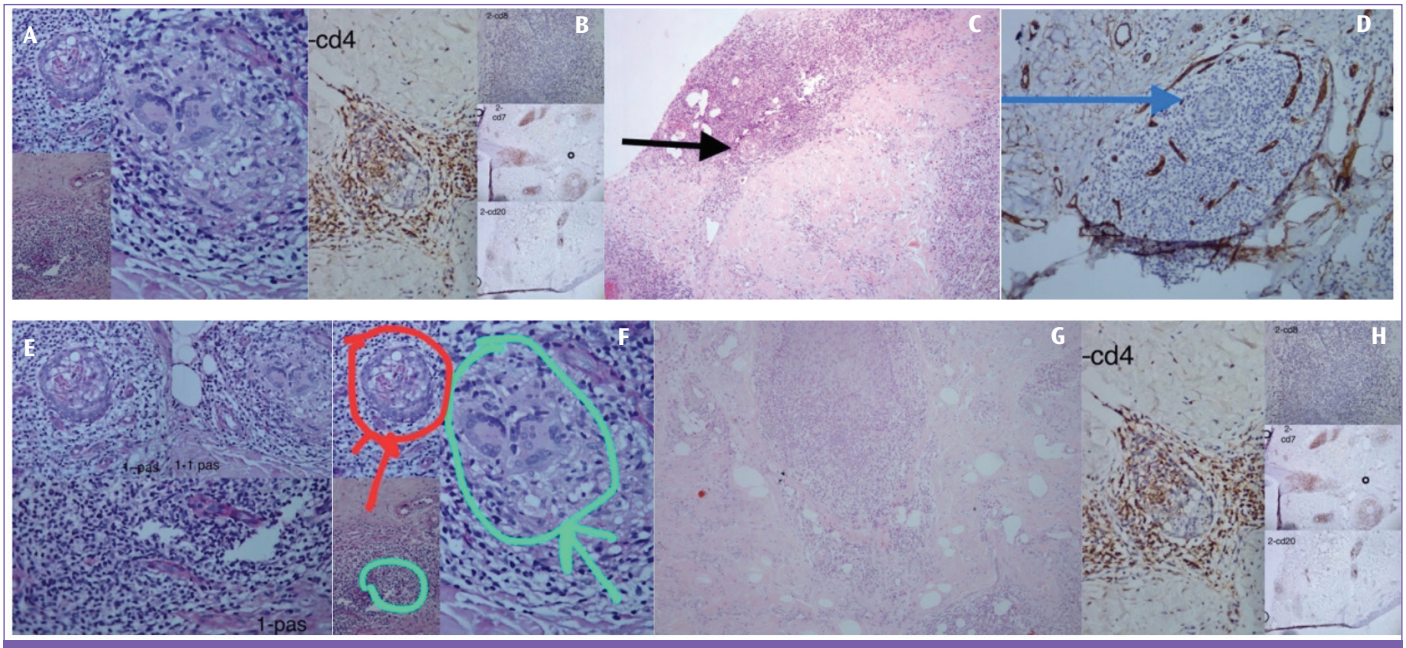

Figure 2. A: Lymphcyte, plasma cell, eosinophil and neutrophil infiltraion (H&E), B: Lymphcytic infiltration involving eccrine glands, C and D: Lymphocytic infiltration involving eccrine glands, E: Granulomatous infiltration and folliculotropism , F: Red arrow: syringometaplasia, yellow arrow: granulomatous infiltration with two multi nuclear giant cells, G: Perifollicular lymphocytic infiltration, H: Perifollicular and follicular lymphocytic. infiltration Mostly positive for CD4, and CD7, Less predominantly positive for CD8 and CD20

and syringometaplasia), neutrophilic eccrine hidradenitis (infiltrate is mostly neutrophilic). Syringometaplasia can also be seen in a number of conditions including skin reactions to chemotherapy, cutaneous ischemia, and radiation dermatitis, in which there were no prominent lymphoid infiltration cutaneous lymphoproliferative T-cell and B-cell disorders other than SMF can also cause hyperplasia of the hair follicles and/or eccrine glands [6]. In classical MF, usually in the tumoral stages, we expect lymphoid infiltrates around the eccrine glands, but syringometaplasia and syringotropism are absent [3,4,6]. Folliculotropism may also be present in some cases [8,10]. In our case, folliculotropism was present.

