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Correspondence

Erythema multiforme and Kawasaki disease associated with COVID-19 infection in children

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Dear Editor

We read with interest the publications in the JEADV which reported dermatological manifestations associated with COVID-19, such as pityriasis rosea, urticaria, rash, vascular signs, or chilblain-like lesions[1-6]. Herein, we report two life-threatening cases of children presenting with fever and eruptions with mucous membrane involvement – erythema multiforme and Kawasaki disease – associated with COVID-19.

Case 1

A 6-year-old male was hospitalized for painful cheilitis that develop during the week before admission and rapidly became associated with a rash of the extremities, and conjunctivitis. The patient was reported to have had a loss of appetite, without any other symptoms. The father reported having transient anosmia 2 weeks before. There was no history of recent medication. At admission, clinical examination revealed severe erosive cheilitis (Fig. 1A) with diffuse gingival erosions and thick hemorrhagic crusts, bilateral conjunctivitis, associated with multiple target lesions (Fig. 1B, 1C). Respiratory function was normal. The clinical picture led to a diagnosis of erythema multiforme. *Mycoplasma pneumoniae* serology was negative. The herpes simplex virus (HSV) polymerase chain reaction (PCR) test, on buccal erosions, was also negative. A first COVID-19 test, carried out by PCR, was negative; however, a second test was positive. The child's condition improved and he was discharged 2 weeks after.

Case 2

A 3-year-old male was hospitalized for fever > 39.0°C for 8 days. The fever was associated with asthenia, generalized exanthema, cheilitis, stomatitis, and bilateral conjunctivitis. His mother had been diagnosed with COVID-19, 3 weeks earlier. Clinical examination revealed generalized exanthema (Fig. 2A), bilateral palmar edema, glossitis, and cervical lymphadenopathy. Desquamation of the extremities was noted during a subsequent examination (Fig 2B).Laboratory tests showed an increase in inflammatory biomarkers: CRP = 195 mg/L, and hyperleukocytosis (leukocytes=17,400/mm^3). A COVID-19 PCR test performed at admission was negative. The CT scan revealed ground-glass opacities and consolidation in the right posterobasal area (<10% of the lung parenchyma), suggestive of COVID-19 pneumonia (Fig. 2C). We concluded a final diagnosis of COVID-19-associated Kawasaki disease. The child was treated with an initial dose of intravenous gamma globulin (2g/kg).

This case report provides a detailed description of severe cutaneous manifestations occurring in two children with COVID-19. The manifestations reported in our first case are typical of erythema multiforme, with particularly severe mucosal lesions being noted in this child. The main causes of erythema multiforme in children are *Mycoplasma pneumoniae* and HSV[7]. Other viruses and bacteria, together with some vaccines, have also been reported to trigger erythema multiforme[7]. In our case, the absence of any serologic and biologic evidence of HSV or of mycoplasma infection, together with the positive result for the second COVID-19 test led us to a final diagnosis of COVID-19-associated erythema multiforme.

The skin condition in our second case was diagnosed as Kawasaki disease. Kawasaki disease is a systemic vasculitis for which the etiology remains unknown, although it seems likely that immunologic and infectious mechanisms, associated with either viruses or bacteria, are involved[8-9]. Several studies have investigated whether there is a link between the common human coronavirus (HCoV) NL-63 and Kawasaki disease, but no associations have been identified so far. A 2014 study indicated that HCoV-229E could be a possible causative agent for Kawasaki disease[10]. Although the COVID-19 PCR test performed on the child described in our case report was negative, the results of the CT scan were very suggestive of COVID-19 pneumonia. This case strongly suggests that Sars-CoV-2 is a trigger for Kawasaki disease.

Finally, it is interesting to note that neither of the two children with COVID-19 described in this report had respiratory symptoms and that cutaneous manifestations were at the forefront of the clinical picture.

