Radiology

Pediatric Abdominal US in Times of a COVID-19 Pandemic

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In December 2019, a novel coronavirus disease (COVID-19) caused by SARS-CoV-2 was diagnosed in the Chinese city of Wuhan. Due to the rapid spread of the virus worldwide, the World Health Organization officially declared a global pandemic on March 11, 2020. Although this virus generally causes more severe disease in middle-aged and older adults as compared with children, a novel specific pediatric presentation emerged concurrently with COVID-19. This novel disease in children is referred to as pediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS), or multisystem inflammatory syndrome in children (MIS-C).

In April 2020, Riphagen et al (1) were the first to describe a group of children with hyperinflammatory syndrome with multiorgan involvement. PIMS-TS is a severe inflammatory disease, usually developing 3–6 weeks after SARS-CoV-2 infection. Partly due to this long interval after initial infection, the molecular diagnostic tests to confirm a SARS-CoV-2 infection (reverse transcription polymerase chain reaction test from a nasopharyngeal swab) can be negative, hampering the diagnosis of PIMS-TS (2). However, detection of humoral immune responses to diagnose if a child had a past SARS-CoV-2 infection can aid in this context. Humoral immunity to SARS-CoV-2 is usually monitored by the detection of SARS-CoV-2–specific antibodies (mainly of the immunoglobulin G [IgG] isotype) in blood.

In children with PIMS-TS, only a minority present with positive circulating SARS-CoV-2 IgG antibodies. A recent study reported on detectable SARS-CoV-2 IgG in saliva, whereas circulating IgG levels were undetectable (3). Adults (presenting with COVID-19) usually show antispike (S) immunoglobulins G, M, and A antibodies and antinucleocapsid (N) IgG antibody, while children (with or without PIMS-TS) respond with IgG antibodies specific for the S protein but not the N protein (4).

MIS-C affects mainly children in their late childhood. Severe COVID-19 in children is associated with young age, comorbidity (usually obesity), and respiratory dysfunction. But, in contrast to COVID-19 infections, comorbidities are only present in a minority of pediatric patients with MIS-C (2). The clinical findings of PIMS-TS, with data based on a systematic review by Hoste et al (5), typically consist of an ubiquitously present fever (922 of 928 patients, 99.4%) in combination with gastrointestinal complaints in 85.6% (598 of 699 patients) (eg, abdominal pain [315 of 539 patients, 58.4%], vomiting [306 of 532 patients, 57.5%] and/or diarrhea [268 of 532 patients, 50.4%]), rashes (466 of 849 patients, 54.9%), cardiovascular dysfunction (307 of 387 patients, 79.3%; eg, tachycardia [194 of 253 patients, 76.7%], myocarditis [128 of 309 patients, 41.4%], and hemodynamic shock or hypotension [416 of 695 patients, 59.9%]), and respiratory tract symptoms (50%; eg, upper respiratory tract symptoms [95 of 397 patients, 23.9%], dyspnea [101 of 378 patients, 26.7%], and [multiple] infiltrates at imaging [114 of 321 patients, 35.5%]) (5). A quarter of children (130 of 557, 23.3%) with PIMS-TS presented with clinical symptoms fulfilling the criteria for the diagnosis of Kawasaki disease (fever, mucocutaneous abnormalities, conjunctivitis, palmar edema, and/or erythema) and another quarter (99 of 411, 24.1%) fulfilled two of three criteria (5). Thus, Kawasaki disease and PIMS-TS are sometimes indistinguishable. Typically, children with PIMS-TS present with multiorgan inflammation and dysfunction, necessitating hospitalization (6). Children with PIMS-TS usually present with cardiovascular dysfunction, ranging from tachycardia to cardiac shock necessitating cardiovascular support. Furthermore, in contrast to children with Kawasaki disease, children with PIMS-TS often present with gastrointestinal symptoms (2). The majority of children with PIMS-TS are usually treated with a combination of intravenous immunoglobulin, steroids, or immune-suppressive antibodies such as infliximab (anti–tumor necrosis factor), anakinra (interleukin 1 receptor antagonist), or interleukin

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Conflicts of interest are listed at the end of this article.

See also the article by Meshaka et al in this issue.

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6 inhibitors (tociluzimab or siltuximab). The mortality rate of MIS-C is reported to be low (1.5%) (2).

