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Research Article

Incidence of Erythema Multiforme among Patients with ORF Disease in Al-Kindy Teaching Hospital

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A B S T R A C T

Background: ORF virus has a worldwide distribution among sheep and goats. The hypersensitivity reaction, erythema multiforme (EM) is a known complication of ORF infection in humans; however, its occurrence is poorly understood and has not been extensively reviewed.

Aims of the Study: To assess the incidence of EM among patients with ORF infection and to find the association of EM incidence to age, gender, and occupation of the patients.

Method: A cross-sectional study of analytic design was conducted between 1st January 2018 and 31st December 2018 at Al-Kindy Teaching Hospital. Thirty cases of age ranging from 16 to 65 years who were clinically confirmed with ORF with and without EM eruption were included in this study. Data related to age, gender, occupation, complete clinical history, time of getting ORF infection and EM eruption was collected.

Results: The finding of the current study showed that the mean age of studied sample was 36.1 ± 9.1, 19 (63.3%) participants were less than 40 years of age, 24 (80%) were female, 24 (80%) were housewives, and 9 (30%) ORF patients were presented with EM. 4 (44.4%) patients got EM infection in the first week of ORF infection and 3 (33.3%) in the 2nd week. No significant association ($p \geq 0.005$ for all) was found between the status of EM and age category, gender and occupation of the patients.

Conclusion: We could conclude that the incidence of EM was relatively high among patients who had ORF infection.

Keywords: Incidence, Erythema Multiforme, ORF Disease, Al-Kindy Teaching Hospital

Introduction

Erythema multiforme (EM) is an acute, self-limiting but often relapsing, mucocutaneous inflammatory condition. It is considered to be a hypersensitivity reaction that is associated with certain infections, vaccinations, and, less commonly, medications. In general, the lesions of EM cover < 10% of the total body surface area. Mild symptoms of an upper respiratory infection, including low-grade fever, can sometimes be noted prior to and at the start of an episode of EM. Orolabial lesions are noted in two-thirds of patients; while 40.9% of cases have oral lesions alone. Erosions, blisters, and crusts can be noted in any of the mucous membranes and are typically painful and tender.[1] EM is reported worldwide without any ethnic predilection. It occurs at any age, more frequently in young adults. The average age of occurrence is between 20 and 30 years, and 20% of cases occur in children. Erythema multiforme is currently more common in younger males (male-to-female ratio in the range of 3:2 to 2:1) (mainly second to fourth decades, but can include children and adolescents) (20%).[2] The aetiology of EM is still unclear to this day. It is considered as a reaction against certain microorganisms, radiotherapy, systemic diseases, malignancy, and food or drug allergy.[3] Though HSV type 1 is the most commonly associated cause, HSV type 2 can also induce EM.[4] Drug-associated EM is reported in less than 10% of cases. Although numerous causative drugs have been identified, the most common disease-inducing medications are nonsteroidal anti-inflammatory drugs, sulfonamides, antiepileptic, and antibiotics. Laboratory evaluation and histopathology may assist in confirming the diagnosis, determining the causative factor and also excluding other diseases in the differential diagnosis. Although histopathologic changes are not always diagnostic of EM, they can be helpful in excluding other disorders. Similarly, although no specific DIF findings of EM exist, performing a DIF study of perilesional skin can rule out autoimmune bullous disease if that is considered in the differential diagnosis. Indirect immunofluorescence (IDIF) testing can also be useful in making a diagnosis of autoimmune bullous disease.[5] ORF is a mucocutaneous disease caused by double-stranded DNA parapoxvirus that is also known as sheep pox, ecthyma contagiosum, and contagious pustular dermatitis. Transmission to humans occurs when damaged skin comes into contact with infected sheep, goat saliva, or their dead bodies. The incubation period varies from 3 to 10 days and then single or multiple lesions evolve. At the onset of the disease, primary lesions are papules that gradually progress to nodular lesions. The nodules change into tubercules or crusted form within 4-6 weeks. The lesions may be complicated by lymphangitis or secondary bacterial infection but systemic complications such as erythema multiforme, maculopapular rash, and generalised lymphadenopathy are rare.[6] Differential diagnoses of ORF include pyoderma, herpetic whitlow, cowpox, cat-scratch disease, anthrax, tularemia, tuberculosis, other mycobacterial infections, syphilis, sportrichosis, keratoacanthoma, and pyogenic granuloma. Diagnosis of ORF is usually based on clinical findings and history of exposure of non-intact skin to contaminated sheep, goat saliva, or their dead bodies.[7,8] This study was conducted to assess the incidence of EM among patients with ORF infection and find the association of EM incidence to age, gender and occupation of the patients.

Method

A cross-sectional study of analytic design, this study was carried out during the period from 1st January 2018 to 31st December 2018 at Al-Kindy Teaching Hospital. A convenience sample of 30 patients of age ranging from 16 to 65 years who were clinically confirmed with ORF was considered for the study. The data were collected from thirty patients with clinically confirmed ORF with or without EM who attended outpatient clinics of Al-Kindy Teaching Hospital via a direct interview with the patients. The collected data were related to age, gender, occupation, clinical history regarding infection, drugs history, and any chronic illness especially the connective tissue disease, time of onset of ORF and EM, status of EM (first attack or recurrent), and prescribed medications for ORF. Topical steroid and antihistamines were prescribed for the patients and followed up for six weeks.