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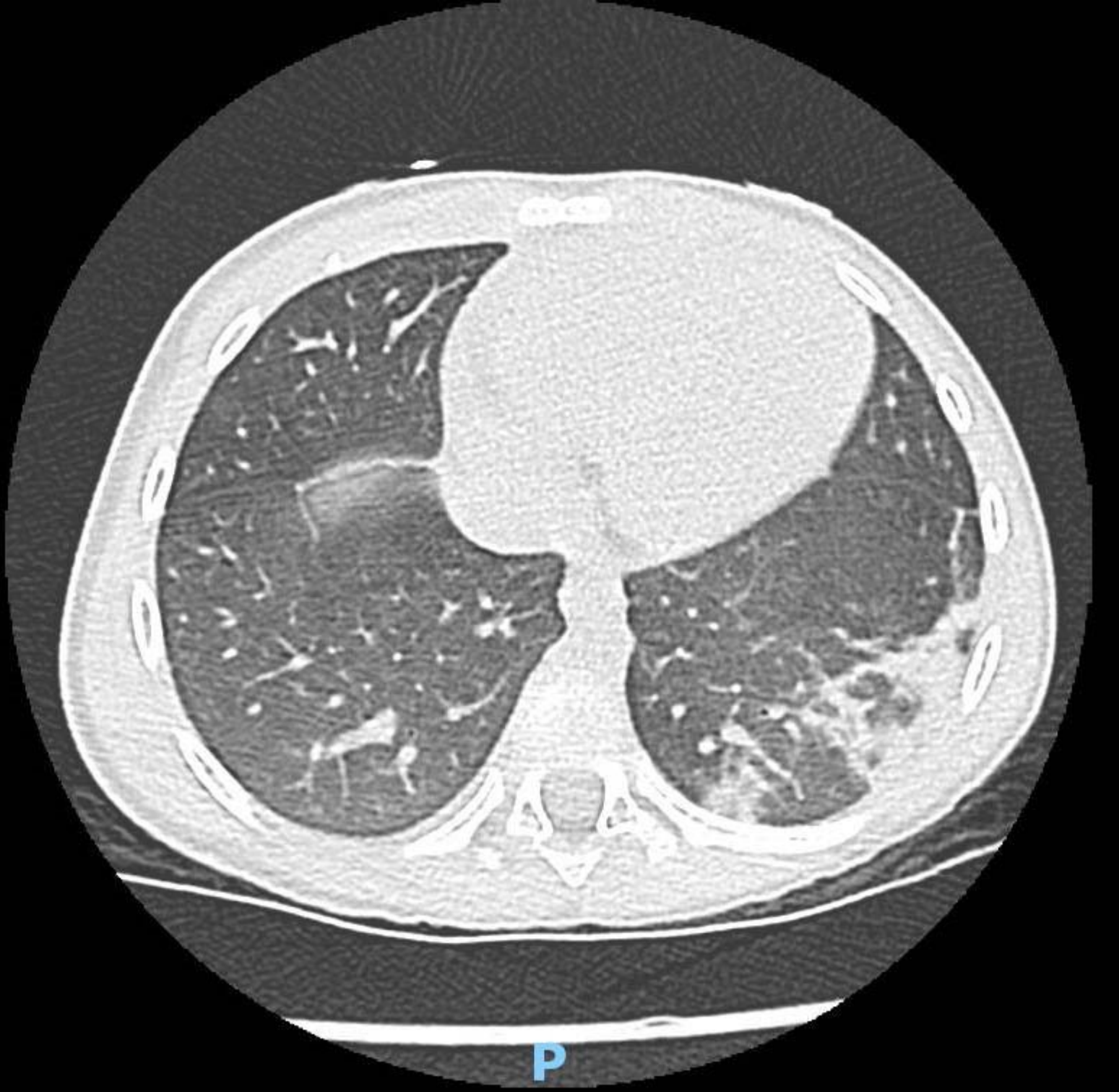
Figures

Figure 1. Erythema multiforme in a 6-year-old boy (case 1). **A**. Severe erosive cheilitis and a typical "target" lesion on the right cheek. **B**. A typical "target" lesion on the right foot and, **C**. left hand.

Figure 2. Kawasaki disease in a 3-year-old boy (case 2). **A**. Generalized exanthemas with desquamation. **B**. Finger desquamation. C. A CT scan showing typical signs of COVID-19 pulmonary involvement (case 2)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