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Report

Eosinophilic folliculitis due to wearing protective gear in citizens volunteering for sanitation services during the COVID-19 pandemic – an original epidemiological, clinical, dermoscopic, and laboratory-based study

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Abstract

Background An association between wearing protective gear and eosinophilic folliculitis has not been reported. We aimed to investigate such during the COVID-19 pandemic.

Methods In three outpatient clinics, we hand-reviewed records of all patients having consulted us during a *Study Period* (90 days) in the early phase of the pandemic. Our inclusion criteria for *Study Subjects* were: (i) clear clinical diagnosis, (ii) dermoscopic confirmation, (iii) differential diagnoses excluded, (iv) eosinophilia, (v) protective gear worn during sanitation services, (vi) temporal correlation, (vii) distributional correlation, (viii) physician-assessed association, and (ix) patient-assessed association. *Control Periods* in the same season were elected.

Results Twenty-five study subjects fulfilled all inclusion criteria. The incidence was significantly higher than in the control periods (IR: 3.57, 95% CI: 1.79–7.43). Male predominance was significant ($P < 0.001$). Such for patients in the control periods were insignificant. Study subjects were 21.2 (95% CI: 11.0–31.4) years younger than patients in the control periods. For the study subjects, the distribution of erythematous or skin-colored folliculocentric dome-shaped papules and pustules were all compatible with body parts covered by the gear. Lesional biopsy performed on two patients revealed eosinophilic dermal infiltrates within and around the pilosebaceous units. Polarized dermoscopy revealed folliculitis with peri-/interfollicular vascular proliferation. Lesion onsets were 6.4 (SD: 2.1) days after wearing gear. Remissions were 16.7 (SD: 7.5) days after ceasing to wear gear and treatments.

Conclusions Wearing protective gear in volunteered sanitizing works could be associated with eosinophilic folliculitis. Owing to the significant temporal and distributional correlations, the association might be causal.

Introduction

An association between wearing protective gear in sanitation works and the development of eosinophilic folliculitis (EF) has not been reported. In this study, we aim to investigate this association in civilians wearing gear during volunteered sanitation works during the early phase of the COVID-19 pandemic in Hong Kong.

Materials and methods

Our settings were three primary care clinics operating in two geographically different practices attached to a university teaching hospital. All patients were managed by a physician with training and qualifications in dermatology. He has published regarding clinical and dermoscopic diagnoses of different types of folliculitis previously[1–3] and should be able to make valid and reliable clinical diagnoses of EF.

Hong Kong saw its first confirmed patient with COVID-19, then known as *Wuhan pneumonia*, on January 23, 2020. We searched our computerized registers and hand-reviewed the medical records of all patients who have consulted us during a study period from February 1 to April 30, 2020 (90 days), and diagnosed as having EF.

Our criteria for inclusion as study subjects were (i) clear clinical diagnosis of EF (erythematous or skin-colored hemispherical or urticarial papules and pustules, sometimes edematous, and usually pruritic), (ii) dermoscopic confirmation (folliculocentric lesions usually with perifollicular and/or interfollicular vascular proliferation), (iii) differential diagnoses

including irritant and allergic dermatitis, other types of dermatitis, dermatophytoses, other infections or infestations, miliaria, and other types of folliculitis being considered highly unlikely, (iv) eosinophilia (higher than 0.5×10^9/l), (v) that the patient did wear protective gear during volunteer sanitation works (usually at home, neighboring areas, and working areas), (vi) temporal sequence (rash appearing after wearing gear, remission after ceasing to wear protective gear and treatments), (vii) distribution of EF being correlated to such covered by the protective gear, (viii) the physician being convinced that the EF was related to the protective gear, and (ix) that the patient also concurred to such a relationship.

To eliminate the confounding variable of seasonal variation, we traced back two periods – February 1 to May 1, 2019 (90 days), and February 1 to May 1, 2018 (90 days) – as control periods 1 and 2, respectively, and reviewed records of all patients diagnosed with EF within such periods.

For all study subjects and patients in the control periods, we retrieved their demographic details, clinical manifestations, rash distributions, clinical photos (where available), dermoscopic images (where available), temporal relationship between wearing and ceasing to wear protective gear, and the onset and remission of EF, complete blood picture, HIV-1 and -2 antibodies, and P24 antigen results (where available), and treatments.