Distunguishing SMF from FMF is important since their prognosis is different [10]. SMF has better prognosis than its clinically undistinguishable counterpart, FMF [8,9,10]. SMF is a rare disease, thus there is no guideline about its treatment [2,8]. Since the malignant cells are located deep in the dermis, SMF is more refractory to conventional skin directed therapies, such as topical corticostreroids and narrow band UVB, which are usually more effective at classical MF [2,3,9,10]. Radiotherapy is the most effective treatment for local disease [3,8]. Oral retinoids (alitretinoin), interferon alpha, systemic chemotherapy (VELP; vincristine sulfate, etoposide, L-asparaginase, and prednisone acetate), vorinostat, extraphotopheresis, psoralen and UVA are the agents that are used to treat generalised SMF [2,3,8].

In conclusion, SMF is a clinically and histopathologically different variant of MF. It is clinically undistinguisable from FMF, since their prognosis is quite different, they should be differentiated. Clinicians and pathologist should be aware of this entity to prevent delayed treatment.

Ethics

Informed Consent: Informed consent was taken from the patient for possible case report publication.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.E., H.E., Concept: F.E., Design: F.E., Data Collection or Processing: F.E., H.E., Analysis or Interpretation: F.E., H.E., Literature Search: F.E., Writing: F.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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CASE REPORT

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Neutrophilic Dermatosis Overlap Syndrome with Temporal Relationship to Cocaine Usage: A Case Report

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ABSTRACT

Neutrophilic dermatoses (ND) are conditions historically attributed to an undetected bacterial infection. Three of the more common ND are pyoderma gangrenosum (PG), Sweet's syndrome (SS) and neutrophilic dermatosis of the dorsal hands (NDDH), which have many points of clinical overlap. We herein report a rare presentation of recurring cocaine-induced ND overlap syndrome including PG, SS, and NDDH in an adult Caucasian female with a longstanding history of cocaine use. The patient presented with a generalized eruption of juicy, eroded, erythematous papules and nodules. Biopsies obtained revealed marked papillary dermal edema with a robust infiltrate of neutrophils and her labs revealed elevated inflammatory markers and elevated perinuclear anti-neutrophil cytoplasmic antibodies. The rash resolved after cocaine cessation and a prednisone taper. This case highlights a unique temporal relationship between cocaine use and recurrence of ND.

Keywords: Neutrophilic dermatoses, pyoderma gangrenosum, Sweet's syndrome, neutrophilic dermatosis of the dorsal hands, leukocytoclastic vasculitis

Introduction

Historically, neutrophilic dermatoses (ND) were attributed to an undetected bacterial infection; however, current theories include a clonal response to antigenic stimuli, neutrophilic dyscrasia, neutrophil dysfunction, and genetic influences [1,2,3,4]. Three of the more common ND are pyoderma gangrenosum (PG), Sweet's syndrome (SS), and neutrophilic dermatosis of the dorsal hands (NDDH). These diseases have many points of clinical overlap.

PG is a form of ND with an incidence of 3-10 cases per million people each year. It is most common in women 40 to 60 years old and may be associated with medical conditions such as inflammatory bowel disease (IBD), rheumatoid arthritis, and hematologic malignancies. Clinical subtypes of PG include ulcerative (most common), bullous, vegetative, pustular, and peristomal. Classic PG is a painful, ulcerative lesion with a cribriform pattern, violaceous border, and an undermined epidermal edge [5].

SS, otherwise known as acute febrile neutrophilic dermatosis, is another example of ND. It generally presents in females 47 to 57 years old with fever, leukocytosis, painful plaques, and neutrophils on pathology without infection. There are three types, including classic, malignancy-associated, and drug-induced. Common triggers for classic SS include prior infection, vaccination, inflammatory disorder, and pregnancy [5].

