CASE REPORT

Disseminated aspergillosis causing intestinal failure following colectomy for perforated colitis

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ABSTRACT

Disseminated aspergillosis is a rare, invasive, opportunistic, fungal infection associated with a high mortality. We report a non-fatal case diagnosed following extensive enterectomy for intestinal infarction in a patient recovering from emergency abdominal colectomy for perforated ulcerative colitis. This resulted in intestinal failure necessitating life-long parenteral nutrition and prolonged antifungal therapy.

BACKGROUND

To our knowledge, this is the first reported case of intestinal failure due to disseminated aspergillosis.

CASE PRESENTATION

A 49-year-old Caucasian female presented with diarrhoea, rectal bleeding and anaemia. She had no other comorbidity, history of HIV, immunosuppressant therapy or foreign travel. Eosinophil count was $0.10 \times 10^9/L$ (0.04–0.4), white cell count was $5.1 \times 10^9/L$ (4.0–10.0) and neutrophil count was $3.61 \times 10^9/L$ (2.0–7.5). Stool cultures were negative. Acute proctosigmoiditis was diagnosed at colonoscopy. Endoscopic biopsies demonstrated a mixed inflammatory infiltrate of lymphocytes, plasma cells, as well as acute inflammatory cells within the lamina propria. Additionally, mucin depletion and crypt architectural glandular distortion were in keeping with a degree of chronicity and consistent with ulcerative colitis. Following inpatient treatment with intravenous hydrocortisone for 1 week, a regimen of oral prednisolone and mesalazine was commenced. Her symptoms initially improved and she did not require thiopurine or antitumour necrosis factor therapy. However, 5 weeks later she was

admitted as an emergency to our hospital with septic shock and generalised peritonitis. She was neutropenic with a white cell count of $2.1 \times 10^9/L$ and neutrophils of $1.43 \times 10^9/L$. C-reactive protein was elevated at 75 (1–5) mg/L.

Laparotomy revealed faecal peritonitis due to severe colitis with caecal perforation. An abdominal colectomy, end ileostomy, rectal mucous fistula and abdominal lavage were performed. She was transferred to the intensive care unit postoperatively, and intravenous fluconazole, gentamicin, metronidazole and piperacillin/tazobactam were commenced. Intravenous hydrocortisone was administered for 5 days postoperatively.

Six days later, she developed respiratory failure requiring reintubation and ventilatory support. A chest X-ray and CT scan demonstrated right-sided pulmonary consolidation and bilateral pleural effusions. Initial sputum cultures were negative. Over the next 12 days, nasogastric aspirates increased and her abdomen became distended. A CT scan showed distended small bowel and free fluid. After further deterioration and bleeding per ileostomy, a second CT scan showed pockets of free intra-abdominal gas, increased free fluid and thickened small bowel consistent with an intra-abdominal perforation (figure 1). A splenic infarct was also identified.

A second laparotomy revealed ischaemic small bowel with multiple perforations necessitating an extensive enterectomy and high jejunostomy. Just 80 cm of viable small bowel remained. Three days later, a further perforation, just distal to the duodenojejunal flexure, necessitated another laparotomy. The

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Figure 1 (A and B) Coronal and axial images from a contrast-enhanced CT scan of abdomen demonstrating thickened enhancing loops of small bowel (white) indicating an inflammatory process consistent with intestinal aspergillosis. There is also extensive ascites (yellow) and locules of free intraperitoneal air (red) due to intestinal perforation.

perforation was exteriorised as a loop jejunostomy through a midline Vicryl mesh as fascial closure was not possible. Parenteral nutrition was commenced and antibiotic and antifungal therapy continued.

Four days later, the histopathological report of the enterectomy specimen from the second laparotomy revealed multiple intestinal perforations with evidence of extensive ulceration and transmural necrosis. Fungi with acutely branching hyphae were identified within the vasculature and submucosa consistent with a diagnosis of intestinal aspergillosis (figure 2). Intravenous antifungal therapy was then changed to amphotericin-B and voriconazole.

Figure 2 (A) Low-power view showing area of small intestinal ischaemic mucosal ulceration with marked submucosal vascular congestion and oedema. Note, large obliterated submucosal vein (arrowed) (H&E $\times 20$). (B) High-power view of submucosal vein showing neutrophils mixed with acute branching, narrow fungal hyphae (arrowed), consistent with aspergillus (periodic acid-schiff $\times 200$). (C) High-power view of the serosal surface adjacent to an intestinal perforation, showing fungal hyphae (arrowed) mixed with fibrinopurulent debris, indicating fungal peritonitis (Grocott $\times 400$).