Inclusion Criteria

Any patient of any age and any gender with ORF.

Exclusion Criteria

Patients with recurrent attacks of EM, patients on immunosuppressive medications, patients with EM and a history of drug intake, history of pregnancy, radiotherapy or insect bite, patients with oral or genital herpes.

The analysis of data was carried out using SPSS version 23. Number and percentage were used to represent the categorical data. Chi-square test and linear regression were used to confirm significance. Statistical significance was considered whenever the P-value was less than 0.05. Approval was obtained from concerned authorities to carry out the study in January 2018 and consent was obtained from the participants. Difficulty in obtaining an accurate and complete clinical history, small sample size and short duration of study are the limitations of this study.

Results

The finding of the current study showed that the mean age of the studied sample was 36.1 ± 9.1. The results revealed that 19 (63.3%) participants were less than 40 years of age, 24 (80%) were female, and 24 (80%) were homemakers. The results of this study demonstrated that 9 (30%) ORF patients were presented with EM. The results revealed that

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19 (63.3%) patients had ORF on the left hand, 8 (26.7%) on the right hand, and 3 (10%) had ORF on both hands. About two-thirds (70%) of patients had one lesion of ORF, 7 (23.3%) had two lesions, and just 2 (6.7%) had three lesions of ORF. The majority of cases of EM (88.9%) were of acral type and only one patient had EM of generalised form as displayed in Table 1.

Table 1.Sociodemographic and Other Data of Study Participants

Variables		Frequency	Percentage
Age groups (years)	< 40	19	63.3
	≥ 40	11	36.7
Gender	Female	24	80.0
	Male	6	20.0
Occupation	Housewife	24	80.0
	Restaurant worker	2	6.7
	Butcher	2	6.7
	Others	2	6.7
Incidence of EM	Yes	9	30
	No	21	70
Site of ORF	LH	19	63.3
	RH	8	26.7
	RH & LH	3	10.0
No. of ORF lesions	One	21	70.0
	Two	7	23.3
	Three	2	6.7
Type of EM	Acral	8	88.9
	Generalised	1	11.1

Table 2.Association of EM Incidence and Sociodemographic Characteristics of the Patients and Status of Co-morbid Illness

Presence of EM						P-value
		Yes		No		
		No.	%	No.	%	
Age groups (year)	< 40	7	36.8	12	63.2	0.2
	≥ 40	2	18.2	9	81.8	
Sex	Female	7	29.2	17	70.8	0.8
	Male	2	33.3	4	66.7	
Occupation	Butcher	0	0.0	2	100.0	0.6
	Housewife	7	29.2	17	70.8	
	Restaurant worker	1	50.0	1	50.0	
	Others	1	50.0	1	50.0	
Comorbidity	Yes	1	50.0	1	50.0	0.2
	No	8	28.6	20	71.4	

P-value ≤ 0.05 (significant).

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Table 3.Frequency of Patients according to the Month of ORF Infection, Frequency of Patients according to Annual Quarter, and Frequency of Patients according to Sequence of Time in Weeks of getting EM after ORF

	No. of Patients	%
Months		
October	10	33.3
November	5	16.7
June	3	10.0
May	3	10.0
April	2	6.7
July	2	6.7
March	2	6.7
August	1	3.3
December	1	3.3
September	1	3.3
Total	30	100.0
Annual Quarter		
Autumn	16	53.4
Summer	4	13.3
Spring	6	20.0
Winter	4	13.3
Total	30	100.0
Sequence of time in weeks		
1	4	44.4
2	3	33.3
3	0	0.0
4	2	22.3
Total	30	100.0

The highest percentage of patients (33.3%) got ORF in October followed by November (16.7%), June (10%), May (10%) and the remainder got the infection on different months of the year. The findings showed that about half of the patients (16, 53.4%) got ORF infection in the 4th quarter of the year, 4 (13.3%) got the infection in the 3rd quarter of the year, 6 (20%) in the 2nd quarter, and 4 (13.3%) in the first quarter of the year. The results showed that 4 (44.4%) patients got EM infection in the first week of ORF infection, 3 (33.3%) got EM in the 2nd week of ORF infection, nobody got EM in the 3rd week, and 2 (22.3%) got EM in the 4th week of ORF infection as illustrated in Table 3.

The findings showed there was no significant association ($p = 0.2$) between age category and status of EM eruption as the results showed that out of 19 patients of age less than 40 years, 7 patients developed EM, and out of 11 patients older than 40 years, 2 patients developed EM so the difference did not reach the significant level. The same non-significant association was reported with gender distribution ($p = 0.8$) and occupation of the patients ($p = 0.6$). The results of the current study showed there was no significant association ($p = 0.2$) between comorbidity statuses in terms of present or absent and status of EM, as the EM was reported with patients who had chronic illnesses and with patients who were free of chronic illnesses as seen in Table 2.