Results

Incidence

Twenty-nine patients were diagnosed with EF during the study period (Table 1). This incidence was significantly higher than in the first control period (incidence ratio [IR]: 3.63, 95% CI: 1.62–9.18), second control period (IR: 4.83, 95% CI: 1.97–14.2), and the two control periods combined (IR: 4.14, 95% CI: 2.12–8.48). All patients with EF did not have COVID-19 diagnosed. All were not healthcare professionals and not being engaged in cleaning as a job.

Twenty-five patients in the study period fulfilled all nine inclusion criteria and became our study subjects. The incidence for the study subjects alone was significantly higher than in the two control periods and the two combined (IR: 3.57, 95% CI: 1.79–7.43).

Demographics

Twenty-one (84%) study subjects were males, and four (16%) were females. Male predominance was significant ($z = 3.4$, $P < 0.001$). In contrast, one male and three female patients with EF diagnosed in the study period but not related to wearing protective gear, and the patients in both control periods demonstrated insignificant sex predilection.

The 25 study subjects ranged in age from 15 to 81 years (mean: 33.5 years, SD: 13.6 years). Although the range was

Table 1 Incidence ratios, sex, and age differences of patients with eosinophilic folliculitis during the COVID-19 pandemic as compared to two control periods in the same season

Periods	Number of days	Incidence of eosinophilic folliculitis (males/females)	Incidence ratio of Study Period (all patients) against Control Periods	Incidence ratio of Study Period (related to protective gear) against Control Periods	Age	Age differences of Study Period (related to protective gear) compared to Control Periods
Study period (related to protective gear)	90	25 (21/4)[a] M/F z = 3.4, $P < 0.001$	–	–	15–81 years mean: 33.5, SD: 13.6	–
Study period (unrelated to protective gear)	90	4 (1/3) M/F z = 1.00, $P = 0.32$	–	–	23–85 years mean: 61.0, SD: 23.3	−27.5 years[a] 95% CI: −44.1 to −10.9
Control period 1	90	8 (5/3) M/F z = 0.71, $P = 0.48$	3.63[a] 95% CI: 1.62–9.18	3.13[a] 95% CI: 1.37–8.02	23–76 years mean: 53.5, SD: 16.2	−20.0 years[a] 95% CI: −31.8 to −8.2
Control period 2	90	6 (3/3) M/F z = 0.00, $P = 1.00$	4.83[a] 95% CI: 1.97–14.2	4.17[a] 95% CI: 1.67–12.4	24–79 years mean: 56.3, SD: 18.6	−22.8 years[a] 95% CI: −36.4 to −9.24
Control periods 1 and 2 combined	180	14 (8/6) M/F z = 0.53, $P = 0.59$	4.14[a] 95% CI: 2.12–8.48	3.57[a] 95% CI: 1.79–7.43	23–79 years mean: 54.7, SD: 17.4	−21.2 years[a] 95% CI: −31.4 to −11.0

CI, confidence interval; M/F, males/females; SD, standard deviation.
[a]Statistically significant.

wide, they were actually significantly younger by 20.0 (95% CI: 8.2–31.8) years than patients in control period 1 and by 22.8 (95% CI: 9.24–36.4) years than patients in control period 2.

Clinical

For all patients in the study and control periods, multiple edematous inflammed folliculocentric papules and pustules were seen. The lesions were pruritic. Figures 1a–4a depict lesions of four study subjects. The lesions were clustered together, except for the patient in Figure 2a who was in partial remission when the clinical photo was taken.

Lesional histopathology

Lesional biopsy was performed on two study subjects, such as revealing intense eosinophilic dermal infiltrates within and around the pilosebaceous units. However, histopathological images were not available for publication.

Dermoscopy

Polarized dermoscopic images from four study subjects are shown in Figures 1b–4b. All confirmed that the inflammation and pus were at the hair follicles. Perifollicular and interfollicular capillaries are dilated in Figures 1b, 3b, and 4b. Perifollicular vascular proliferation are shown in Figure 2b. For the patient in Figure 2a, the lesions were sparsely spaced on the upper back. All are typical dermoscopic appearances of EF.