NDDH is debated as a separate disease from SS; however, it is clearly a neutrophilic dermatosis as it exhibits a neutrophilic infiltrate without an active infection [6]. NDDH is most common in women and presents as a sudden onset of fever, leukocytosis, and painful plaques on the dorsal hand(s). Unlike in SS, bullae are common and may ulcerate. NDDH also is more often associated with vasculitis,

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where SS is not. The connection to an underlying malignancy warrants cancer screening in these patients [7].

Levamisole is an anti-helminthic drug used primarily in veterinary medicine. Previously, the FDA-approved its use in colon cancer post-resection, [8] however it was removed from the market in 2000 due to adverse reactions including neutropenia, agranulocytosis, and vasculitis [9,10,11]. Due to its similar appearance, cheaper cost, and ability to increase and prolong the euphoria from cocaine, it is a common bulking agent in cocaine sold in the United States. Cocaine inhibits monoamine transporters for serotonin (SERT), norepinephrine (NET) and dopamine (DAT). Aminorex is a levamisole metabolite that also inhibits NET and DAT, and causes efflux of SERT; which explains its ability to produce similar amphetamine-like properties and prolong the associated euphoria [8]. It has been found to increase the half-life of cocaine from 1 hour to 5.5-6 hours [12]. The United States Drug Enforcement Administration reports that the amount of seized cocaine containing levamisole rose from <10% in 2008 to 87% in 2016, before declining to 40% in 2017 [13,14,15].

We present a case of cocaine-induced ND overlap syndrome, including PG, Sweet's syndrome, and ND of the dorsal hands. Based upon cocaine's common contamination with levamisole, it is reasonable to think that this drug may play a contributory role in this patient's findings.

Case Report

A 47-year-old Caucasian female with an extensive history of cocaine use was seen in the hospital with a recurrent, painful, and non-pruritic rash. She presented with a generalized eruption of juicy, eroded, erythematous papules and nodules. Evidence of the juicy lesions were visible on her buttock (Figure 1) her dorsal hallux at the interphalangeal joint (Figure 2), and an erythematous ulcer with central necrosis and violaceous borders was present on her left thigh (Figure 3). She was seen multiple times prior to our consultation for recurrence of the same rash.

Biopsies obtained from her buttock lesions exhibited marked papillary dermal edema with a robust infiltrate of neutrophils (Figure 4) and tissue culture was negative for bacteria, fungi, and mycobacteria. The patient has no known underlying disease process associated with a neutrophilic dermatosis, such as IBD, leukemia, multiple myeloma, or rheumatoid arthritis. Her labs were unremarkable except for elevated inflammatory markers and an elevated perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA). Her erythrocyte sedimentation rate and C-reactive protein were elevated at 65 and 62.1, respectively. During her admission, she was treated with a 6-week 1 mg/kg prednisone taper along with cocaine cessation, and her rash resolved completely.

Of note, she was readmitted to the hospital several months later with the same rash, which occurred 2 weeks after she had relapsed on cocaine. The rash recurrence exemplifies the temporal relationship between cocaine use and her rash. Moreover, her rash completely resolved again after cocaine cessation and a prednisone taper.

Blood cultures have been negative over the course of her hospital admissions and she has not had any response to antibiotics. She has had multiple debridements over the course of her disease due

