

DMARDS Complicated With Acute Pancreatitis in Young Boy with Ankylosing Spondylitis

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Case Report

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Abstract: Acute pancreatitis is defined as an acute inflammation of the pancreas that may also involve peripancreatic tissues and/or remote organ systems. Although the common causes of acute pancreatitis are gallstones and alcohol consumption, drug-induced cases are also reported frequently. While disease-modifying anti-rheumatic drugs (DMARDs) induced pancreatitis cases were less and rarely reported so the true incidence is unknown, quality of the evidence is limited since the availability of studies is very less. DMARDs are a commonly used in rheumatological conditions. It is a challenge to physicians to diagnose the drug-induced pancreatitis than other causes. In this case report, we describe a 20-year-old male patient who had received dual DMARDs tablets for Ankylosing spondylitis (AS) complicated with acute pancreatitis.

Keywords: Disease-modifying anti-rheumatic drugs, Methotrexate, sulfasalazine and pancreatitis

INTRODUCTION

Ankylosing spondylitis (AS) is an inflammatory condition that affects the joints, especially in the spine. Spondylitis simply means inflammation of the spine. As part of the body's reaction to inflammation; calcium is laid down where the ligaments attach to the bones that make up the spine. Disease-modifying anti-rheumatic drugs (DMARDs) are the treatments for AS when peripheral joints are involved. Drugs such as sulfasalazine and methotrexate can be helpful for arthritis in the joints of your arms or legs, though they are not usually effective for spinal symptoms [1].

They have used either alone or in combination with newer biological agents. Methotrexate acts as an anti-inflammatory drug and is now the most frequently used DMARD, particularly for severe disease. Methotrexate it starts working within 3 - 6 weeks, but its full effect may not occur until after 12 weeks of treatment.

Acute pancreatitis typically, presenting as abdominal pain with elevated levels of pancreatic enzymes. The majority cases of acute pancreatitis are related to gallstones or alcohol abuse held responsible for about 80% of all cases with other etiologic factors being less frequent. In 1959s, first-time thiazide-induced pancreatitis was reported, thereafter number of drug-induced pancreatitis were reported in the literature [2].

DMARD induced pancreatitis is very rare however, all DMARDs may produce stomach and intestinal side effects, and, over the long-term, each

poses some risk for rare but serious reactions. Commonly reported side effects of sulfasalazine include, gastric distress, headache, nausea, oligospermia, vomiting, and anorexia. Methotrexate can cause serious or life-threatening side effects on your liver, lungs, or kidneys, upper stomach pain, loss of appetite, dark urine, clay-colored stools, jaundice (yellowing of the skin or eyes), dry cough, shortness of breath, blood in your urine, and little or no urinating.

We reported a case with dual DMARDs including methotrexate and sulphasalazine, presented with a rare complication of pancreatitis. Generally, drug-induced pancreatitis is an acute oedematous pancreatitis of a benign course and good prognosis but fatal outcomes have been also reported.

In this case, the patient presented with typical epigastric pain with episodes of vomiting and elevated serum amylase and serum lipase as well as imaging. Ultrasonography revealed no evidence of Cholelithiasis

or liver abnormality. In addition, other possible causes of acute pancreatitis were excluded.

CASE REPORT

A 20-year-old student from Batticaloa Sri Lanka, with an unremarkable medical history, presented to Teaching Hospital Batticaloa with backache before 3 years. One year later, he had right knee-joint pain and swelling. He had no family history of rheumatic or skin diseases. On physical examination, he had swollen, tender right sided knee joint. Rheumatic factor and anti-cyclic citrullinated peptide (Anti-CCP) were negative, HLA-B27 was (positive) and 2D Echo was normal. X-ray pelvis was taken, which revealed evidence of sacroiliitis. He was diagnosed to have ankylosing spondylitis. Initially we have started non-steroidal anti-inflammatory drugs, but back pain and knee pain not responded. Then we started on methotrexate, sulfasalazine and prednisolone. After 1 year he defaulted treatment and followed indigenous medical advice. He defaulted indigenous medical treatment as well after another 1 year and again came back to the clinic.