Temporal and distributional correlations

All 25 study subjects did not have a previous history of EF or skin rashes akin to EF. All developed EF after wearing protective gear for three to 12 (mean: 6.4, SD: 2.1) days. The time from ceasing to wear gear and treatments to complete remission was seven to 32 (mean: 16.7, SD: 7.5) days. There exists an insignificant difference for male, female, and all study subjects (Table 2). The time from onset of rash to complete remission was also insignificantly different for study subjects and patients in the control periods.

The most commonly involved areas were the upper or lower back (84%), anterior trunk (48%), and lateral aspects of trunk (28%) (Table 3). The protective gear ranged from plastic aprons to full bodysuits. Many dtudy dubjects wore different combinations of protective gear on multiple occasions. However, for

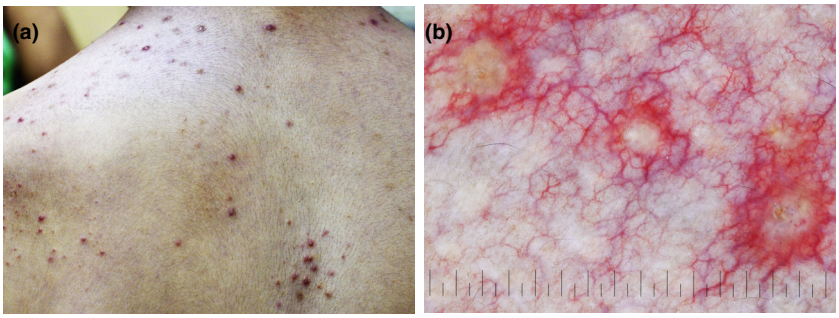

Figure 1 (a) Clustering of lesions on the upper back of a patient with eosinophilic folliculitis. The lesions were dark-red hemispherical papules and pustules. All were folliculocentric. Excoriations are seen. This was taken at a later phase of the disease. Lesions were no longer in bright erythema. (b) Polarized dermoscopy showing four lesions of eosinophilic folliculitis for the patient in Fig. 1a. Perivascular and interfollicular regions are intensely perfused. This image was taken on the cluster of lesions at the right lower part of Fig. 1a

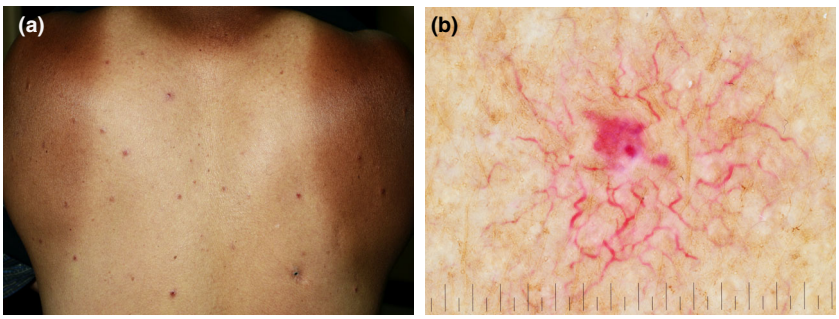

Figure 2 (a) Lesions of eosinophilic folliculitis on the upper back of a middle-aged patient. Lesions are sparsely apart from each other. All are erythematous dome-shaped papules and pustules around hair follicles. (b) Polarized dermoscopy on one lesion from the upper back of the patient in Fig. 2a. The hair follicle is out of polarization-focus but still identifiable in the center of the figure. Numerous perifollicular capillaries are dilated

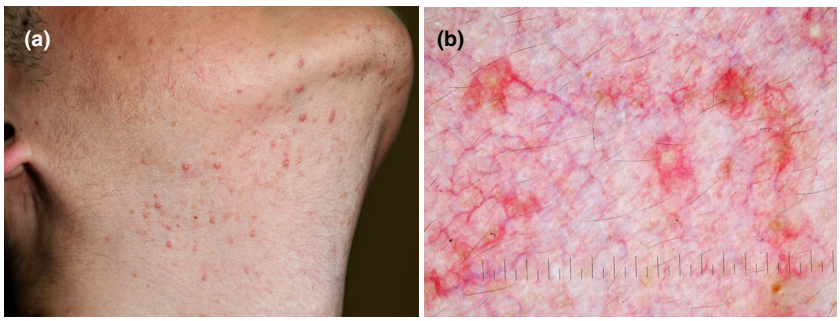

Figure 3 (a) Lesions of eosinophilic folliculitis on the face, chin, and neck of a young patient. Erythematous perifollicular pustules are seen. Blood vessels are dilated for the larger lesions. The patient sometimes left his surgical mask hanging on his neck, which might account for lesions on his there. (b) Polarized dermoscopy on the neck of the patient in Fig. 3a. Around 10 lesions of eosinophilic folliculitis are seen. Perifollicular blood vessels are dilated