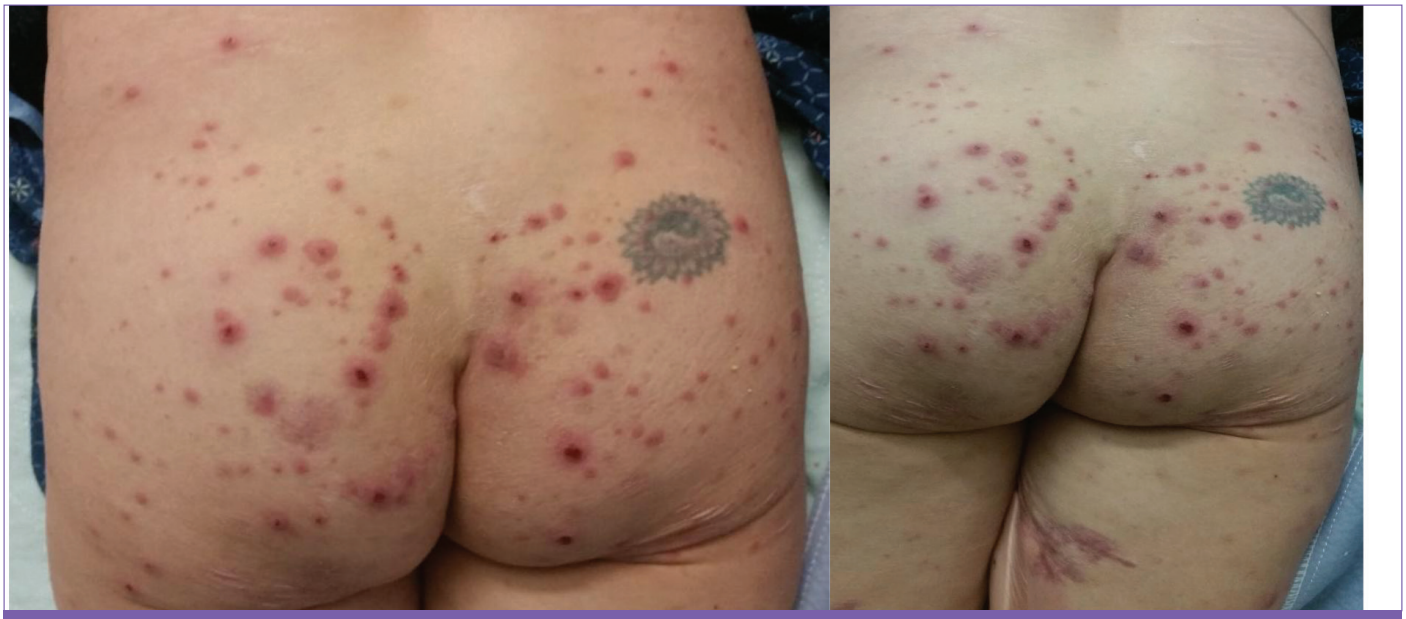

Figure 1. Numerous juicy eroded erythematous papules and nodules scattered on the buttocks

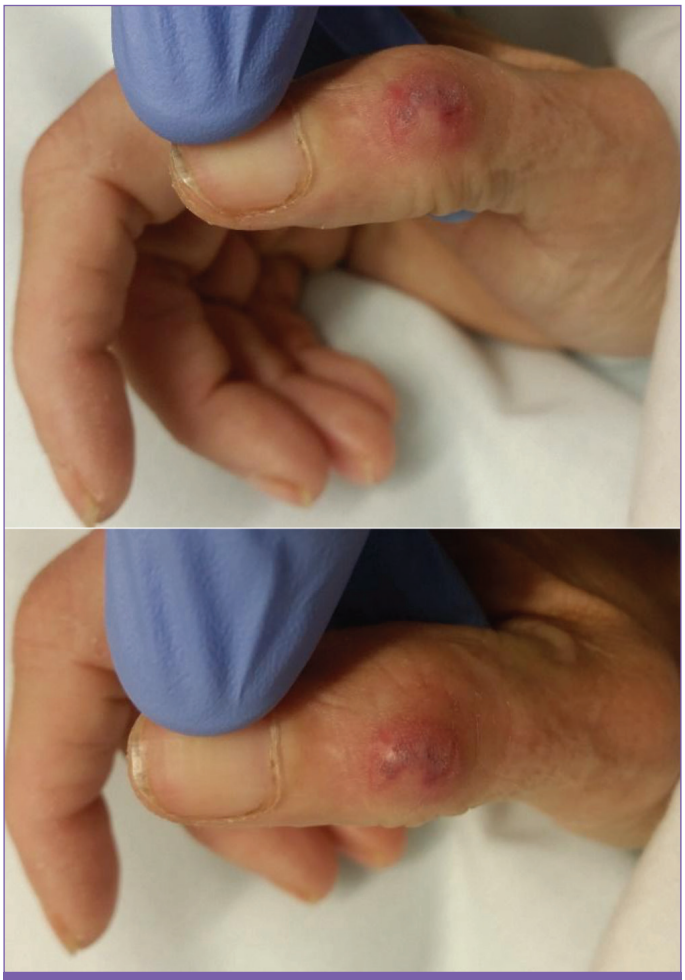

Figure 2. A juicy erythematous nodule with a central erosion on the interphalangeal joint of the right dorsal thumb

to presumed infection resulting in considerable scarring, most notably on her lower extremities. The patient has a cocaine-induced neutrophilic dermatosis overlap syndrome with concurrent PG, Sweet's syndrome, and NDDH.

