Rare disease

A likely diagnosis of Crohn's disease in a 95-year-old woman

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Summary

Crohn's disease (CD) has a bimodal distribution in incidence, with a second peak in the elderly. However, its diagnosis in the elderly is difficult due to a wider range of more common differential diagnoses such as diverticulitis, ischaemic colitis and colorectal cancer. We report a likely case of CD in a 95-year-old woman. She presented with diarrhoea and rectal bleeding and was found to have multiple pleomorphic ulcers with a patchy cobblestone mucosa on sigmoidoscopy. Histopathology demonstrated focal ulceration, altered crypt architecture and adjacent neutrophil polymorph infiltration with no granulomata or features of malignancy. The patient passed away after steroid treatment was started. This case is a reminder that CD can present in the elderly and highlights the challenging diagnosis and high mortality of CD-related hospitalisation in the elderly. When considering management, attention should be given to comorbid disease, age-related changes in pharmacokinetics and patients social circumstances.

BACKGROUND

Crohn's disease (CD), a form of inflammatory bowel disease (IBD), is a relapsing and remitting inflammatory disorder that can affect any part of the gastrointestinal tract. Although significant efforts have been made to understand the aetiopathogenesis of CD, this remains an idiopathic disorder.

CD is primarily considered to affect adolescents and young adults; however, recent epidemiological studies have demonstrated an increased prevalence and incidence of CD in elderly individuals¹ and a bimodal distribution in incidence with a second peak between the ages of 60 and 90 years.^{2–3} These findings however are not widely recognised and the diagnosis of CD in the elderly is often overlooked due to a higher incidence in this population of differential diagnoses such as ischaemic colitis, diverticulitis and colorectal cancer. CD diagnosed in individuals above 90 years of age has rarely been reported.⁴ Here we report the case of a 95-year-old woman who presented with diarrhoea and per rectal (PR) bleeding and was found to have macroscopic and microscopic features in keeping with CD on endoscopy and histopathological examination, respectively.

CASE PRESENTATION

A 95-year-old woman presented with confusion, following a fall at her home. A collateral history revealed that she had symptoms of nausea, vomiting and diarrhoea for the past 3 weeks with some PR bleeding. Her medical history included hypertension, haemorrhoids, glaucoma and atrial fibrillation and there was no significant family history. She was a non-smoker, did not drink alcohol and lived alone, supported by her family. Her regular medications included amiodarone, aspirin, co-codamol, furosemide and latanoprost eye drops.

Examination of her chest, heart and neurological system did not reveal any abnormalities. Some suprapubic

tenderness and a urinary catheter were noted on abdominal examination and her abbreviated mental test score was 6/10.

INVESTIGATIONS

Routine laboratory investigations on admission were normal apart from a reduced albumin level (27 g/l [35–50]) and raised white cells count ($16.1 \times 10^9/l$ [4.0–11.0]), neutrophil count ($13.9 \times 10^9/l$ [2.0–7.5]), C reactive protein (CRP; 107.1 mg/l [<10.0]), urea (18.3 mmol/l [2.5–6.7]) and creatinine (188 $\mu\text{mol/l}$ [53–97]). Interestingly blood tests taken 9 months prior to admission revealed a B12 deficiency (119 ng/l [150–620]) and negative intrinsic factor antibodies. Her stool cultures and stool clostridium difficile toxin were negative, and her urine dip was positive for blood, nitrites and leucocytes.

To investigate her gastrointestinal symptoms, a flexible sigmoidoscopy was arranged. Macroscopically, this demonstrated multiple pleomorphic ulcers in the rectum with a patchy cobblestone mucosa at the rectum (figure 1), in keeping with a diagnosis of CD. Histopathological analysis of the colorectal mucosa also demonstrated focal ulceration with altered crypt architecture and adjacent mucosal reactive changes, in keeping with an acute on chronic inflammatory process (figure 2). There was no granulomata, viral inclusions or features of dysplasia or malignancy visible.

DIFFERENTIAL DIAGNOSIS

Alterations in bowel habit and PR bleeding are common presentations in the elderly and the differential diagnosis is broad. Infective colitis should be considered particularly in those with an abrupt clinical onset and evidence in the stool of an inflammatory process (such as pus, mucous and blood). Stool cultures are imperative in aiding the diagnosis and the histology of infectious-type colitis may also be useful as it generally shows a picture of active inflammation with normal mucosal architecture, unlike in

Figure 1 Images of the colorectal mucosa obtained at sigmoidoscopy. There are multiple pleomorphic ulcers visible with a patchy cobblestone mucosa at rectum.

IBD. Colitis associated with diverticular disease is also common in the elderly and can present with altered bowel habit and PR bleeding. Mucosal biopsies may show features of IBD, providing a diagnostic challenge; however, the colonic mucosa both proximal and distal to the sigmoid colon is usually normal and there may be a history of diverticular disease with radiological or endoscopic evidence of diverticulae formation. Ischaemic colitis is also common in the elderly; however, it is usually localised to the splenic colonic flexure. The diseased segment is also usually short and the patient's history usually includes other atherosclerotic manifestations. Neoplasia should always be ruled out before considering IBD and is more common in the elderly. Radiological studies are often useful in identify an underlying malignancy and histopathological specimens will demonstrate features of dysplasia or malignant cells.

