EJCRIM
European Journal
of Case Reports
in Internal Medicine

ISCHAEMIC COLITIS FROM AN UNUSUAL CAUSE: ORAL CONTRACEPTIVES

Mark A. Colantonio[1], Nathan Williams[2], Tahreem Ahmad[1], Waqas Ali[1]

[1] Department of Medicine, West Virginia University, Morgantown, USA
[2] Department of Pathology, University of Maryland, Baltimore, USA

Corresponding author's e-mail: macolantonio@hsc.wvu.edu

Received: 25/06/2024
Accepted: 08/07/2024
Published: 26/07/2024

Conflicts of Interests: Each author certifies that they, or a member of their immediate family, has no commercial association (i.e. consultancies, stock ownership, equity interest, patent/licensing arrangements) that might pose a conflict of interest in connection with the submitted manuscript. The authors have not used generative artificial intelligence or artificial intelligence associated technologies.
Patient Consent: Consent has been obtained from the patient and they have agreed to the use of their clinical information.
Acknowledgements: We would like to thank the teaching staff for affording us the opportunity to learn from clinical cases.

How to cite this article: Colantonio MA, Williams N, Ahmad T, Ali W. Ischaemic colitis from an unusual cause: oral contraceptives. *EJCRIM* 2024;**11**:doi:10.12890/2024_004731

ABSTRACT

Ischaemic colitis is responsible for more than half of the presentations of gastrointestinal ischaemia and develops due to an interruption of intestinal blood flow. Risk factors include increasing age and conditions associated with decreased perfusion. Infrequently, ischaemic colitis may develop in young females prescribed oral contraceptives. Here, we present a case of ischaemic colitis secondary to oral contraceptives that resolved with medication discontinuation.

KEYWORDS

Ischaemic colitis, oral contraceptives, gastrointestinal ischaemia, haematochezia

LEARNING POINTS

- Ischaemic colitis is due to insufficiency of intestinal blood flow and is responsible for half of the cases of gastrointestinal ischaemia.
- Oral contraceptives have an increased odd of 1.05 predisposing development of ischaemic colitis.
- Symptoms typically resolve with removal of the oral contraceptive.

INTRODUCTION

Ischaemic colitis (IC) is characterised as an interruption in intestinal blood flow leading to inadequate oxygen supply to vital regions of the gastrointestinal tract[1]. Not uncommon, IC is responsible for roughly 50% of cases of gastrointestinal ischaemia[1]. Affected areas most commonly include intestinal watershed areas, as these areas are especially sensitive to disruptions in blood flow due to limitations in collateral blood flow[1]. Colonic hypoperfusion leading to ischaemia can be secondary to an embolic arterial occlusion, vein thrombosis or non-occlusive aetiology[1]. Risk factors linked to various aetiologies have been associated with IC, as have pathologies related to a decrease in perfusion, including chronic systolic/diastolic heart failure, shock and mechanical obstruction[1]. Medications have also been found to be connected to IC, including non-steroidal anti-inflammatory drugs, diuretics, vasopressors and hormonal therapies[1]. Cubiella Fernández et al. performed a retrospective case

EFIM European Federation of Internal Medicine

Publisher smc media srl

control study analysing specific risk factors linked to IC[2]. Out of 161 cases, diabetes, hyperlipidaemia, heart failure, arterial disease, non-steroidal anti-inflammatory drugs and digoxin were common associations[2].

When assessing a patient with suspected IC, classification is important to further identify the aetiology. IC can be broadly categorised into gangrenous and non-gangrenous subtypes and further sub-classified according to the Brandt and Boley classification system, which ranges from reversible in aetiology to fulminant, universal ischaemia[1]. IC can present with a broad range of symptoms. Abdominal pain is the most frequent symptom, occurring in 87% of cases, whereas haematochezia occurs in 84% of cases and diarrhoea in 56% of cases[3]. Haematochezia is more common in left-sided IC due to splenic flexure proximity, whereas right-sided colitis presents more frequently with abdominal pain[3].