Discussion

Cocaine has been associated with ND [16], including 8 cases of PG with cocaine use reported by Jeong et al. [17]. These cases of PG have had +p-ANCA, + human neutrophilic elastase antibody titers (the most specific marker for levamisole-associated vasculitis), and even histopathologic findings of vasculitis in common with levamisole associated leukocytoclastic vasculitis [18]. Table 1 further

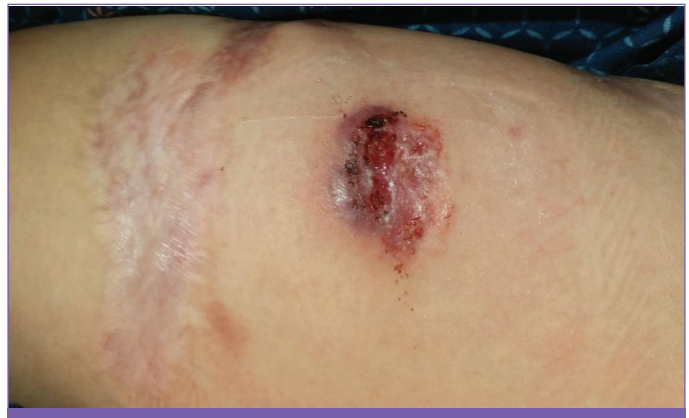

Figure 3. An erythematous to violaceous ulceration with some necrosis on the left thigh adjacent to a cribriform scar from prior PG that had been debrided

PG: Pyoderma gangrenosum

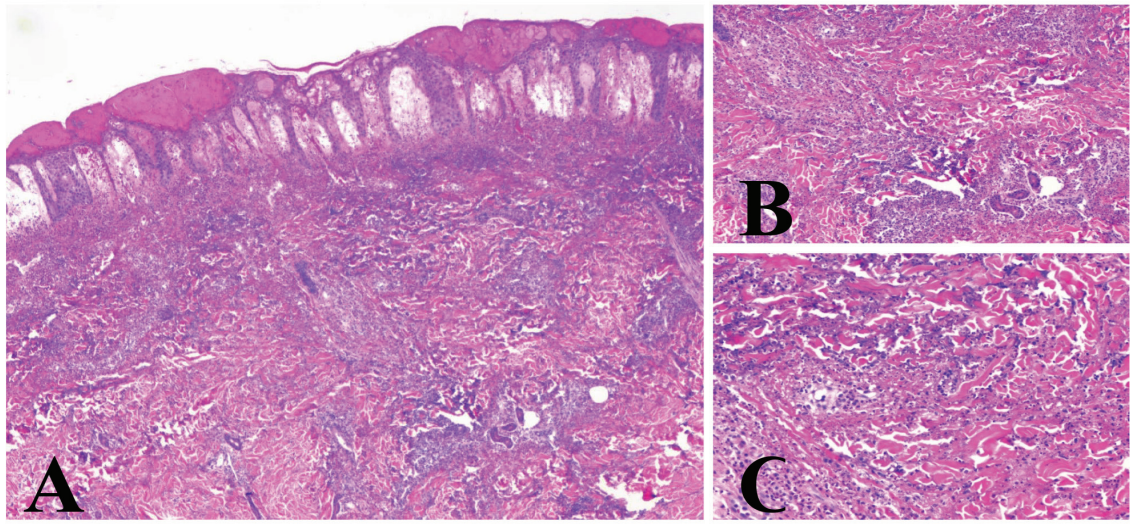

Figure 4. A biopsy taken from a nodule located on patient's buttock. A) 40X reveals marked dermal edema with a robust neutrophilic infiltrate consistent with sweets. B) 100X C) On 200X marked dermal neutrophilic infiltrate without signs of infection or vasculitis

