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Letter to the Editor

SARS-CoV-2 induced necrotizing pancreatitis

Pancreatitis necrotizante inducida por SARS-CoV-2

Dear Editor,

Acute pancreatitis diagnosis is a combination of clinical, laboratory and imaging findings. Common etiologies are alcohol, biliary obstruction/gall stones, drugs, trauma, and severe hypertriglyceridemia. While viral pancreatitis by HIV (human immunodeficiency virus), Cytomegalovirus, Coxsackievirus B, EBV (Epstein-Barr virus), Mumps and Influenza A (H1N1) has been reported, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) induced pancreatitis was rarely reported in the literature. We here-below present such a case.

A 62-year-old male presented to the Emergency Department complaining of shortness of breath at rest, watery diarrhea, vomiting and associated decrease in oral intake of two weeks' duration. His past medical history is significant for hypertension, type 2 diabetes mellitus and end stage renal disease status post kidney transplant four years ago.

Vital signs, including temperature, were within normal range. Physical exam was unremarkable except for decreased bilateral air entry. Initial blood tests were only suggestive of mild leukopenia with a white blood cell count (WBC) of 3600/cu.mm (reference range 4000–11,000/cu.mm) and acute kidney injury with creatinine level of 2.3 mg/dL compared to a baseline of 1.9 mg/dL (normal range). C-reactive peptide (CRP) was 58 mg/L (reference range 0–2.5 mg/L) and pro-calcitonin level was 0.2 ng/mL (reference range <0.05 ng/mL). Patient tested positive for SARS-CoV-2 on polymerase chain reaction (PCR). The patient was admitted to the SARS-CoV-2 unit at our institution.

On the second day, he reported severe epigastric pain radiating to the back. Physical exam revealed a soft abdomen with epigastric tenderness. Laboratory tests were significant for elevated lipase levels reaching 4361 U/L (reference range 13–60 U/L). Thus, the diagnosis of acute pancreatitis was made.

On further history, patient denied trauma, alcohol or steroid intake, scorpion sting, recent endoscopic retrograde cholangiopancreatography (ERCP) or previous pancreatitis. Medications were carefully reviewed with none associated with pancreatitis except for saxagliptin in less than one percent of cases. Saxagliptin was thus discontinued. Abdominal ultrasound showed no acute finding of cholelithiasis or cholecystitis, with no evidence of gallstones. Triglyceride level and liver function tests were unremarkable.

Epigastric pain failed to improve a week later despite treatment with perfalgan, hydration and cessation of saxagliptin. Resonance imaging (MRI) of the abdomen with gadolinium was positive for acute necrotizing pancreatitis involving the peripancreatic tissue with an acute necrotic collection supero-anterior to the pancreatic tail.

In the setting of worsening inflammatory markers, we opted to empirically treat with meropenem for a total of 6 days without CT-guided fine needle aspiration.

At the end of the antibiotic course, inflammatory markers trended down and epigastric pain resolved. By exclusion, and since the patient worsened despite cessation of saxagliptin, SARS-CoV-2 was attributed as a cause of the acute necrotizing pancreatitis.

SARS-CoV-2 induced pancreatitis was rarely described in case reports. Wang et al. reported mild pancreatic injury in 17% of patients with SARS-CoV-2 pneumonia. This was attributed to either direct viral involvement of the pancreas, or secondary to severe illness without substantial pancreatic injury.[1] In a large cohort study, Inamdar et al. showed a low prevalent association between SARS-CoV-2 and acute pancreatitis with a 0.43% incidence compared to 0.27% in patients without SARS-CoV-2.[2] As per the authors, the etiology of pancreatitis was undetermined in a significant proportion of SARS-CoV-2 patients.

The pathogenesis of SARS-CoV-2 induced pancreatic injury is thought to be related to the increased expression of angiotensin converting enzyme-2 (ACE-2) in the pancreatic islet cells of affected individuals.[3] SARS-CoV-2 has high binding affinity to transmembrane ACE-2 and uses a wide array of host proteases include transmembrane protease serine 2 (TMPRSS2) to facilitate cell entry following receptor binding.[4] ACE-2 mediated anti-oxidant, anti-hypertrophic and vasodilatory effects are lost following endocytosis to the enzyme along with SARS-CoV-2. In a cohort of SARS-CoV-2 patients, circulating angiotensin II (pro-inflammatory mediator) levels were markedly elevated compared to healthy control and markedly correlated to the viral load.[5] Indeed, ischemia, inflammation and pancreatic edema induced by SARS-CoV-2 ACE-2 blockade could be the culprits of this entity.

In conclusion, SARS-CoV-2 is a newly described cause of acute necrotizing pancreatitis. Given the overall low prevalence of pancreatitis compared to other gastrointestinal manifestations, this entity has mainly been reported in case reports. We suggest including pancreatitis in the list of SARS-CoV-2 gastrointestinal complications.