OUTCOME AND FOLLOW-UP

The patient was initially treated for a suspected urinary tract infection with trimethoprim. Her confusion however persisted and she continued to report diarrhoea and

further episodes of PR bleeding. This resulted in a drop in her haemoglobin to 8.8 g/dl, for which she was transfused 2 units of blood. Following her sigmoidoscopy, she was treated with 40 mg oral prednisolone, a pentasa suppository and an asacol foam enema for a presumed diagnosis of CD, but unfortunately passed away 1 day after the treatment was started.

DISCUSSION

Epidemiology, clinical presentation and outcome

Although CD is rarer in the elderly, this case report is a reminder that it should be considered as part of the differential diagnosis in any elderly patient presenting with typical gastrointestinal symptoms. This is confirmed by epidemiological studies that demonstrate a bimodal distribution in the incidence of CD with a first peak between the ages of 20–29 years and comparable second peak between the ages of 60–89, in some studies,^{2 3 5} although not in all.^{6–8} It should be recognised that up to 25% of cases are thought to occur in patients aged 60 years or older,⁵ and with improved diagnosis and prolonged survival these figures are likely to increase further.

The clinical presentation of CD in the elderly can overlap with a number of other medical disorders, providing a diagnostic challenge. This is clearly reflected by the greater mean time to diagnosis of 6.4 years in those aged 64–85 years compared to 2.4 years in those aged 20–61.⁹ The correct diagnosis however is important, due to the worse prognosis of CD in the elderly.¹⁰ A collaborative approach using clinical presentation, laboratory investigations as well as radiological and histological findings is required for the diagnosis.

This patient presented acutely with symptoms of confusion, nausea, vomiting, diarrhoea and PR bleeding, which could be ascribed to a number of conditions including IBD, infective colitis, diverticulitis, ischaemic colitis and colorectal cancer. An acute presentation is more common with an infective aetiology; however, this was not supported by the negative stool cultures and abnormal mucosal architecture found on histology. Diverticulitis can also present acutely; however, there was no history of diverticular disease, and the macroscopic and microscopic features were localised to the rectum without involvement of the sigmoid colon and without evidence of diverticulae formation. CT imaging would have been useful here. Ischaemic colitis can also present acutely, but usually effects the splenic flexure. The macroscopic and microscopic findings located in the rectum make a diagnosis of acute ischaemic colitis less likely; however, a CT angiogram would have been useful to identify potential ischaemia.

It is worth mentioning that some differences in the frequency of presenting symptoms have been reported between younger and elderly patients presenting with CD, providing a further diagnostic challenge. For example, as with this particular case report, some studies have demonstrated a lower frequency of abdominal pain in elderly patients diagnosed with CD.^{9 11} However, this is not supported by all studies,¹² and diarrhoea, PR bleeding, abdominal pain and weight loss are still the most consistently reported symptoms in patients initially diagnosed with CD after 50 years.¹³ This diagnosis should therefore be considered in any elderly patient presenting with these

Figure 2 Histopathological specimens of rectal mucosal biopsies obtained at sigmoidoscopy. (A) Shows altered crypt architecture. The crypts are irregularly distributed and show branching (H&E $\times 5$). (B) Show an area of altered crypt architecture with crypt atrophy together with an increased number of inflammatory cells including neutrophils (H&E $\times 5$). (C) Higher power view demonstrating inflammatory cell infiltration and altered crypt architecture (H&E $\times 10$).

symptoms. This patient also denied any significant family history, particularly of IBD. This is an important consideration as an older age at the diagnosis of CD is associated with less of a prevalence for a family history for CD,¹⁴ possibly suggesting less of a genetic influence in the aetiology of CD in the elderly.

Her laboratory results revealed some abnormalities that are commonly found in elderly patients with CD; anaemia, leukocytosis, hypoalbuminaemia and a raised CRP.¹⁵ Another common finding, a serum B12 deficiency with normal intrinsic factor antibodies,¹⁶ was also noted and may reflect malabsorption of vitamin B12 at the terminal ileum. Possible terminal ileum involvement could not be confirmed, due to this patient's limited sigmoidoscopy.

In this case, the patient passed away soon after the treatment was started, after a delayed diagnosis. Her hospital admission was characterised by a number of complications including anaemia, hypovolaemia and the requirement for blood transfusions, which are more commonly reported in elderly patients with IBD.¹⁰ Her clinical course is a reminder of the higher in hospital mortality associated with CD in the elderly in some studies.

Macroscopic findings

In this particular case, the patient underwent a flexible sigmoidoscopy to investigate her symptoms. Although this investigation does not allow full characterisation of disease location and behaviour within the gastrointestinal tract, this would appear to be an appropriate initial investigation, due to her presentation of active disease, where the risk of bowel perforation is increased with colonoscopy.¹⁷ Her sigmoidoscopy revealed several important macroscopic features in keeping with CD, including the appearance of discontinuous ulcers of different sizes, skip

lesions and a cobblestone appearance of the rectal mucosa. From this limited examination there was no evidence of stricturing or penetrative disease that is in keeping with the inflammatory subtype of disease with a preference for distal colonic involvement, reported in the elderly.^{18–20} An ileocolonoscopy when stable, however, would have allowed for better characterisation of her macroscopic features in terms of disease location and behaviour.