Table 1. A comparison of neutrophilic dermatoses associated with cocaine use

	Pyoderma gangrenosum	Sweet syndrome	Neutrophilic dermatosis of the dorsal hands	Levamisole vasculitis
Clinical presentation	Painful, well-demarcated ulcer with undermined, violaceous border	Tender, erythematous papules and nodules coalesce to plaques	Tender, erythematous papules and nodules coalesce to plaques +/- ulceration	Painful, palpable purpura, +/- bullae that may ulcerate
Lesion location	Lower legs Atypically: hands or elsewhere	Face, arms, neck	Dorsal hands	Lower legs Higher specificity: Helix and zygomatic arch
p-ANCA	+/-	+	+/-	+
Associated co-morbidities	Malignancy, IBD, systemic disease, vasculitis	Fever and leukocytosis, pregnancy, malignancy, drug-induced, post-vaccination, infection	Fever and leukocytosis, malignancy	Cocaine use
Pathergy	Yes	Yes	Yes	Yes
Treatment*	Topical or systemic corticosteroids, dapsone, potassium iodide, cyclosporine, TNF-Alpha inhibitors	Topical or systemic corticosteroids, dapsone, potassium iodide colchicine if corticosteroids are contraindicated	Topical or systemic corticosteroids, dapsone, potassium iodide colchicine if corticosteroids are contraindicated	Systemic corticosteroids cyclophosphamide, rituximab, methotrexate, thalidomide, cocaine cessation

*In all cases, stopping the offending agent, such as cocaine, is paramount in stopping the disease progression
p-ANCA: Perinuclear anti-neutrophilic cytoplasmic antibodies, IBD: Inflammatory bowel disease, TNF: Tumor necrosis factor alpha

distinguishes PG, SS, NDDH, and levamisole vasculitis clinical findings and treatment options [6,19]. Most notably, PG generally lacks the fever and leukocytosis common to both SS and NDDH. NDDH diagnosis is distinguished from SS based upon the location of the lesions. A leukocytoclastic vasculitis may be present in any of the diseases; however, levamisole vasculitis has specific clinical and laboratory findings, including +c-ANCA and palpable purpura, commonly on lower extremities and helices.

Among her widespread lesions, the juicy generalized nodules on her buttock (Figure 1) are suggestive of SS. The lesions on her dorsal hands (Figure 2) coincide with the location of NDDH. The ulcerations most prominent on her thigh (Figure 3) particularly calls to mind PG.

Unfortunately, she has had multiple debridements over the course of her disease. Some ND, including PG, exhibit pathergy. Otherwise insignificant trauma to the skin, may lead to ulcers that are resistant to healing [5]. This phenomenon in the presence of debriding these lesions led to substantial scarring that could have been avoided with earlier diagnosis and treatment.

Ethics

Informed Consent: Written consent obtained from patient for the case presentation.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practicies: M.N., Concept: M.N., Desing: M.N., M.T., M.G.P., Data Collection or Processing: M.N., Analysis or Interpretation: M.N., T.K., M.G.P., Literature Search: M.N., M.T., M.G.P., Writing: M.T., T.K., M.G.P., M.N.

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A Rare Disease That Causes Facial Nodules in Children: Idiopathic Facial Aseptic Granuloma

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Dear Editor,

Idiopathic facial aseptic granuloma (IFAG) is a benign but uncommon pediatric skin disorder [1,2]. Here we present a case of 2-year-old girl who showed nodular lesions on the cheek and eyelids.