He was started again on methotrexate, sulfasalazine and prednisolone. But still back pain and right knee joint pain were persisted. Three months later back pain partially resolved but right knee joint persisted as same. We liaised with rheumatologist and he suggested starting biological agent riluximab. He was admitted for assessment. While, in the ward he developed abdominal pain and vomiting. On examination abdomen was tender. C-reactive Protein 295 mg/dl, Blood urea 25mmol/l, Serum creatinine 0.6mmol/l, Serum amylase was 820 IU/L (reference range: 0-90 IU/L) and urinary amylase was 2,000 IU/L (reference range: 0-460 IU/L). His lactate dehydrogenase was 341 IU/L (reference range: 100-350 IU/L) and he had a leucocytosis of $11.6 \times 10^9 /L$ (reference range: $4.0-11.0 \times 10^9 /L$). Liver function tests, calcium level and lipid profile were all normal liver function test normal and ultra sound abdomen revealed, bulky pancreas, with isoechoic texture, free fluid in Morrison pouch and pouch of Douglas. The patient's chest X-ray was normal, Mantoux was positive while Acid Fast Bacillus (AFB) in sputum was negative. Patient was treated for acute pancreatitis; methotrexate and sulfasalazine were omitted and started on hydroxychloroquine.

DISCUSSION

Drug-induced acute pancreatitis mechanisms are currently based on facts extracted from case reports, case-control studies, animal studies, and other experimental data. Possible mechanisms for drug-induced acute pancreatitis include pancreatic duct constriction, cytotoxic and metabolic effects,

accumulation of a toxic metabolite or intermediary, and hypersensitivity reactions [3].

The diagnosis could be sulfasalazine induced acute pancreatitis which was an immune-mediated or hypersensitivity reaction and discontinuation of drug sulfasalazine resulted in resolution of symptoms [4,5]. Methotrexate has never been reported to be linked to pancreatitis, but available literature indicated that methotrexate combined with other immunosuppressant caused acute pancreatitis [6].

Last six month period, this patient was a number of medications including steroid, non-steroidal anti-inflammatory drugs (NSAIDs), DMARDs and indigenous medicine. We exactly can't say which medication responsible for acute pancreatitis. Non-steroidal anti-inflammatory drugs (NSAIDs) have rarely been identified as a definitive cause for acute pancreatitis. However, Paul Magill *et al.* reported a case in which NSAID responsible for the acute pancreatitis [7]. In addition to that, prednisolone medication is the well-known cause for the pancreatitis [8]. But recent study conducted by Chi Ching Chang *et al* which clearly stated that rheumatoid arthritis (RA) are at increased risk of acute pancreatitis compared with those without RA and to determine if the risk of acute pancreatitis varied by anti-RA drug use. Use of oral corticosteroid decreased the risk of acute pancreatitis (adjusted HR 0.83, 95% CI 0.73–0.94) but without a dose-dependent effect [9].

Even though the patient was on a number of medications, at present patient on Dual DMARDs, we felt that these two drugs could be a cause for acute pancreatitis. In a critical review, Mallory *et al* suggested that the sulfonamide component of Sulfasalazine was accountable for this adverse effect because of the structural resemblance of the sulfonamides to the thiazide diuretics, which are a well-recognized cause of drug-induced pancreatitis [10, 11]. However, sulphasalazine seems to be the most likely agent to have caused acute pancreatitis.

CONCLUSION

All patients with acute pancreatitis of unknown etiology should be carefully questioned on drugs possibly responsible for the induction of the disease and, in confirmed cases, the drug held responsible should be withdrawn and avoided in the future. Here we reported a case where DMARDs, NSAIDs and prednisolone were culprits for acute pancreatitis. However, sulphasalazine seems to be the most likely agent to have caused acute pancreatitis. It concludes that the continuous intake of prednisolone and NSAIDs may cause acute pancreatitis. However, Oral corticosteroid use decreased the risk of acute pancreatitis.

Conflict of interest

None to be declared

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