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CASE REPORT

Biologic therapy for paediatric inflammatory bowel disease in Ghana: a case series

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Background: Inflammatory bowel disease (IBD) comprises Crohn's disease and ulcerative colitis. It is a chronic inflammatory disease of the gastrointestinal tract (GIT) that can affect all ages. Globally, paediatric IBD is rising, with approximately 10% of IBD cases diagnosed in children < 16 years. Paediatric IBD can present in various atypical forms, making recognition challenging to distinguish from other intestinal pathologies. In Africa, children with IBD present a considerable diagnostic challenge.

Methods: Four patients in Ghana were diagnosed with IBD following clinical, laboratory, and special investigations, confirmed by upper and lower gastrointestinal endoscopy and histology. Three patients were initially managed with oral therapy but did not achieve remission and became steroid dependent. One patient was started on a biologic at the time of diagnosis.

Results: All four patients were eventually managed with infliximab (IFX), an anti-tumour necrosis factor alpha (TNFα) agent. Their clinical features improved remarkably.

Conclusion: Biologic therapy is effective in improving the outcome and quality of life of African children, but it is extremely expensive. Access to these agents can be improved through partnerships with non-governmental organisations and support groups with an interest in paediatric IBD.

Keywords: inflammatory bowel disease, endoscopy, children, infliximab, Ghana

Introduction

IBD comprises Crohn's disease and ulcerative colitis. Both are chronic inflammatory diseases of the GIT that can occur at any age. Previously considered a disease of high-income countries, recent reports indicate a rapid rise in newly industrialised countries in South America, Eastern Europe, Asia, and Africa.[1] Approximately 4.9 million cases of IBD were reported in 2019, and this number is projected to increase.[1] About 10% of IBD is diagnosed in children < 16 years.[2] The clinical course of paediatric-onset IBD is characterised by a greater disease burden compared with adult-onset IBD.[3]

Few studies have been conducted in sub-Saharan Africa. An IBD Africa registry based in Cape Town reports that 9.7% of cases involve children and adolescents aged ≤ 18 years at diagnosis, a finding similar to that in Western countries.[4,13,14] Reports on paediatric IBD from Ghana and other sub-Saharan African countries remain scarce, with South Africa and Nigeria being the only countries with reports of paediatric IBD cases in the literature.[5]

IBD diagnosis involves proper history-taking, relevant investigations, endoscopy, and specific tissue histology in patients with relevant clinical features. The disease is associated with remissions and relapses, even in patients undergoing treatment. A delay in diagnosis or a misdiagnosis resulting in untreated IBD can lead to worsened clinical outcomes. This includes persistent inflammation, the development of systemic symptoms, potential complications such as bowel stenosis and fistulae, an increased risk of bowel surgery, and worsening nutritional deficiencies.[6]

In Africa, children with IBD present a considerable diagnostic challenge. Underlying pathologies, such as chronic diarrhoea, iron deficiency anaemia, malnutrition, and failure to thrive due to chronic enteric infections, parasites, intestinal tuberculosis, and environmental enteropathy, are pervasive clinical problems. Differentiating these common intestinal maladies from IBD is clinically challenging.[7] Furthermore, paediatric IBD can present with various atypical forms, making recognition even more challenging to decipher from other intestinal pathologies.[8]

IBD management includes exclusive enteral nutrition, pharmacotherapy, and surgery for patients with complications. In this series, four patients were managed with pharmacotherapy, as this is the main treatment option available locally.

Cases

Four patients from the paediatric gastroenterology clinics at Korle Bu Teaching Hospital and the Lister Hospital in Accra, Ghana, were diagnosed with IBD. They were ultimately managed with IFX, an anti-TNFα agent. Parents were counselled on the mode of administration, frequency, cost, and potential therapy complications. The patients were screened for hepatitis B and C, human immunodeficiency virus (HIV), and latent tuberculosis. The details of the four cases are presented in Table I.

Case 1

An 11-year-old female with sickle cell disease presented with an eight-month history of abdominal pain, bloody diarrhoea (5–7 times daily), and nocturnal bowel emptying (2–3 times nightly). No abnormality was detected during her physical examination, except for being small for her age. At endoscopy, no abnormality was seen in the upper GIT. Diffuse ulcerations from the rectum to the ascending colon were seen during colonoscopy. Biopsies were taken from the upper and lower GIT to confirm an ulcerative colitis diagnosis.