Postoperatively, the patient also developed digital ischaemia and a transoesophageal echocardiogram demonstrated an aortic valve vegetation. Serum aspergillus antigen testing was negative. A chest CT showed widespread focal consolidation and cavitory change

Figure 3 Coronal image from a contrast-enhanced CT scan of chest showing multiple cavitary lung lesions, with an upper lobe predominance, typical of pulmonary aspergillosis.

(figure 3). Bronchoscopy was performed 7 days following the third laparotomy. Bronchoalveolar lavage washings isolated *Aspergillus fumigatus* and were aspergillus antigen positive. MRI of brain identified multiple areas of T2 hyperintensity consistent with cerebral and cerebellar aspergillosis (figure 4).

Figure 4 Axial T2 weighted image from an MRI scan of brain demonstrating multifocal white matter abnormalities consistent with cerebral involvement in the systemic aspergillosis.

After 8 weeks in the intensive care unit she was transferred to the surgical ward. Here, intestinal failure due to extremely short bowel (just 5 cm proximal to the jejunostomy) was managed with parenteral nutrition and fluids. With insufficient small bowel for adequate enteral absorption, antifungal therapy (voriconazole) was continued intravenously.

OUTCOME AND FOLLOW-UP

Four months following admission she developed severe mental disturbance with extreme agitation, pressure of speech, disinhibition and personality change. A further brain MRI confirmed persistent multiple lesions consistent with cerebral aspergillosis. Intravenous antifungals were continued and her neurocognitive symptoms continued for several months.

Ten months later, after nutritional optimisation and delayed healing of her open wound, reversal of loop jejunostomy and abdominal wall repair were performed. This facilitated conversion to oral antifungals. However, with just 70 cm of small bowel remaining to an end jejunostomy, short bowel syndrome necessitated life-long parenteral nutrition. Despite disseminated aspergillosis there were no issues with fungal line infections.

No cardiac intervention was required, and despite significant cerebral involvement, there was no persistent neurological or cognitive deficit. She was discharged from hospital with home parenteral nutrition some 20 months following initial admission, and remains systemically well after 2 years' follow-up.

DISCUSSION

Disseminated aspergillosis is a rare, opportunistic fungal infection usually affecting immunocompromised patients.¹ It is rapidly progressive with reported mortality rates of 80–90%.^{2,3} A detailed medical, drug and travel history is therefore paramount in cases of critically unwell patients in whom the pathogenesis is unusually aggressive. Predisposing factors include haematological malignancy, post-transplantation, chemotherapy and corticosteroid treatment.⁴ It has also been reported following anti-tumour necrosis factor (TNF) therapy for inflammatory bowel disease.⁵ In this case, corticosteroid therapy and profound sepsis were the predominant factors.

The European Crohn's and Colitis Organisation (ECCO) has issued guidelines for the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. However, no specific screening or prophylaxis measures are recommended for opportunistic fungal infection in patients with IBD. Other opportunistic infections such as strongyloides (which also progresses with steroid use) can also present catastrophically in these often immunosuppressed patients.⁶

Around 25% of patients with primary pulmonary aspergillosis will develop extrapulmonary

dissemination.⁷ Of those with invasive disease, 41–47% will have involvement of the gastrointestinal tract.² These patients may develop bowel obstruction and other complications including intestinal ischaemia, bleeding, necrosis and perforation.³ However, diagnosis of gastrointestinal aspergillosis is difficult. It is usually histological, and often postmortem. Here, the patient survived, but a prolonged hospital stay and lifelong dependence on parenteral nutrition demonstrate the considerable morbidity in non-fatal cases. To our knowledge, this is the first reported case of intestinal failure due to disseminated aspergillosis.

Most patients (94%) will have clinical or radiological evidence of pulmonary aspergillosis at presentation.² This is the usual portal of entry leading to systemic haematogenous spread. However, primary GI aspergillosis has been reported in the absence of pulmonary involvement.^{8–9} One author reports this in the presence of a pre-existing enterocolitis.¹ This has some similarities to our case where a background of acute colitis with subsequent intestinal aspergillosis may suggest an intestinal portal of entry with subsequent dissemination. However, as respiratory failure and pulmonary infiltrates were early features in our case, dissemination from primary pulmonary involvement seems more likely. Primary colonic aspergillosis presenting with toxic megacolon has also been reported but, in our case, subsequent re-examination of the previously resected colon showed no evidence of fungal invasion.¹⁰