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High adenosine deaminase level in the pleural effusion of a case with leukemia

Nivel alto de adenosina desaminasa en el derrame pleural de un caso con leucemia

Dear Editor:

Tuberculosis, pneumonia and malignancies are among the most common causes of pleural effusions in adults. Elevated levels of adenosine deaminase (ADA) in patients with pleural effusion help clinicians to diagnose areas where tuberculosis is endemic. We present a case of T-cell leukemia associated with elevated ADA in a pleural effusion in a patient presenting with massive pleural effusion.

A 21-year-old female patient was admitted to our outpatient clinic with dyspnea and weight loss of 8 kg in 3 months. She had no cough, sputum, hemoptysis or fever. Although the patient migrated from Syria, which had a high prevalence of TB, she had no contact with TB. Her family history revealed that her sister was diagnosed with leukemia. On her physical examination, a mobile, 2 cm sized lymphadenopathy extending to the thyroid was found in the left supraclavicular fossa. On examination of the respiratory system, the left hemithorax was less involved in breathing and there was a matite up to the upper zone. Abdominal examination revealed splenomegaly and mild ascites, no hepatomegaly. In the laboratory findings; the blood white cell count was 8410 per microliter (mcL) and 71.5% were neutrophils and 19.1% were lymphocytes. The erythrocyte sedimentation rate was 10 mm/h. On chest X-ray, diffuse opacity reaching the apex was observed on the left. Computed tomography of the thorax which was taken four days ago in another health center; bilateral left greater pleural effusion, pericardial effusion close to 1 cm, and conglomerated lymphadenopathies surrounding the vascular structures of the mediastinum were observed. The patient was hospitalized and thoracentesis was performed on the left side. The pleural fluid was yellow in color, exudative, LDH level value was found 1959 units per liter (U/L) and white blood cell count was 59 310 mcL and the device could not distinguish lymphocytes. The right pleural fluid ADA level was reported as >150 U/L. Right thoracentesis was performed two days later, pleural fluid was yellow, exudative, LDH value 2444 U/L, white cell count was 37 680 mcL, 71.8% lymphocyte predominance. The left pleural fluid ADA level was reported as >150 U/L. Bilateral pleural fluid gram staining showed no bacterial and no culture growth. Acid-resistant bacilli (ARB) test and *Mycobacterium tuberculosis* polymerase chain reaction examination were negative and their cultures were negative. Interferon gamma release test for latent TB was negative. Cytological examination of fluid showed atypical T-cell proliferation and was found to be compatible with T-cell lymphoma or leukemia. Excisional biopsy of the left supraclavicular lymphadenopathy was performed for definitive diagnosis, reported as T-lymphoblastic type leukemia and treatment was initiated. Hematoxylin–Eosin stained preparations of lymph node showed diffuse infiltration of lymphoid blastic cells. In the immunehistochemical study, blastic cells were positive for CD3, CD4, CD5, CD7, Bcl-2 and TdT.

Written informed consent was obtained from the patient who participated in this case.

In adults, tuberculosis and parapneumonic effusions are the most common causes of benign pleural effusions, but malignant causes should be kept in mind. Lympho-proliferative diseases, especially lymphoma, are among the causes of massive pleural effusion.

Adult T-cell leukemia; the rate of chronic leukemia in adults is 2% and clinical findings include B-symptoms, conglomerated lymph nodes. Pleural or peritoneal effusion can be seen in the diagnosis at a rate of 25%.[1]

ADA is an enzyme involved in purine metabolism, especially in T-lymphocyte proliferation and maturation, which has an effect on the immune system in all cells. In diseases such as leukemia and lymphoma, ADA may be elevated in pleural fluid. Intracellular microorganisms such as Mycobacterium tuberculosis increase ADA secretion by stimulating lymphocytes.[2] Therefore, ADA is used as a biomarker in the diagnosis of tuberculous pleurisy. In a study, pleural effusion was detected in 30% of patients with Large B-cell lymphoma, and ADA level >35 U/L was found in 35% of fluids.[3]

ADA in pleural fluid has a very high sensitivity for tuberculosis. When pleural fluid is tested for TB, it is an extremely valuable biomarker for the clinician with high diagnostic sensitivity, specificity, positive probability ratio and negative probability ratio (92%, 90%, 9.03 and 0.10) according to the results of meta-analysis.[4]

Although pleural effusion cases with ADA elevation have been reported with lymphoma, there are no case reports of leukemia. In conclusion, in patients with lymphocytic pleural effusion with ADA elevation, other causes must be ruled out before diagnosis of tuberculosis, especially for the diseases that cause lymphocyte cell proliferation such as lymphoma and leukemia.

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