A 2-year-old girl presented with asymptomatic nodules on the cheek and eyelids. The nodules had appeared approximately four months before the physical examination. The patient's family didn't describe any trauma or insect bite. The patient had a history of cerebral palsy and right hemiparesis. She was receiving physical therapy. In dermatological examination, there were red-violaceous papulonodular lesions on the upper eyelids and on the left cheek (Figure 1). She was afebrile and regional palpable lymphadenopathy wasn't detected. A 3 mm punch biopsy was taken from the lesion on the left cheek. The histological examination revealed a granulomatous dermal infiltrate consisting of lymphocytes, epitelioid histiocytes, neutrophils, sparse plasma cells, foreign body type giant cells and negative results of staining (Gram, EZN, PAS) for detection of microorganisms (Figure 2). Diagnosis of IFAG was made based on clinical and histopathological findings. No treatment was prescribed. In the controls, it was observed that the lesions started to regress.

IFAG is a recently described childhood disease characterized by chronic, painless, red-to-violaceous facial nodules. It occurs in children between 8 months and 13 years of age. It has a characteristic location. In two-thirds of cases, it is located in the triangle formed by angulus oris, lateral eye canthus and earlobe. The nodule is generally solitary and typically located on the cheeks or eyelids or both. In addition, it resolves spontaneously less than one year, about 11 months [1,2,3]. It can be difficult to distinguish eyelid nodules from chalazion, but the latter is normally found in the tarsal plate [2,4,5].

The etiopathogenesis of this pediatric condition has not yet been determined. It's still unclear. One of the actual hypotheses is that IFAG may be within the spectrum of childhood granulomatous rosacea. The presence of concurrent chalazions which are usually associated with rosacea, development of rosacea lesions in follow-up, detection of lymphohistiocytic perifollicular infiltrate which is typical of granulomatous rosacea, response to antibiotherapy used for rosacea treatment are some of the features suggesting an association with granulomatous rosacea [2,3,6].

The possibility of an infectious etiology seems to be ruled out. Therefore, the disease is considered aseptic. Another hypothesis is that the development of a granulomatous response to an embryonal remnant. Finally, other suggested etiologies include a persistent reaction to an insect bite or traumatic injury [1,2].

The histopathology of this condition is characterised by a chronic granulomatous infiltrate. Therefore, in the histopathological examination, we can see lymphohistiocytic infiltrate, neutrophils and foreign body type giant cells in the dermis. We don't expect to see ghost cells and calcification which is characterized pilomatrixoma [1].

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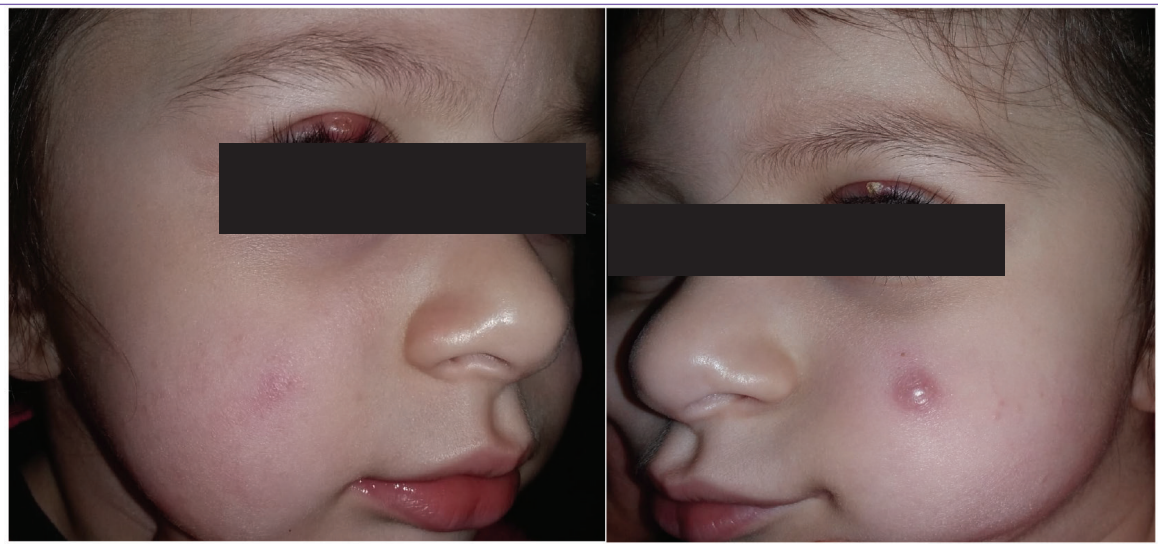