Aspergillus fumigatus is the usual organism involved. Angio-invasion by fungal hyphae leads to vascular occlusion and subsequent infarction.¹¹ In this case, diagnosis was achieved on histological examination of the enterectomy specimen. Typical features of transmural necrosis plus fibrin thrombi and aggregates of fungal hyphae within the submucosal vasculature were identified.¹²

Other organs involved in disseminated disease include brain, kidneys, heart and skin. *Aspergillus* serology should be performed in suspected cases and, as the majority have pulmonary involvement, broncho-alveolar lavage fluid should also be tested. As already emphasised, intestinal aspergillosis is difficult to diagnose, but CT may demonstrate non-specific findings, such as peri-enteric mesenteric inflammation or obstruction due segmental small bowel thickening.⁷ Cerebral imaging and echocardiography should also be performed to establish the extent of dissemination.

Upon diagnosis, voriconazole is the gold standard systemic antifungal agent, though liposomal amphotericin B is a suitable primary alternative. Caspofungin may be introduced in refractory cases, and combination therapies are often used.¹³ As in this case, surgery may be required for gastrointestinal complications, such as obstruction, peritonitis or bleeding. Resection of involved intestine is performed, and a low threshold for further laparotomy adopted as

progressive ischaemia may lead to further intra-abdominal complications. Successful primary anastomosis has been reported but exteriorisation is recommended in these invariably critically ill patients.⁷

Intestinal aspergillosis should be considered in immunocompromised patients with abdominal signs and symptoms even without evidence of pulmonary involvement. This case demonstrates the difficulty in diagnosis and the role of operative intervention in intestinal aspergillosis. Here, intestinal failure highlights the considerable morbidity for those surviving this rare, but often fatal, invasive fungal infection.

Contributors We, the authors, have all contributed to and approved the manuscript. We agree to its publication and it has not been published elsewhere (KM, MBL, SG, KG).

Competing interests None.

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REFERENCES

- 1 Fieber JH, Atladóttir J, Solomon DG, *et al.* Disseminated enteroinvasive aspergillosis in a critically ill patient without severe immunocompromise. *J Surg Case Rep* 2013;2013:rjt091.
- 2 Cohen R, Heffner JE. Bowel infarction as the initial manifestation of disseminated aspergillosis. *Chest* 1992;101:877–79.
- 3 Tresallet C, Nguyen-Thanh Q, Aubriot-Lorton MH, *et al.* Small-bowel infarction from disseminated aspergillosis. *Dis Colon Rectum* 2004;47:1515–18.
- 4 Kontoyiannis DP, Bodey GP. Invasive aspergillosis in 2002: an update. *Eur J Clin Microbiol Infect Dis* 2002;21:161–72.
- 5 Alderson JW, Van Dinter TG Jr, Opatowsky MJ, *et al.* Disseminated aspergillosis following infliximab therapy in an immunosuppressed patient with Crohn's disease and chronic hepatitis C: a case study and review of the literature. *Med Gen Med* 2005;7:7.
- 6 Rahier JF, Ben-Horin S, Chowers Y, *et al.* European evidence-based Consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. *J Crohns Colitis* 2009;3:47–91.
- 7 Shah SS, Birnbaum BA, Jacobs JE. Disseminated aspergillosis inciting intestinal ischaemia and obstruction. *Br J Radiol* 2001;74:1145–7.
- 8 Catalano L, Picardi M, Anzivino D, *et al.* Small bowel infarction by *Aspergillus*. *Haematologica* 1997;82:182–3.
- 9 Eggimann P, Chevrolet JC, Starobinski M, *et al.* Primary invasive aspergillosis of the digestive tract: report of two cases and review of the literature. *Infection* 2006;34:333–8.
- 10 Mohite U, Kell J, Haj MA, *et al.* Invasive aspergillosis localised to the colon presenting as toxic megacolon. *Eur J Haematol* 2007;78:270–3.
- 11 Marterre WF Jr, Mong AT, Pulito AR. Locally invasive aspergillosis of the bowel. *J Pediatr Surg* 1992;27:1611–13.
- 12 Prescott RJ, Harris M, Banerjee SS. Fungal infections of the small and large intestine. *J Clin Pathol* 1992;45:806–11.
- 13 Maschmeyer G, Haas A, Cornely OA. Invasive aspergillosis: epidemiology, diagnosis and management in immunocompromised patients. *Drugs* 2007;67:1567–601.