In this issue of *Radiology*, Meshaka et al (7) present their findings of abdominal US in PIMS-TS. The authors report on a single-center retrospective consecutive case series of 140 children and young adults with a clinical suspicion of PIMS-TS referred for abdominal US in a tertiary referral center. Of these 140 patients, 120 were subsequently diagnosed with PIMS-TS and 102 underwent abdominal US. The US examinations were performed according to the local protocols by radiology residents. All patients with PIMS-TS were invited for clinical follow-up at 6 weeks and 6 months after discharge, with 115 of 120 (96%) reviewed at 6 weeks and 56 of 120 (47%) reviewed at 6 months at the time of writing the original report. Children had at least one gastrointestinal clinical symptom in combination with fever at the time of abdominal US.

At the initial US examination, 86 of 102 examinations (84%; 95% CI: 77, 91) showed abnormalities, with the following abnormalities being most prevalent: ascites in 65 of 102 patients (64%), increased periportal echogenicity in 21 (21%), hyperechoic inflammatory mesenteric fat in 16 (16%), enlarged kidneys in 17 (17%), gallbladder debris in 15 (15%), mesenteric lymphadenopathy in 14 (14%), and bowel wall thickening in 14 (14%). In addition to these abdominal imaging findings, the fecal calprotectin level was tested in 54 patients; calprotectin levels were raised in 25 (46%).

After 6 weeks, only a minority of patients (14 of 115, 7%) had persisting abdominal symptoms and, in 18 of 43 tested patients (42%), the fecal calprotectin level was still raised. In only 31 of 120 patients (26%), follow-up US was performed at intervals ranging from 8 to 269 days, whereas seven patients underwent US at follow-up without undergoing US at presentation. Of the patients who underwent US at presentation and less than 2 months of follow-up (24 of 27, 89%), 20 of 24 (83%) had an abnormality at presentation. That number was reduced to 11 of 20 (55%) within 2 months. Seven of 27 patients (26%) had mesenteric inflammation, and three of 27 (11%) still had visible bowel inflammation at follow-up, albeit at significantly reduced levels as compared with levels at initial presentation. The incidence of other abnormal findings was also reduced.

At 6-month follow-up, seven of 56 patients (13%) had persisting abdominal symptoms. Of the 17 patients who underwent US more than 2 months after initial presentation, all abdominal abnormalities had resolved (except in one patient with hemophagocytic lymphohistiocytosis with persistent splenomegaly).

A major strength of this study is the relatively homogeneous study population seen in a large tertiary center dedicated to pediatrics and the availability of follow-up data. It underscores the fact that, although PIMS-TS is a relatively rare disease, it can cause clinically significant disease with abdominal illness as shown with US examination. Fortunately, most of the abdominal illness due to SARS-CoV-2 is time-limited—but not in all children. The impact of long COVID in children with respect to the rate of incidence, impact, and clinical findings is still under evaluation (8). The reported incidence of long-term abdominal symptoms in 13% of patients at 6-month follow-up by Meshaka and colleagues (7) is in keeping with the data presented by Stephenson et al (9), indicating that long COVID can be a clinically significant health care problem in children.

Of note, an important limitation of this study is that follow-up US was performed in only a small subgroup of patients. However, the indication for US studies was based on clinical findings, so it is relatively safe to assume that no clinically significant abnormalities would have been found at abdominal US in asymptomatic patients.

Meshaka and colleagues (7) refer to a clinical dilemma that has arisen to differentiate acute appendicitis from PIMS-TS. There have been conflicting reports on an increase in the incidence and severity of acute abdominal presentations, including appendicitis, in children (10). In the study by Meshaka et al, two children underwent an appendectomy at a general hospital before being referred to a tertiary center and diagnosed with PIMS-TS. These were the only two children diagnosed with appendicitis in this cohort of children with PIMS-TS. The low number of patients with clinical suspicion of appendicitis within this study must be seen in the perspective that the Great Ormond Street Hospital for Children has no emergency department and only receives patients out-of-hours or complex cases as referrals from surrounding secondary level medical units. Therefore, the findings of this study may underreport the true incidence and severity of appendicitis.

Meshaka and colleagues (7) have shown the importance of abdominal imaging findings in PIMS-TS in a pediatric population. Lack of awareness of PIMS-TS–related US findings could lead to incorrect diagnoses, erroneous therapies, or, in extreme cases, unnecessary abdominal surgery.

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