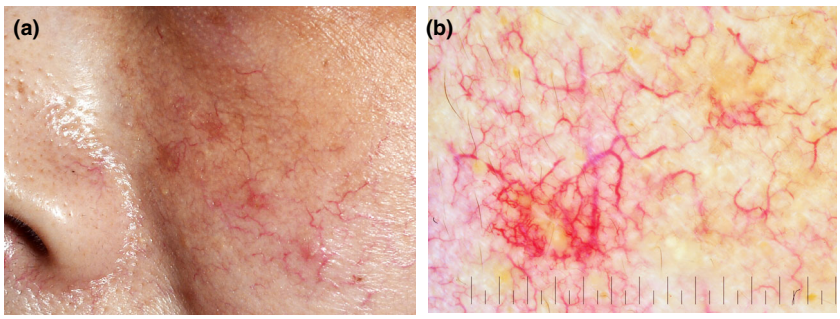

Figure 4 (a) Folliculocentric skin-colored and dome-shaped papules and pustules with perilesional and interlesional vascular proliferation on the face of a study subject wearing the same face masks repeatedly during sanitation work. (b) Polarized dermoscopy shows three lesions of eosinophilic folliculitis with the inflammation being most spectacular for the lesion on the left lower part of the figure. These correspond directly with the lesions seen in Fig. 4a

Table 2 Temporal correlations for 25 study subjects with eosinophilic folliculitis and wearing protective gear in sanitation works during the COVID-19 pandemic

	Male Study Subjects (N = 21)	**Female Study Subjects (N = 4)**	**All Study Subjects (N = 25)**
Time from wearing protective gear to the onset of eosinophilic folliculitis	3–12 days Mean: 6.5 days, SD: 1.9 days	3–9 days Mean: 6 days, SD: 2.5 days	3–12 days Mean: 6.4 days, SD:2.1 days
Comparisons	Comparison with female study subjects SE: 1.1, 95% CI: −2.7 to 1.7	Comparison with all study subjects SE: 1.2, 95% CI: −2.0 to 2.8	Comparison with male study subjects SE: 0.6, 96% CI: −1.1 to 1.3
Time from ceasing to wear protective gear and treatments to remission of eosinophilic folliculitis	7–32 days Mean: 16.8 days, SD: 7.6 days	9–28 days Mean: 16.5, SD: 7.0 days	7–32 days Mean: 16.7 days, SD: 7.5 days
Comparisons	Comparison with female study subjects: SE: 4.1, 95% CI: −8.8 to 8.2	Comparison with all study subjects: SE: 4.0, 95% CI: −8.0 to 8.4	Comparison with male study subjects SE: 2.2, 95% CI: −4.4 to 4.6

CI, confidence interval; N, total number of Subjects; SD, standard deviation; SE, standard error.

every part of the body with lesions of EF seen, protective gear had been worn over such area. Figure 5 shows a re-creation of a typical set of disposable protective gear.

Laboratory results

All 25 study subjects were confirmed to exhibit eosinophilia, with the mean value of the 21 males being 2.81 (SD: 1.00) $\times$ 10^9/l,

Table 3 Distribution correlations of lesions for 25 dtudy subjects with eosinophilic folliculitis and wearing protective gear in sanitation works during the COVID-19 pandemic

Distribution of lesions of eosinophilic folliculitis	Number of Study Subjects affected (%; N = 25)[a]	Protective gear worn[b]
Upper or lower back	21 (84%)	All of these 21 study subjects wore full-body suits covering the trunk and four extremities.
Anterior trunk	12 (48%)	
Lateral aspects of trunk	7 (28%)	
Upper limbs	5 (20%)	
Lower limbs	4 (16%)	
Neck	2 (8%)	These two study subjects wore full-body suits covering the trunk, four extremities, neck, and head.
Face	2 (8%)	These two sudy subjects reused disposable surgical face masks repeatedly.

N, total number of study subjects.
[a]The figures add up to be more than 25 as many study subjects had multiple sites affected.
[b]Many study subjects wore different combinations of protective gear on multiple occasions.

the four females being 3.33 (SD: 0.51) $\times$ 10^9/l (insignificantly different from the male patients). All study subjects were HIV Ab negative and P24 Ag negative.