The patient started on prednisone and azathioprine, with good response until eight months, when the symptoms recurred. The treatment was changed to methotrexate, 6-mercaptopurine, and, later, to mesalamine, due to poor response and symptom recurrence. Each therapy included a course of prednisolone and then tapered down, but none of the medications had the desired result. With all the medications, she responded well until 5 mg of prednisolone and full doses of the other medications, when the symptoms recurred.

After 18 months of treatment, she was initiated on IFX at a dose of 5 mg/kg. Symptoms resolved completely, with significant weight gain after the induction phase of the therapy. She continued with eight weekly therapies for a year. Due to the weight gain, the dose requirement increased, causing a spiralling financial burden due to the high cost of IFX, and the parents were unable to continue the therapy. Her symptoms recurred within five months after IFX discontinuation, and the family resorted to alternative therapy.

Case 2

An 11-year-old male presented with abdominal pain and intermittent rectal bleeding for two years. He had haematochezia about 3–5 times and nocturnal bowel emptying once daily. Physical examination findings were normal. He was admitted and started on ciprofloxacin and metronidazole. Intravenous (IV) methylprednisolone was added when his laboratory results were obtained. Upper endoscopy was normal, but colonoscopy showed diffuse ulcerations with exudates from the rectum to the caecum, with mucosal oedema. Biopsies were taken, and ulcerative colitis was diagnosed.

The patient started on IFX at a dose of 10 mg/kg. Symptoms resolved and calprotectin normalised by seven months. Surveillance endoscopy after one year of therapy showed small ulcerations in the rectum. Repeat colonoscopy at 18 months of treatment showed complete mucosal healing.

After 33 months of therapy, the patient developed a soft swelling on the forehead with headache, without previous head trauma. A magnetic resonance imaging (MRI) scan showed a left skull bone osteomyelitis with overlying subgaleal extension and dural enhancement secondary to chronic frontal sinusitis, chronic left maxillary, and ethmoidal sinusitis. The abscess was drained, and he recovered fully after treatment. An extensive discussion with

Table I: Clinical features and laboratory results of the four patients with inflammatory bowel disease

Variable	Case 1	Case 2	Case 3	Case 4
Age (years)	11	11	10	8
Gender	Female	Male	Female	Male
Duration of symptoms	8 months	2 years	4 months	1 year
Symptoms at presentation	Abdominal pain, bloody diarrhoea Nocturnal diarrhoea thrice nightly	Abdominal pain, bloody stools	Abdominal pain, bloody diarrhoea, weight loss. Nocturnal diarrhoea twice nightly	Abdominal pain, bloody diarrhoea, weight loss, poor appetite
Physical findings	Small for age	Normal	Small for age, mouth ulcers	Thin, finger clubbing, lip sores
Full blood count				
Haemoglobin (g/dL)	8.6	9.8	10.3	9.2
White blood cells ($X10^9$/L)	6.2	7.3	10.0	7.5
Platelets ($X10^9$/L)	510	488	359	695
Endoscopy findings	Diffuse ulcerations with exudate from rectum to caecum	Diffuse ulcerations with exudate from rectum to caecum	Ulcerations with pseudopolyps, the rectum was spared	Pancolitis
Histology findings	Ulcerative colitis	Ulcerative colitis	Crohn's disease	Ulcerative colitis
Calprotectin (µ/g) at presentation	2 231	5 346	1 240	1 682
Calprotectin (µ/g) during treatment	753	29	238	76
Extraintestinal features	None	Arthralgia	Arthralgia, joint swelling	None
Comorbidities	Sickle cell disease	None	None	None

the neurosurgeon led to a decision to continue with the therapy after a second MRI showed no lesion. Therapy was continued as scheduled with close monitoring from the neurosurgery team.

Case 3

A 10-year-old female presented with abdominal pain, weight loss, and bloody diarrhoea for four months. Diarrhoea occurred 4–5 times daily and twice nightly. She also had two months of right ankle joint pain. She was small for her age, with moderate pallor and a swollen right ankle joint. Colonoscopy and mucosal biopsies confirmed Crohn's disease with extraintestinal manifestation (arthritis of the right ankle joint).