Microscopic findings

Microscopically there were a number of features observed that would suggest a diagnosis of CD. Firstly, neutrophil polymorph infiltration of the mucosa was seen, which is a common feature of IBD, and also acute infective colitis. The negative stool cultures and other histological features of chronic inflammation however would go against an acute infective colitis. For example, a number of mucosal architectural abnormalities were observed including crypt distortion (non-parallel), crypt branching (represents growth or regeneration) and crypt shortening (atrophy). These features are commonly seen in IBD and rarely seen in the normal mucosa or acute infective colitis. The discontinuous nature of the architectural disturbance observed here is more in keeping with CD, rather than ulcerative colitis (UC) where a continuous disturbance is more often seen. Other features of chronic inflammation observed included an increased lamina propria cellularity. Again a discontinuous increase in lamina propria cellularity was observed, which is more in keeping with CD rather than UC.

A further feature of chronic inflammation in CD is the presence of granuloma, which was not observed here. Although the presence of granulomas are a specific feature of CD, it should be noted that their presence is not a

sensitive feature of CD, being seen in as few as 18% of biopsy specimens.²¹ The detection of granulomas is highly dependent on tissue sampling (number of examinations performed, biopsies taken and sections examined) and it is also known that a higher frequency of granulomas are detected on surgical specimens compared to endoscopic specimens, which were obtained here. Age may also be an important factor as interestingly fewer granulomas are detected from surgical specimens obtained from older patients. Thus, the absence of granulomas reported in the histology in this case does not rule out a diagnosis of CD.

Epithelial abnormalities can also give important diagnostic clues. For example, dysplastic changes that can be seen in colorectal cancer were not observed. Mucin depletion which can be seen in CD, although more commonly in UC, was observed in the mucosal biopsies of ulcerated lesions. The biopsies taken consisted of mucosa and scanty muscularis mucosa and as such were too superficial to assess for other features of CD such as hypertrophy/hyperplasia of the nerve fibre layer within the submucosa, or expansion of the muscularis mucosa that can be seen with strictures.

Management of CD in the elderly

The management of CD in the elderly and younger adults is similar.²² The general approach involves treatment to induce remission followed by maintenance therapy and consideration should be given to the disease location, severity and behaviour (inflammatory, penetrating and stricturing).

For active ileal, ileocolonic or isolated colonic disease, of mild severity, five aminosalicylates (5-ASA) derivatives may be effective. For moderate disease, or disease unresponsive to 5-ASA derivatives, oral prednisolone is recommended or budesonide in patients with isolated ileo-caecal disease. As budesonide interferes with bone metabolism less than conventional steroids this is an important consideration in elderly patients at risk of osteoporosis. For patients with severe disease intravenous hydrocortisone is recommended. Azathioprine or mercaptopurine may also be used in active CD as adjunctive therapy and infliximab in refractory disease. For perianal CD, metronidazole is recommended as first-line treatment.

The evidence for the use of 5-ASA derivatives for maintenance therapy is weak, especially if steroid treatment was required for induction. However, maintenance with azathioprine or mercaptopurine has been shown to be effective and infliximab is also effective in maintaining remission in luminal or fistulating CD. Although there are no specific trials that have evaluated the safety or efficiency of these medications in elderly patients, they appear to be well tolerated. Surgical treatment for CD may be indicated to treat complications (ie, obstruction and fistulae) or for medically refractory disease.

Although the general approach to treatment of CD in elderly and younger individuals is similar, in elderly patients, additional thought should be given to comorbidities which may influence the choice and outcome of treatment. The risk of drug interactions and the increased risk of adverse effects from steroid use and immune suppressing medication should also be given extra thought. As with all elderly patients, consideration should be given

to the elderly patient's social circumstances and home environment, which can considerably improve their overall quality of life.

Learning points

- Crohn's disease (CD) is a common inflammatory disorder affecting young adults as well as the elderly.
- Although the clinical presentation in the elderly is similar to that of younger individuals, the diagnosis remains difficult due to a wider range of more common differential diagnoses.
- CD in the elderly is associated with a higher rate of systemic complications and hospital-related mortality in elderly patients compared to younger individuals.
- The diagnosis should be made collectively using clinical history, radiological, endoscopic and histological findings where possible.
- Treatment options for the elderly are generally similar to younger individuals; however, additional consideration should be given to comorbidities, drug interactions, the potential adverse effect of treatments used, as well as patient social circumstances.

Acknowledgements We would like to thank the Department of Histopathology, Royal Oldham Hospital, Oldham, United Kingdom, for their expert histopathological analysis.

Competing interests None.

Patient consent Obtained.

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Parmar KR, Patel E, McCann P. A likely diagnosis of Crohn's disease in a 95-year-old woman. *BMJ Case Reports* 2012;10.1136/bcr-2012-006445, Published XXX

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