Oral contraceptive pills (OCP) are the most common type of birth control prescribed in the United States[4]. Most commonly prescribed to prevent pregnancy, OCPs are also used for the management of endometriosis, menstrual pain and even acne[4]. Although 25% of women from 15 to 44 years old are prescribed OCPs, these medications are not without side effects[4]. To date, few studies have explored the association between IC and oral contraceptive use. Here, we present an unusual case of IC in healthy 20-year-old female prescribed oral contraceptives.

CASE DESCRIPTION

The patient is a 20-year-old female with past medical history of seasonal allergies, asthma and endometriosis, who presented to the emergency department with a complaint of lower abdominal pain and bloody stools that abruptly woke her up the morning before with nausea and vomiting. During the interview, the patient denied a family history of inflammatory bowel disease. She stated that she had developed recurrent episodes of diarrhoea with associated haematochezia and denied a previous occurrence of these episodes. Initial work-up revealed a white blood cell count of 20.4 × 10^3/µl; otherwise, the patient's complete blood count, including haemoglobin, was within normal limits. The basic metabolic panel, beta hCG, hepatic function panel, carcinoembryonic antigen, lipase and erythrocyte sedimentation rate (ESR) were within normal limits. C-reactive protein (CRP) was elevated to 13.4 mg/dl; a BioFire® GI and *Clostridium difficile* test were also ordered, which were both negative. Computed tomography (CT) of the chest, abdomen and pelvis revealed diffuse colonic wall thickening with mucosal fatty infiltration of the ascending colon with scattered diverticula, concerning for chronic inflammatory colitis. Gastroenterology was subsequently consulted and recommended a colonoscopy for further evaluation. Antibiotics were withheld as the patient was afebrile throughout her admission. The elevation of inflammatory markers including her white blood cell count and CRP were thought to be secondary to inflammation. A terminal ileum biopsy and left colon biopsy were performed during the colonoscopy. The terminal ileum biopsy revealed small bowel mucosa with no diagnostic abnormalities recognised; however, the left colon biopsy revealed colonic epithelium with areas of atrophic crypts, lamina propria haemorrhage and superficial acute inflammation. These findings were most consistent with IC. Pseudomembranous colitis could also have been considered; however, *C. difficile testing* was negative. Per Gastroenterology, it was recommended to discontinue oral contraceptive pills as this is a risk factor for IC. A repeat colonoscopy in 3 months was scheduled to evaluate the response to therapy. At follow-up, the patient denied abdominal pain, haematochezia or melena. She also reported having at least one formed bowel movement daily without evidence of blood or mucus. She continues to follow-up with Gastroenterology and will undergo a colonoscopy later this year.

DISCUSSION

IC is one of the most common subtypes of gastrointestinal ischaemia[1]. Without a high suspicion, IC is often misdiagnosed as an inflammatory bowel subtype, including Crohn's disease or ulcerative colitis[1]. Clinicians should have a high suspicion for IC especially in the elderly, as advancing age is a known risk factor[5]. Park et al. sought to identify risk factors associated with IC in a case control study, identifying age greater than 60 as an independent risk factor[5]. Further research has shown that 90% of IC cases occur in the elderly[6]. Our case demonstrated a rare presentation of IC in an otherwise healthy, 20-year-old female. When assessing an otherwise young, healthy patient presenting with symptoms consistent with IC, other risk factors must be explored. Although multicentre trials have not explored the relationship between OCP use and IC, observational studies have sought to identify a relationship, with the first known documentation in 1972 by Gelfand[6]. This case demonstrated recovery and resolution of symptoms after discontinuation of the offending OCP, similar to our case. Thrombotic

