Exanthema and eosinophilia in COVID-19 patients: has viral infection a role in drug induced exanthemas?

To the Editor

At the present time, the whole world is faced with coronavirus disease 2019 (COVID-19). Cutaneous manifestations in these patients are becoming frequent in our daily practice, and they pose a challenge regarding their pathogenesis.

We present a retrospective case series of twelve adult patients (6 male/6 female) with a mean age of 66.3 years (47–79). All patients had pneumonia and nasopharyngeal swab PCR positive for SARS-CoV-2 and had received treatment for COVID-19 per protocol established. Table 1 shows the characteristics of these patients. All patients developed an itching papular exanthema after an average of 20.4 days (10–28) from their admission. At the exanthema onset, all the drugs had already been discontinued; therefore, topical corticosteroids were prescribed. However, the exanthema showed a cephalocaudal progression and confluence with islands of sparing in all cases. Seven patients developed violaceous-areas and/or target-like (Fig. 1) lesions; of them, three developed fever and facial oedema. In one patient, the progression of the cutaneous lesions coincided with reintroduction of hydroxychloroquine and lopinavir/ritonavir. Cutaneous biopsy was performed in two of these patients: one of them showed a superficial perivascular inflammation with eosinophils and the other showed a lichenoid pattern with eosinophils. Both two were compatible with drug reaction.

Systemic corticosteroids were prescribed in six patients with violaceous areas, starting at 0.5–1 mg/kg and then tapered over the ensuing 2–4 weeks with progressive improvement. The other cases improved with topical corticosteroids.

It has been suggested that underlying viral infections may increase the risk of adverse drug reactions. The association of viral infections and drug reactions has been described in many clinical situations, such as the ampicillin rash in infectious mononucleosis or the increased risk of drug reactions in AIDS patients.2 In DRESS syndrome, viral reactivation (especially HHV-6) is a characteristic feature. Antiviral immune responses may facilitate drug allergy development, and several biological mechanisms have been proposed for this effect, including excessive production of proinflammatory cytokines, which has been observed in COVID-19.3,4

The presence of exanthema and eosinophilia suggests a drug reaction in our patients. DRESS syndrome, although unusual, has been reported related to hydroxychloroquine but it has not been described with lopinavir/ritonavir.5 Other drug reactions have also been reported with the treatments used for COVID-19 management. However, the high frequency we are observing these reactions in the COVID-19 pandemic make us think that SARS-CoV-2 infection may have a role in their pathogenesis. We suggest that several exanthemas may result from interaction between antiviral immune response and drugs. Nevertheless, more studies are needed to confirm this hypothesis. We must be cautious until then. It would be therefore strongly recommended that all COVID-19 patients with exanthema and eosinophilia were investigated for drug sensitization. We suggest that systemic corticosteroids should be considered in those exanthemas that progress to violaceous areas or target-like lesions, since in our experience topical corticosteroids have not been able to achieve an improvement in these cases.

Acknowledgement

The patients in this manuscript have given written informed consent to publication of their case details.
Table 1: Characteristics of 12 patients with atypical exanthems and eosinophilia

| Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 | Case 8 | Case 9 | Case 10 | Case 11 | Case 12 |
|--------|--------|--------|--------|--------|--------|--------|--------|--------|---------|---------|---------|
| **Exanthema** | Violaceous | Generalized | Maculopapular confluent | No fever | Maculopapular confluent | No fever | Maculopapular confluent | No fever | Maculopapular confluent | No fever | Maculopapular confluent |
| **Demographics** | Male, 67 y.o. | Male, 76 y.o. | Female, 61 y.o. | Male, 71 y.o. | Male, 59 y.o. | Female, 62 y.o. | Male, 87 y.o. | Female, 74 y.o. | Male, 47 y.o. | Female, 74 y.o. | Female, 61 y.o. |
| **Lesions** | Maculopapular confluent | No fever | Maculopapular confluent | No fever | Maculopapular confluent | No fever | Maculopapular confluent | No fever | Maculopapular confluent | No fever | Maculopapular confluent |
| **Itch** | ++ | + | Generalized |++ | Itch |++ |++ |++ |+ |++ |++ |
| **Eosinophils** | Eos 1200/l | Eos 1400/l | Eos 2300/l | Eos 1000/l | Eos 800/l | Eos 1000/l | Eos 700/l | Eos 900/l | Eos 1600/l | Eos 900/l | Eos 1000/l |
| **ALT** | 36 U/L | 495 U/L | 153 U/L | 68 U/L | 34 U/L | 32 U/L | 30 U/L | 23 U/L | 20 U/L | 30 U/L | 495 U/L |
| **Reference ranges are as follows: eosinophils 0 to 500 per microlitre; lymphocytes 1300 to 1500 per microlitre and ALT 5 to 41 U/L. y.o. denotes years old, HT hypertension, DL dyslipidemia, CKD chronic kidney disease, HC hydroxychloroquine, LP/RT Lopinavir/Ritonavir, CF ceftriaxone, AZ azithromycin, MP methylprednisolone, TZ tocilizumab, RDS remdesivir Eos eosinophils, Lymp lymphocytes, IV intravenous, BID Bis in die; PO Per os OD Omnie die.**

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Iatrogenic dermatitis in times of COVID-19: a pandemic within a pandemic

Editor

The pandemic of the 21st century COVID-19 emerged in Wuhan, China, and swiftly became a global phenomenon. The frontline barriers for preventing spread are hand hygiene and personal protective equipment (PPE). The amplified hygiene practices and PPE as recommended have brought in its wake a second pandemic – a pandemic of dermatitis.

We reviewed the most prevalent types of iatrogenic skin damage among healthcare workers (HCWs), notably irritant, and allergic contact dermatitis (ACD) to PPE and hand hygiene measures, as well as face mask induced pressure-related skin damage. The prevalence of occupational skin disease among HCWs in earlier studies (pre-COVID era) has been estimated to range from 20 to 50%. However, in two recent studies from Huibe, China, a staggeringly higher number of HCWs (97%, n = 526/542 and 71%, n = 234/330) HCWs engaged in the care of COVID-19 patients reported self-perceived skin barrier damage. Majority experienced skin dryness/tightness (70.3%) and desquamation (62.2%) commonly occurring on the nasal bridge (83.1%) (Fig. 1). Skin damage was more prevalent among HCWs wearing N95 masks and goggles for more than 6 h a day, whereas the face shield produced no such effect on prolonged wearing. Goggles were reported as the commonest (51.92%) culprit among PPE and about a fifth of patients reported work absenteeism because of dermatitis. Face mask and headgear worn tightly for prolonged hours result in ACD, ICD, pressure urticaria, friction dermatitis, abrasions and aggravation of pre-existing dermatoses. N95 respirators may contain formaldehyde, a known allergen. Retro-auricular skin is vulnerable to frictional dermatitis due to ear loops of the facemasks. Frequent...