

An Emerging Clinical Form of Acute Pancreatitis in Covid-19

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Abstract: Background: As the global severe acute respiratory syndrome coronavirus (SARS-CoV-2) pandemic continues, new clinical forms of the disease continue to emerge. While the coronavirus is responsible for gastrointestinal symptoms and acute hepatitis, researchers at the Royal University Hospital of Liverpool say they have identified cases of COVID-19-linked pancreatitis in young patients with COVID-19. Objectives: To establish influence of concomitant COVID-19 on clinical presentation and treatment strategy of patients with AP. Methods: This is a case report of pediatric patient admitted to a Pediatric Gastroenterology Unit, A. Harouchi Hospital, CHU Ibn Rochd, Casablanca, Morocco in October 2020 during the COVID-19 pandemic. Results: We report the observation of a 16-year-old girl, who received symptomatic outpatient treatment for influenza-like illness with a fever of 38.5°C before rapidly evolving in 1 week to stage E pancreatitis, where a SARS-CoV2 IgG and IgM viral serology was requested coming back positive with a negative nasopharyngeal PCR covid. Conclusion: In conclusion, pancreatitis caused by SARS-CoV-2 is a real but rare entity; in fact COVID-19 can present as pancreatitis. This case highlights acute pancreatitis as a complication associated with COVID-19 and underlines the importance of measuring pancreas-specific plasma amylase in patients with COVID-19 and abdominal pain. This diagnosis is important for adequate treatment and better management of systemic repercussions, such as SIRS, decreasing SARS-CoV-2 mortality.

Keywords: Pancreatitis, COVID-19, SARS-COV2, Gastroenterology

1. Introduction

Acute pancreatitis is rare in children. It is a serious condition and still presents diagnostic and management difficulties. Its causes are multiple, dominated by viral, biliary, traumatic and drug-related origins [1].

In children pancreatitis occurs in about 1/10,000 children per year. Viral infections are identified as a cause of acute pancreatitis in about 8%-10% [2]. The mechanism by which COVID-19 infection can cause pancreatitis is not as clear. Many studies have confirmed that SARS-CoV-2 infections can cause multiple organ damage. The lungs, heart, kidneys, immune system, and coagulation system are common targets of SARS-CoV-2 [3, 4]. It has been reported that COVID 19 can be combined with pancreatic injury [5, 6].

Angiotensin-converting enzyme-2 (ACE2), the functional virus host cell receptor, expressed in both exocrine and

endocrine pancreatic cells, plays a role in this disease process. The mechanisms of pancreatic injury in SARS-CoV-2 infection include direct cytopathic effects or indirect systemic inflammatory and immune-mediated cellular responses, resulting in organ damage or secondary enzyme abnormalities [7].

In the current pandemic, screening for SARS CoV-2 in children with acute pancreatitis should be considered in order to guide the workup and tailor the treatment. To date, the association between COVID-19 and pancreatitis has been limited to a few published cases in pediatrics and our observation constitutes one of the rare cases reported in the literature.

2. Observation

The young patient Hiba was admitted to the department for

a rather violent epigastric pain with transfixing irradiation without vomiting or transit disorder evolving for 2 days and occurring one week after an influenza-like syndrome made of headaches, myalgias and a fever of 38.5°C. However, she had no particular pathological history, notably no notion of contact with a confirmed covid-positive case, no drug intake, no toxic products and no notion of thoraco-abdominal traumatism.

On admission, the patient was conscious, with good hemodynamic constants, regular breathing, and afebrile. The abdominal examination was normal except for epigastric tenderness. This clinical picture of acute excruciating epigastric pain was suggestive of acute pancreatitis supported by an elevated lipase of 1124 IU/L.

The abdominal computed tomography (CT) scan (Figure 1) confirmed the diagnosis by showing a swollen pancreas with a collection in the corporal-caudal portion and heterogeneous enhancement after injection of the contrast medium. The presence of necrosis flows in the back cavity of the epiploica and the left pararenal space led to the conclusion of a stage E pancreatitis, without biliary, hepatic, renal or splenic anomalies. There was also a small right pleurisy with adjacent pulmonary collapse and a calcified nodule under the left posterobasal pleural space.