Some of the laboratory data were missing for patients in the control periods. Comparison of the existing data to those of the study subjects revealed insignificant differences.

Treatments

Treatments delivered to the patients included topical corticosteroids, topical permethrin, topical tacrolimus, oral indomethacin, and oral itraconazole. Systemic indomethacin at a dose of 50 mg daily proved to be of high efficacy to achieve clinical remissions for at least six study subjects and many of the patients in the control periods. For the study subjects, we also counseled them regarding their predilection to develop EF upon wearing the protective gear right after clinical diagnoses were made. General hygienic measures and the use of skin protective agents were advocated. We also advised that gear meant to be disposable should not be used repeatedly. The time from stopping wear gear to total symptomatic remission ranged from seven to 32 (mean: 16.7, SD: 7.5) days.

Other fit family members would take up their responsibility alternatively so that consecutive wearing of gear for each person was kept to a minimum. Responses to treatments were similar for patients in the study and control periods.

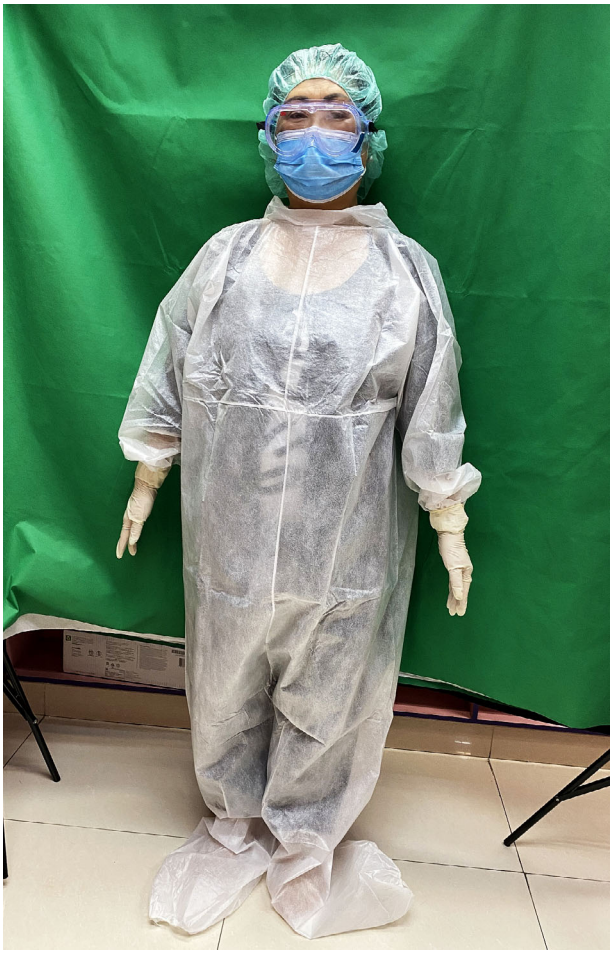

Figure 5 A re-creation of the full protective gear meant for singleuse. One would feel hot after wearing such for 15 minutes without air conditioning. Another version covers the head and neck as well. Other gears in this figure include an elastic cover for the scalp and ears, goggles, surgical face mask, and unsterilized surgical gloves

Comment

EF is usually a very pruritic rash. In some countries and regions, the commonest associated factor is HIV infection.[4] For these patients, the trunk of males and the face and trunk of females are principally affected.[4]

It has been controversial whether EF and *eosinophilic pustular folliculitis* (EPF) are the same or different disease entities. Patients with EPF were mainly reported in Japan. Some investigators consider EF and EPF as belonging to the same spectrum of diseases.[4–6] The four subtypes would be (i) EF/ERP described in this article (principally affecting the trunk, associated with HIV or not),[7,8] (ii) EPF principally affecting the face of adults not associated with HIV infection (also known as Ofuji disease),[4–6,9] (iii) infantile EPF principally affecting the scalp and face,[10,11] and (iv) EPF associated with hematological malignancies and transplantations.[12,13]

In Hong Kong, patients with EF associated or not associated with HIV infection are seen. However, since the seroprevalence of HIV is low (0.14% of the total population in 2019),[14] most patients with EF do not have HIV infection, like our patients in the study and control periods. For this type of EF, no genetic predisposition has been reported.

