

Elevated Fecal Calprotectin Levels Can be Misleading if Guidelines are Not Properly Followed

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Patients can present with various gastrointestinal symptoms that might need thorough workup and intensive follow up. Many gastrointestinal diseases can cause an abnormally elevated levels of fecal calprotectin including, inflammatory bowel disease, colorectal cancer, intestinal cystic fibrosis, coeliac disease, infectious colitis, and necrotizing enterocolitis [1].

Calprotectin can be defined as a 24 kDa dimer. This is a dimer of calcium binding proteins S100A8 and S100A9. Calprotectin has recently emerged as an important test in the GI clinics. The calprotectin complex is resistant to degradation by most enzymes. This has led to the feasibility of its measurement in feces [2]. It has been reaffirmed in a recent paper that surgeons need to revise their medical knowledge especially during the COVID-19 era because of the new challenges that this new disease is presenting to GI surgeons and gastroenterologists [3].

Fecal calprotectin is usually measured in patients presenting with lower GI symptoms. Fecal calprotectin testing is recommended by the British NICE guidelines to help clinicians differentiate between inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) provided that gastrointestinal cancer is not suspected (for example, newly diagnosed iron deficiency anemia (IDA)) [4].

Two patients presented with abdominal pain and recent changes in bowel habits. The first patient, a 38-year-old female who presented with new onset severe bloody diarrhea and abdominal pain two months after hemorrhoidectomy surgery. The same surgeon referred the patient to a gastroenterologist who investigated her with fecal calprotectin and found it to be $> 1000 \mu\text{g/g}$ (quite elevated, negative $< 50 \mu\text{g/g}$). No fecal microscopy or culture were requested or done. The patient was rushed into a colonoscopy that showed inflamed and ulcerated colon. Random colonic biopsies confirmed Colitis (probably Ulcerative Colitis). The patient was started on 5-ASA (5-amino salicylate, Pentasa) but the patient failed to improve. Then the patient was referred to me and a short course of antibiotics and prednisolone were immediately started and improved the symptoms dramatically. The patient had a miscarriage at 4 months of her pregnancy and decided to stop the 5-ASA (Pentasa) because she did not have any GI symptoms at all for the previous few months. The patient presented to my clinic recently, 14 months after stopping her medications and she was still in remission. A proctoscopy was done in the clinic that showed a normal rectum. A repeat colonoscopy was done by me and showed normal colonic mucosa and a normal terminal ileum. Biopsies showed mild non-specific superficial colitis. No medications were restarted at all.

A second 41-year-old male patient presented with epigastric pain of 3 days duration. He was seen by a gastroenterologist who also requested fecal calprotectin levels. It was severely elevated at > 1000 µg/g. No fecal microscopy or culture were requested. He was fast tracked for double endoscopy and biopsies. His upper GI endoscopy showed duodenitis and evidence of gastric *Helicobacter pylori*. The *H. pylori* eradication triple therapy was started immediately (esomeprazole, clarithromycin and amoxicillin). The colon was normal but there was evidence of terminal ileitis. This was confirmed by magnetic resonance enterography (MRE). Biopsies confirmed enteritis probably Crohn's disease. The patient significantly improved after the double endoscopy and just before starting his 5-ASA (Asacol) and budesonide (Enterocort) tablets. The patient then presented to my clinic for a second opinion. He still did not have any recurrences of his lower GI symptoms despite not taking his IBD medications. I repeated his calprotectin levels and it was normal, less than 2 weeks after the first reading, despite him not having his CD medications.

These two cases confirm that elevated calprotectin can be associated with enteritis or colitis. Milder elevation of calprotectin can be associated with microscopic colitis. But the type of inflammation can be missed if a complete workup was missed before the endoscopy. Fecal microscopy, stool culture, iron levels, ferritin, CBC and also probably COVID-19 tests are all so vital to be done before performing lower GI endoscopy and biopsy. Otherwise the patient can be wrongly labelled with IBD while they might be suffering from temporary, probably infectious colitis and enteritis or even as a sequelae to a recent COVID-19 infection [5,6].

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