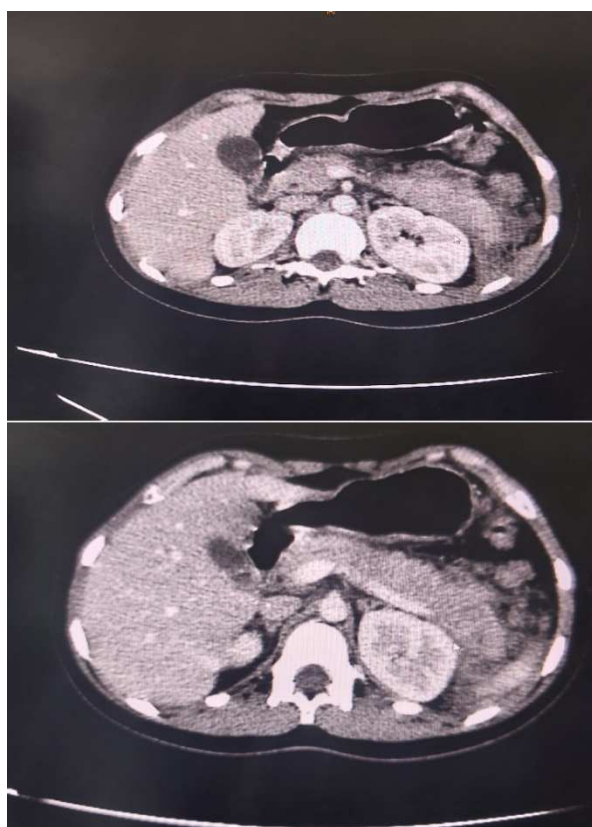


Figure 1. ABDOMINOPELVIAN CT scan: Aspect of acute pancreatitis classified as stage E according to BALHAZAR.

The biological workup was disturbed, showing an inflammatory syndrome with a C-reactive protein (CRP) elevated to 233 mg/L, a hyperleukocytosis to 20300/ mm³

with a predominance of neutrophils (78%), as well as a lymphopenia to 1400, contrasting with a negative procalcitonin to 0,06. The blood ionogram showed a hyponatremia of 133 mmol/day, the renal, kalemia, glycemia, calcemia and hepatic tests were normal.

As part of the etiological assessment of the acute pancreatitis, a lipidic assessment was requested, showing a normal level of cholesterol and triglyceride, the dosage of antinuclear antibodies (AAN) and anti-DNA in search of an autoimmune origin came back negative, the viral serologies of Epstein-Barr (EBV) and Cytomegalovirus (CMV) are also negative.

Because of the current context of the SARS cov 2 pandemic and the notion of a precessive influenza syndrome with a fever of 38.5°C reported by our patient 1 week before and the presence of lymphopenia, a nasopharyngeal covid PCR was requested and came back negative, but the SARS-COV2 IgG and IgM viral serology proved positive.

The initial management consisted of hydro electrolytic resuscitation, digestive rest, and analgesia with triple antibiotic therapy based on ceftriaxone, Ciprofloxacin and Azithromycin including VIT C and zinc according to the therapeutic protocol for the management of possible or confirmed cases of COVID -19 infection in children.

The disappearance of the pain was obtained after 4 days, with the progressive decrease of the lipase and the CRP, five days later, the girl was fed with a low-fat diet.

The evolution was favorable, marked by a good clinical and biological improvement with a good follow-up of 5 months.

3. Discussion

Acute pancreatitis in children is a rare condition, occurring in about 1/10,000 children per year. Viral infections are identified as the cause of acute pancreatitis in about 8% -10% [1], most commonly mumps, measles, coxsackie, Epstein-Barr virus and hepatitis A virus [2].

Like these viruses, SARS cov can cause pancreatitis, but to date, few studies are available and limited to a few published cases especially in pediatrics.

In our current pandemic context, the first case of pancreatitis in pediatrics was reported in a 7-year-old girl, admitted to the pediatric emergency room at the university hospital in the United States, with transfixing abdominal pain, eupnea in a context of apyrexia, her lipase was elevated to 676 U/L. An abdominal CT scan showed acute necrotic pancreatitis with pleurisy of small volume and she was also positive for COVID-19 by polymerase chain reaction, discovered during her hospital stay [8]. A retrospective study of 8159 pediatric patients admitted to 12 hospitals of a large health system in New York (Northwell Health System) during the COVID-19 pandemic identified 2 covid-positive cases out of 13 cases of acute pancreatitis [9].

The mechanism by which COVID-19 infection can cause pancreatitis is not clear. It is assumed that the pathogenesis of COVID-19 is mediated by the angiotensin-converting

enzyme receptor-2 (ACE-2) to which the coronavirus specular protein binds to enter the infected cell and then interact with the serine protease TMPRSS2, resulting in Viral replication in the contaminated tissue [10]. Yet CEA2 is involved in the regulation of the inflammatory response and is highly expressed in epithelial cells of the proximal and distal small enterocytes, as well as in pancreatic islets [11]. This therefore suggests a rationale for an over-incidence of digestive disorders and in particular diarrhea related to COVID-19 infection.

Although the exact mechanism is unknown, AP in COVID19 could occur due to the direct cytopathic effect of local SARS-CoV-2 replication or indirectly by a virus-induced detrimental immune response [12].

As the global pandemic of severe acute respiratory syndrome coronavirus (SARS-CoV-2) continues, new clinical forms of the disease continue to emerge. While the coronavirus is responsible for gastrointestinal symptoms and acute hepatitis, a group from Wuhan had reported a series of 9 patients susceptible to minor acute pancreatitis (AP) on the basis of mild hyperamylasemia, with a clear upsurge of cases since the start of the coronavirus epidemic [13]. In an autopsy review of 5 patients who died from COVID during their stay in the intensive care unit at the Raymond-Poincaré Hospital in France for a documented severe SARS-COV-2 infection requiring mechanical ventilation, shows that all patients had lesions of acute pancreatitis on examination associated with microfocuses of hemorrhagic suffusions on microscopic examination. Three patients were male and 2 were female, the mean age was 64.6 years. [14]

In our case, the CT scan showed not only a stage E

pancreatitis, but also a right pleurisy of small volume with adjacent pulmonary collapse and a calcified nodule under the left postero-basal pleural, testifying to the possibility of a coincidence between COVID-19-related pulmonary damage and the pancreatitis in a child.