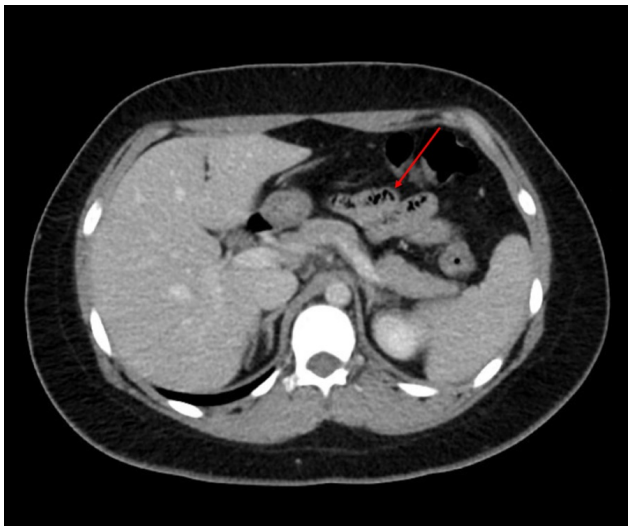

Figure 1. Abdominal CT scan at initial presentation. Red arrow demonstrates dilated, oedematous air-filled bowel representing pneumatosis.

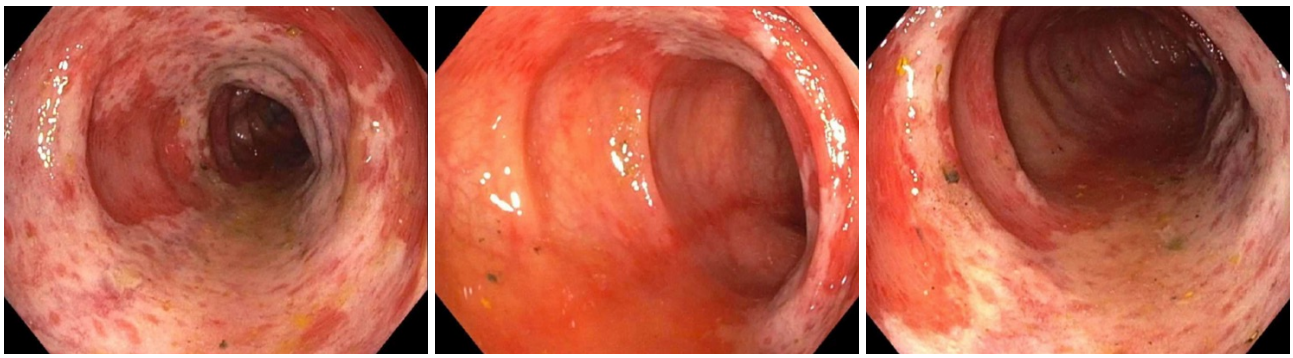

Figure 2. Diagnostic colonoscopy revealing mucosal congestion and friability, both of which are consistent with acute IC.

properties of OCPs are thought to predispose these individuals to the development of IC due to elevated clotting factors and fibrinogen with a relative decline in protein S and antithrombin[6]. Chang et al. sought to determine the odds of developing IC in roughly 8,700 patients prescribed OCPs over a five-year period[7]. This study demonstrated increased odds of 1.05 for the development of IC in this population. To further explore the relationship between OCPs and the development of IC, a Naranjo algorithm score was calculated[8,9]. Based on prior evidence of this documented association, the development of IC after administration of the drug and improvement after discontinuation, a Naranjo score of 4 was calculated, indicating the possibility of IC secondary to OCP exposure[8,9]. As OCPs and other hormonal contraceptives play a vital role in women's health, adverse events – including IC – should be discussed with patients; however, development of this adverse event should not defer use as this population has demonstrated promising recovery once the agent is discontinued[6].

