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Letter

Absence of Severe Complications From SARS-CoV-2 Infection in Children With Rheumatic Diseases Treated With Biologic Drugs

To the Editor:

We read with interest the editorial by Cron and Chatham[1] suggesting a cytokine storm syndrome (CSS) occurring in response to SARS-CoV-2 infection and, consequently, a possible role for targeted approaches to blocking inflammatory cytokines.

Almost 30% of patients with coronavirus disease 2019 (COVID-19) develop severe acute respiratory distress syndrome with a high mortality rate[2]. In those critically ill patients, there are clinical signs and symptoms, as well as laboratory abnormalities, that suggest a CSS is occurring in response to the viral infection[1].

In contrast to adults, pediatric patients with COVID-19 seem to have a milder clinical course and asymptomatic SARS-CoV-2 infections may be frequent[3]. However, albeit rarely, severe infections may occur even in children, with pediatric intensive care unit admission or high-flow ventilation. In a recent Spanish cohort, 60% of confirmed infections in children required hospitalization[4].

COVID-19 pediatric transmission routes include close contact with family members, exposure to epidemic areas, or both. The school community is a place that can rapidly enhance the spread of a highly infectious virus, and Italian children may have been exposed to SARS-CoV-2 infection weeks before the school lockdown decided by the government.

Several concerns have been raised about children with autoimmune or autoinflammatory conditions characterized by an increased infectious risk, due to both the immune dysregulation of the underlying disease and its immunosuppressive treatment, including glucocorticoids, conventional disease-modifying antirheumatic drugs (cDMARD), and biologic DMARD (bDMARD). However, the increasing knowledge about the pathophysiology of SARS-CoV-2 infection is paradoxically supporting the beneficial role of some well-known antirheumatic drugs for the management of severe COVID-19[5]. Preliminary experience has shown that adult patients with chronic arthritis treated with bDMARD or cDMARD do not seem to be at increased risk of respiratory or life-threatening complications from SARS-CoV-2 compared with the general population[6]. Moreover, in another recent report on patients with inflammatory bowel disease treated with cDMARD and/or bDMARD, none of them were affected by a complicated SARS-CoV-2–related pneumonia[7].

Pediatric rheumatologists are certainly involved in decisions related to chronic care and management during this difficult period[8], but to the best of our knowledge, there are no published data yet related to the risk of severe complications from SARS-CoV-2 infection in children affected with rheumatic diseases.

In order to investigate the effect of COVID-19 on pediatric patients with rheumatic diseases treated with bDMARD, with or without cDMARD, a questionnaire was prepared and administered in our pediatric rheumatology clinics in Milan, Lombardy, the most affected region in Italy. The survey evaluated patients' health conditions, direct exposure to subjects known to be affected by COVID-19, modifications of ongoing DMARD treatment, and potential flares of underlying disease during the early weeks of Italian COVID-19 outbreak. All patients had provided their informed consent for the use of personal and clinical data for scientific purposes, and no patient refused to participate.

Between February 25 and April 14, 2020, we collected data from children treated with bDMARD and followed in the ASST Pini and Fondazione IRCCS Cà Granda Policlinico hospitals in Milan. The survey was administered face-to-face to all patients during outpatient clinic visits, or by telephone in those who missed a scheduled visit during the period under review. The final study population included 123 pediatric patients (83 [62%] female, median age 13 yrs, range 4–20) taking bDMARD for chronic rheumatic diseases (89 with juvenile idiopathic arthritis, 5 with chronic uveitis, 5 with autoinflammatory disease, 2 with recurrent pericarditis, and 22 with other chronic rheumatic diseases). As shown in Table 1, none of them were confirmed cases of COVID-19. Eight children presented mild respiratory symptoms; 3 of them were family members of adults suspected for COVID-19 infection. In our region, diagnostic swabs are not routinely performed, and a case is considered probable in the context of epidemic area and compatible clinical signs and symptoms (fever, cough, dyspnea). No patient stopped ongoing therapy or needed hospitalization. All contacted patients declared that they had adopted a preventive strategy against COVID-19 based on social distancing and use of personal protective equipment, even if this usually happened only after the beginning of the outbreak.

Table 1. Characteristics of 123 pediatric patients with chronic rheumatic diseases on bDMARD.

Disease	
JIA	89 (72.3)
Oligoarticular	60 (48.8)
Polyarticular, RF-negative	14 (11.4)
Polyarticular, RF-positive	0
Enthesitis-related arthritis	4 (3.3)
Systemic JIA	7 (5.7)
Psoriatic	4 (3.3)
Autoinflammatory diseases	5 (4.1)
Chronic uveitis	5 (4.1)
Recurrent pericarditis	2 (1.6)
Other	22 (17.9)
Female	83 (62.4)
Disease duration, yrs, median (IQR)	6 (3–10)
bDMARD	
Anti-TNF	95 (77.2)
Etanercept	38 (30.9)
Adalimumab	53 (43.1)
Infliximab	4 (3.3)
Anakinra	7 (5.7)
Tocilizumab	7 (5.7)
Canakinumab	2 (1.6)
Baricitinib	1 (0.8)
Other	11 (8.9)
Concomitant cDMARD	
Methotrexate	77 (62.7)
Colchicine	3 (2.4)
Cyclosporine	1 (0.8)
Mycophenolate mofetil	1 (0.8)
Systemic steroids	6 (4.9)
Confirmed COVID-19 infection	0
Suspected COVID-19 infection	0
Children with mild respiratory symptoms	8[a]

Values are expressed as number (%) unless otherwise indicated. [a] Three of them had adult family members suspected of having COVID-19. bDMARD: biologic disease-modifying antirheumatic drug; cDMARD: conventional disease-modifying antirheumatic drug; COVID-19: coronavirus disease 2019; JIA: juvenile idiopathic arthritis; RF: rheumatoid factor; TNF: tumor necrosis factor.

Our results do not allow any conclusions on the incidence rate of SARS-CoV-2 infection in children with rheumatic diseases, nor on the overall outcome of immunocompromised patients affected by COVID-19. However, according to the above-mentioned observations on adult rheumatology patients[6], our preliminary experience supports the idea that patients with chronic diseases treated with bDMARD do not seem to be at increased risk of respiratory or life-threatening complications from SARS-CoV-2 compared with the general population. Keeping the disease under control may therefore be extremely important even during the epidemic, since it is known that disease activity may be a risk factor for superimposed infections.

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The authors declare no conflicts of interest.

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