Figure 1. Chalazion on the upper eyelids and solitary nodule on the left cheek (3 mm punch biopsy was taken from the lesion on the left cheek)

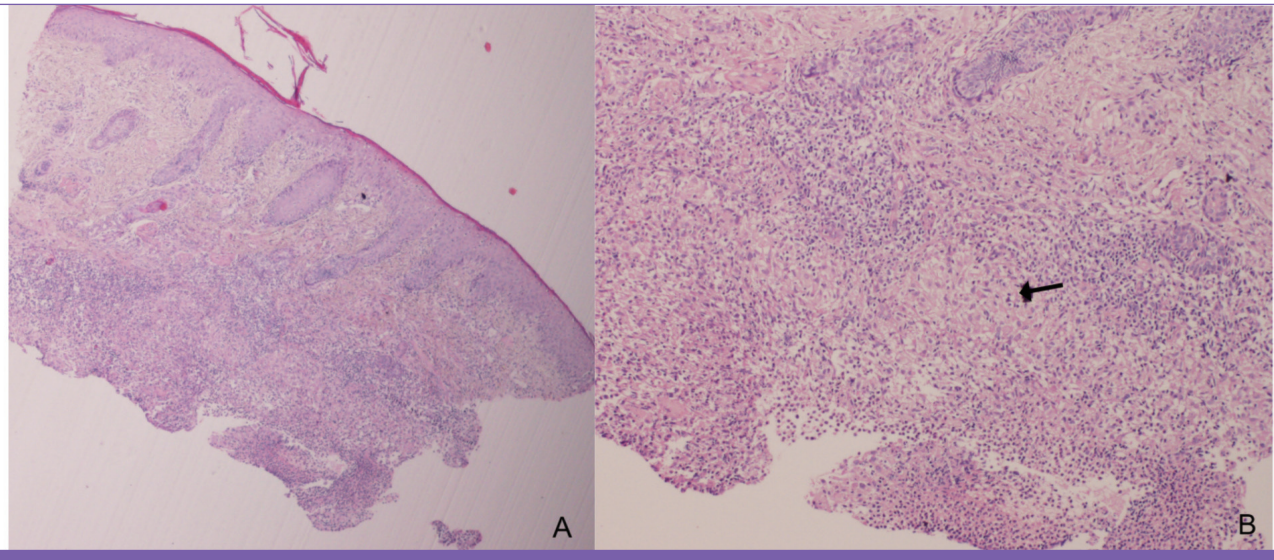

Figure 2. A) Granulomatous inflammation in the middle dermis, H&Ex40, B) Microgranulomas composed of epithelioid histiocytes and surrounding inflammation rich in lymphocytes, H&Ex100

The differential diagnosis includes other causes of facial nodules in childhood such as benign tumors (pilomatricoma, dermoid cyst, epidermoid cyst, juvenile xanthogranuloma, Spitz nevus, chalazion), localized pyoderma (fungal, bacterial, mycobacterial infections), cutaneous leishmaniasis, pyogenic granuloma, vascular malformations, nodulocystic acne [1,5,7].

Most lesions regress spontaneously. Also, good results have been reported with systemic and topical antibiotics [1,3,5].

Our case presented with chalazion and solitary nodule on the cheek. It contained granulomatous dermal infiltrate. The diagnosis was made with clinical and histopathological findings.

IFAG should be kept in mind in the differential diagnosis of facial nodules in children. Families may be worried, so families should be informed about the benign course of the lesions. Lesions should be followed until regression and because of the increased risk of rosacea, especially ocular rosacea, patients should be examined annually by dermatologists and ophthalmologists [5,8].

Ethics

Informed Consent: Informed consent was taken from the patient's father for possible case report publication.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: N.A., D.T., Design: N.A., D.T., Data Collection or Processing: M.M., S.Ş., S.A., S.Al., Analysis or Interpretation: N.A., Literature Search: M.M., Writing: M.M.

Conflict of Interest: No conflict of interest was declared by the authors.

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