Discussion

ORF is a proliferative viral skin disease occurring in people who are in contact with sheep, goats, and cattle that are infected. It is caused by parapoxviruses which are double-stranded DNA viruses belonging to the pox viridae family. Erythema multiforme (EM) is an acute, immunological, vesiculobullous disorder that primarily affects the skin and mucous membranes. The exact aetiology of EM is obscure, although, prior infection with herpes simplex virus (HSV) and the intake of certain drugs are the common precipitating factors.[9,10] Our findings demonstrated that 63.3% of the patients with ORF were less than 40 years of age and these findings are consistent with the report of the Center for Disease Control and Prevention (CDC) that found that the majority of ORF cases were reported within the third or fourth decade of age.[11] The results of our study also revealed that the sites of infection were distributed as follows: right hand in 8 patients (26.7%), left hand in 19 patients (63.3%), and right and left hands in 3 patients (10%). These results are consistent with Lederman ER and Uzel G[12,13] who found that hands are the most common site for ORF infection and the other sites of the body are rarely affected. Uluğ M et al. also found that out of three patients with ORF in their study, two had lesions on only one hand, whereas one patient had additional lesions on the other hand. The lesions were most commonly located on the dorsal aspect of the fingers.[14] The higher incidence of ORF on the left hands of the patients in our study can be explained in part by the way of handling meat in the left hand while cutting it with the right hand which makes the left hand more in contact with infected meat. The results of the current study also showed that the female patients who were housewives (80%) were affected more than male patients and these results might be explained on the basis of the fact that women in our community are concerned more with cooking and hence come into contact with infected meat more than the male subjects. Our findings regarding the gender distribution of infection with ORF are in disagreement with Caravaglio JV who found that ORF infection occurs more commonly in men (70%) owing to the fact that men are more likely to have occupational exposure (eg, ranching, veterinary medicine, animal slaughter).[15] Meier R et al. also reported that the farmers,

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butchers, sheep shearers, and veterinarians are prone to ORF disease.[16] The results of the current study showed that the incidence of ORF infection was more in October (10 patients, 33.3%) followed by November (5 patients, 16.7%). These two months (October and November) coincided with the hijri month (Muharam) and fall within a month of Eid al-Adha when many Muslims slaughter sheep in these religious feasts. This finding is consistent with Shahmoradi Z et al., Veraldi et al., and the CDC report where they also found and reported that the ORF infection is mostly related with Muslim's practice of Eid al-Adha but they also found that it was also seen with Jewish Passover and Christian Easter celebrations.[17] Concerning the ORF distribution according to gender and timing with the feast, Sacar et al. found that male preponderance (30.4%) before the Feast of the Sacrifice, whereas a female preponderance (32.7%) was found after the Feast.[18] Bayındır Y et al.,[19] concluded that the ORF infection tends to occur in the spring and the summer months where they found that all patients who enrolled in their study contracted ORF during these two seasons. The results of our study showed that 9 patients (30%) who presented with ORF developed EM which is a higher incidence than was reported in previous studies which could be due to higher contact with farm animals and meat in our country. Ghislain PD[20] reported that among patients receiving a diagnosis of ORF, an estimated 7–18% experience EM. The results of the current study demonstrated that the mean age of the studied sample with ORF was 36.1 years. In addition, our findings revealed that 7 out of 9 patients with EM were less than 40 years of age and these findings are consistent with the finding of the study that was conducted by Yavuz I H et al.[21] where they also found that the mean age of their patients with EM was 36.7 years. It is also consistent with the results of the study that was carried out by Lerch M et al.[1] who have stated that EM is particularly seen in the second and third decades of life. The current study revealed that 7 of our patients with EM were females and these results are in agreement with the results of Yavuz IH et al.[21] who had also reported a higher percentage of EM among females (66.7% of their patients were females). The findings were also consistent with Samim F et al.[22] who indicated EM is more common in women than men. However, Kondolot et al. reported that there was a male preponderance in their paediatric patients.[23] The highest percentage of patients (44.4%) developed EM within the first week of ORF infection and these findings are partially consistent with Aktaş H et al.[24] who found that the mean time for erythema multiforme development after ORF infection was 6.7 (range 5-9) days. Azizzadeh M and Coskun O et al.[6,24] also related EM disease to ORF infection and they found that ORF associated EM typically develops 2-4 weeks after the onset of primary ORF lesion and is characterised by acute onset of symmetrically distributed papules, macules, bullae, and target lesions. According to the findings of previous literature that confirmed the association between EM and herpes viral infection, the association of EM and ORF infection could be explained by the same mechanisms which are thought to be a cell-mediated immune reaction against viral antigens in the lesions. Some studies have stated that the possible mechanisms of ORF induced cutaneous manifestation include virus mimicry of host proteins and alteration of basement membrane proteins by the virus.[25]

Conclusion

We could conclude that the incidence of EM was relatively high among patients who had ORF infection.

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Conflict of Interest: None

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