It has been postulated that the immunopathogenesis of EF involves eosinophils flaring an intense, probably autoinflammatory,[15] response to the *Demodex folliculorum* and *Demodex brevis* mites in the pilosebaceous units.[16,17] Some reports did demonstrate the effectiveness of topical permethrin in EF.[18,19] This was why we treated some patients with topical permethrin. The autoinflammatory response also targets *Pityrosporum spp* yeasts[16,20] and bacteria[16,21] in the perifollicular regions. However, it was beyond our financial resources to investigate the immunopathogeneses for our patients.

Dermoscopy has been reported to endorse high accuracy in differentiating the various types of folliculitis.[3,22–24] We documented the most severely attacked parts of skin showing inflamed perifollicular and interfollicular vasculatures (Figs. 1b–4b). Such extents of vascular proliferation are much less commonly seen for patients with bacterial folliculitis due to *Staphylococcus aureus* infection.

Having endured SARS in 2003, citizens in Hong Kong have become highly vigilant against epidemics of infectious diseases. Apart from over 98% of the citizens wearing face masks during the COVID-19 pandemic, many also wore protective body suits to clean and sanitize their homes, working spaces, and their neighborhood.[25]

The study subjects were male-predominant and around 20–22 years younger than other patients with EF. This was because young and fit males were more willing to perform sanitation services. An 81-year-old male patient was an exception. His body was good and strong until EF developed on his trunk. Other family members promptly took up his services.

We postulate that the occlusion of protective gear could have compromised physiological skin ventilation, leading to the accumulation of sweat, dirt particles, or bacteria. Such could activate inflammatory responses attacking the mites, yeasts, or bacteria in the hair follicles and the pilosebaceous units as a whole. Moreover, the increased humidity of the skin by wearing protective gear could have caused an imbalance between the Demodex mites and the immunological skin condition of EF.

We were uncertain as to why professionals such as firemen wearing protective gear have not been reported to develop EF. One reason could be that their gear is specifically designed and manufactured with materials of higher quality. Some of the materials might be hypoallergenic and more permeable. Their gear is mostly designed to be worn repeatedly, with proper maintenance of their conditions. However, our study subjects were wearing gear not specifically designed for cleaning and sanitary purposes, and the gear was made of materials of lesser quality. Moreover, some of the protective gear were meant to be disposed after a singleuse. These items were of inadequate supply in the earlier phase of the pandemic and were worn repeatedly with inadequate cleaning and drying by the study subjects.

Another factor could be that citizens in Hong Kong have been in political unrest since June 2019 up to the present moment. It was reported that psychological stress could predispose individuals to higher risks of cutaneous diseases.[26]

The major limitation of this study is that we have performed a lesional biopsy for histopathological investigations for only two study subjects. However, many study subjects and patients in the control periods promptly responded to oral indomethacin treatment. In a proposed diagnostic and therapeutic algorithm, it was stated that if biopsy was not feasible, topical or systemic indomethacin can be used as a diagnostic therapy.[27] Moreover, we have performed dermoscopy for all patients, as dermoscopy has been reported to be highly accurate in diagnosing various types of folliculitis.[2,20–22] We have also demonstrated eosinophilia for all patients.

The involvement of only three clinics by one physician is also an important limitation. Other studies in multiple centers are necessary to confirm the association. Our study being retrospective in nature could be a limitation. However, retrospective assessments might minimize observer bias, which could be a strength in our study.

Although the pandemic is waning in many parts of the world, our findings are important as the association of wearing protective gear and the development of EF has not been reported previously. We now possess the knowledge that EF is sometimes a preventable disease and is nearly always treatable in such a scenario. We should, therefore, be more prepared to prevent and treat EF in epidemics and pandemics in the future.

During 90 days in the early phase of the COVID-19 pandemic, we thus identified 25 patients, predominately being males (21, 84%) with a history of wearing protective gear volunteering to do sanitation services for their homes, working places, and neighborhoods, having developed EF. They were significantly younger by around 20–22 years than other patients with EF.

Wearing protective gear in voluntary sanitizing works could, therefore, be associated with EF. As the temporal and distributional correlations were significant, we believe that the association might be causal.

Acknowledgments

Patient consent: The patients in this manuscript have given written informed consent to the publication of their case details.

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