The SIRS score currently replaces the Ranson score. It is defined by the presence of at least 2 or more of the following criteria: temperature < 36 or $> 38^{\circ}\text{C}$, heart rate > 90 beats/minute, respiratory rate > 20 /minute, and leukocytes < 4 or $> 12 \times 10^3/\text{L}$. The persistence of a high SIRS beyond 48 hours is highly predictive of severe AP [11], of which just one criterion of hyperleukocytosis was present in our patient, but in association with lymphopenia, which is almost constant and seems to be the most common in patients with severe forms of COVID-19.

It is unclear whether our patient's pancreatitis was associated or caused by COVID-19. As children remain PCR positive longer than adults, while our patient had a negative PCR 1 week after the onset of symptoms, but the presence of a positive SARS-COV2 IgM viral serology, as well as the absence of other etiologies, suggest a coronavirus-induced pancreatitis. The presence of IgM on COVID-19 serology, even without IgG and even with a negative PCR, associated with a symptomatology suggestive of COVID-19, requires isolation measures and the continuation of complementary investigations [15]. This confirms the causal link between pancreatitis and sars-cov2 infection in our case despite the negativity of the SARS-COV2 PCR which can be explained by the overlap period between the appearance of IgM and the negativity of the PCR.

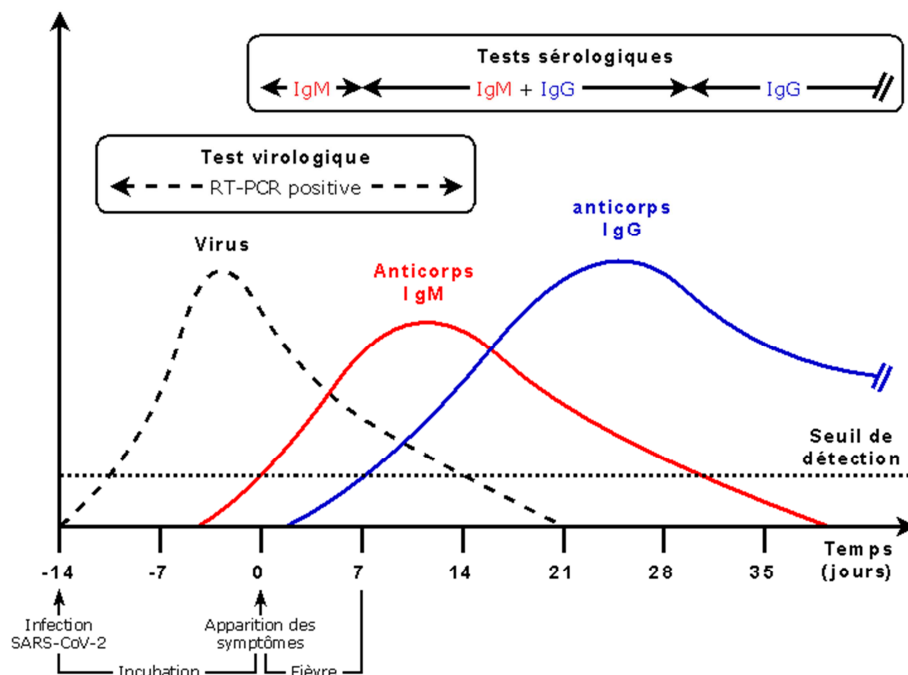


Figure 2. Appearance and temporal progression of different COVID-19-specific analytes as a function of time of exposure to the virus and onset of symptoms.

These cases highlight that, like other viruses, SARS COV2 can have acute pancreatitis as a complication, and underline

the importance of measuring plasma lipasemia in patients with COVID-19, systematically in front of gastrointestinal

symptoms, in order to orientate the assessment and to adapt the therapeutic management.

A classical diagnostic approach is essential for any acute pancreatitis before attributing it to SARS-CoV-2, including the search for a traumatic, drug-induced, autoimmune, toxic, infectious other than covid, and metabolic cause.

4. Conclusion

We believe that clinical presentation of COVID 19 infection and acute pancreatitis overlap with pain abdomen, respiratory involvement and pancreatic enzyme elevation. Great care needs to be taken to establish a diagnose of acute pancreatitis consequent to COVID 19 infection. This diagnosis is important for adequate treatment and better management of systemic repercussions, such as SIRS, decreasing SARS-CoV-2 mortality.

Further research is needed to explore the possibility of a causal link between COVID-19 and the occurrence of acute pancreatitis in children, and this can only be achieved through collaboration of several specialized centers, managing documented SARS-COV-2 infection in children to determine the mechanism of this condition. A better understanding of this relationship will better guide clinicians on early management strategies and focus medical resources toward those patients at risk for worse outcomes.

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