When IC is suspected, abdominal CT with contrast is the diagnostic imaging modality of choice[1]. Typical findings include colonic wall thickening and stranding[1]. Gas cysts, also called pneumatosis coli, is also a hallmark finding in IC, although not specific to IC. CT imaging of our patient revealed both colonic wall oedema and pneumatosis coli, both suggestive of IC *(Fig. 1)*[10]. In cases where there is not a high suspicion for IC, an abdominal X-ray can also be obtained[11]. Common findings include 'thumbprinting', colonic thickening and gas-filled loops of bowel[11]. Although non-specific, laboratory markers can be helpful when determining the severity and acuity of IC[1]. Lactate, amylase and leukocytes are typically normalised in acute presentations of IC; however, they can be elevated in prolonged ischaemic damage[1]. Choi et al. performed a multicentre, retrospective study analysing characteristics of mild and severe cases of IC[12]. In this study, an average CRP of 5.59 mg/dl and 11.70 mg/dl were associated with mild and severe ischaemic, respectively[12]. ESR was also analysed, finding an ESR of 30.23 mm/hr and 40.17 mm/hr associated with mild and severe cases of ischaemia. In our case, CRP was elevated to 13.4 mg/dl whereas ESR was within normal limits. Our case highlights the importance of using multiple laboratory studies to further categorise and stratify disease severity when presented with a case of IC.

Although identifiable on radiographic imaging including CT scan and plain radiography, colonoscopy is the gold standard to confirm the diagnosis of IC[1] *(Fig. 2)*. For the most accurate histological results, biopsy is recommended to be performed within 48 hours of presentation[1]. Common histological findings from biopsy include friable mucosa, along with oedematous tissue fragments[13]. In more advanced, severe cases of IC, a biopsy will show evidence of haemorrhage, as in the findings of our case[14]. Management for OCP-induced IC includes discontinuation of the offending agent, which typically leads to symptom resolution within weeks[6]. Once OCPs were discontinued, the patient's abdominal pain and haematochezia resolved.

REFERENCES

1. Theodoropoulou A, Koutroubakis IE. Ischemic colitis: clinical practice in diagnosis and treatment. *World J Gastroenterol* 2008;**14**:7302–7308.
2. Cubiella Fernández J, Núñez Calvo L, González Vázquez E, García García MJ, Alves Pérez MT, Martínez Silva I, et al. Risk factors associated with the development of ischemic colitis. *World J Gastroenterol* 2010;**16**:4564–4569.
3. Hung A, Calderbank T, Samaan MA, Plumb AA, Webster G. Ischaemic colitis: practical challenges and evidence-based recommendations for management. *Frontline Gastroenterol* 2019;**12**:44–52.
4. Cooper DB, Patel P. Oral contraceptive pills. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.
5. Park CJ, Jang MK, Shin WG, Kim HS, Kim HS, Lee KS, et al. Can we predict the development of ischemic colitis among patients with lower abdominal pain? *Dis Colon Rectum* 2007;**50**:232–238.
6. Rajamanuri M, Garg M, Siddiqui H, Pannala S. Progesterone-only contraceptive-induced ischemic colitis. *ACG Case Rep J* 2024;**11**:e01313.
7. Chang L, Kahler KH, Sarawate C, Quimbo R, Kralstein J: Assessment of potential risk factors associated with ischaemic colitis. *Neurogastroenterol Motil* 2008;**20**:36–42.
8. Adverse Drug Reaction Probability Scale (Naranjo) in Drug Induced Liver Injury. In: *LiverTox: Clinical and Research Information on Drug-Induced Liver Injury* [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012. 2019 May 4.
9. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981;**30**:239–245.
10. Menke J: Diagnostic accuracy of multidetector CT in acute mesenteric ischemia: systematic review and meta-analysis. *Radiology* 2010;**256**:93–101.
11. Green BT, Tendler DA: Ischemic colitis: a clinical review. *South Med J* 2005;**98**:217–222.
12. Choi SR, Jee SR, Song GA, Park SJ, Lee JH, Song CS, et al. Predictive factors for severe outcomes in ischemic colitis. *Gut Liver* 2015;**9**:761–766.
13. Zou X, Cao J, Yao Y, Liu W, Chen L: Endoscopic findings and clinicopathologic characteristics of ischemic colitis: a report of 85 cases. *Dig Dis Sci* 2009;**54**:2009–2015.
14. Dignan CR, Greenson JK: Can ischemic colitis be differentiated from C difficile colitis in biopsy specimens? *Am J Surg Pathol* 1997;**21**:706–710.