The patient was started on prednisone and azathioprine. Her symptoms improved initially (not resolved), and the prednisolone was tapered to 5 mg. All symptoms recurred by three months into the therapy. She was then started on methotrexate, which failed to improve her symptoms. Following this, she was initiated on IFX at 10 mg/kg.

She gained weight, the arthritis resolved, her appetite improved, and other symptoms resolved after the second dose of induction therapy. All symptoms and laboratory results normalised after six months of therapy. However, her parents were unable to sustain the IFX treatment following the weight gain and the need to increase its dose. Shortly after IFX discontinuation, bloody diarrhoea and weight loss were noticed. She had elevated calprotectin with endoscopy evidence of disease.

Case 4

An eight-year-old male presented with abdominal pain, diarrhoea, weight loss, and poor appetite for one year. He was very thin and pale, with an aphthous ulcer on the lower lip and digital clubbing. Colonoscopy and biopsy confirmed ulcerative colitis. He was started on prednisone and azathioprine. Azathioprine was changed to 6-mercaptopurine, then methotrexate. His symptoms improved briefly, then recurred.

Because he never had remission on any of the above medications, he was started on budesonide, which also did not achieve remission. He was then started on IFX at a dose of 10 mg/kg. His symptoms resolved before the end of the induction therapy. He gained weight, and his appetite improved. He remains in remission after 10 months of therapy with IFX.

Discussion

Previously considered a disease of industrialised countries, IBD is well recognised in Africa, with documented reports from Sub-Saharan Africa.[9] Here, we report our small paediatric experience in Ghana. The presentation in all four children was similar, with abdominal pain, bloody diarrhoea, and growth retardation. The patients all had anaemia and elevated stool calprotectin, while three of them had thrombocytosis at presentation. As an extraintestinal manifestation of IBD, all patients were anaemic, driven by iron deficiency, chronic disease, vitamin deficiencies, haemolysis, and the myelosuppressive effect of medications.[10] Two of the four patients had arthralgia, with one large joint swelling similar to findings in the literature, which reports up to 50% of patients with IBD to have arthralgia in their lifetime.[11]

Three patients were started on corticosteroids due to the cost implications for Ghanaian patients. All patients achieved a clinical response within 3–6 weeks. Symptoms recurred on tapering, suggesting steroid dependence and an indication for biologic therapy. Biologics in paediatric IBD revolutionised the approach to treatment.[12] Biologics can induce and maintain remission, achieve mucosal healing, improve growth and development, and improve some extraintestinal manifestations of paediatric IBD after careful patient selection.[11]

The anti-TNFα agent, IFX, was the first biologic used in paediatric IBD in 2006.[13] Little is documented about paediatric IBD in Africa, with scarce reports of biologic use in this population. In low-resource countries where biologics are used, they are often initiated late due to cost and availability challenges.[14] A similar scenario occurred in our setting, where therapy was terminated because it was unaffordable. Following IFX treatment, all patients achieved clinical response during induction, and none experienced any initial adverse reactions during therapy. The patients' parents financed the therapy, as it is not covered by health insurance (both national and private health insurance).

The first patient in this series was given a dose of 5 mg/kg of IFX. After significant weight gain during therapy, the parents could not afford to finance the increasing dose requirement, leading to underexposure and subsequent treatment failure.[15] The other patients were given IFX up to 10 mg/kg; these were rounded up to the nearest hundred to not waste the drug. Arthralgia and joint swelling resolved during remission induction. Two patients with sufficient funds to continue therapy achieved clinical response and biochemical and mucosal healing, as indicated by the normalisation of calprotectin and clearance of mucosal ulcers at endoscopy, respectively. Notably, the patient who developed an infection due to chronic sinusitis responded to the same treatment, with close monitoring after adequate infection treatment.

The management gap in these patients is the unavailability of therapeutic drug monitoring.[16] Hence, those with secondary response loss over time will be difficult to detect in this setting.[17] In this case series, after the first patient received IFX at 5 mg/kg, subsequent patients were treated with 10 mg/kg. This allows the patient and healthcare providers to quickly identify primary non-responders. Partnering with non-governmental organisations and support groups with an interest in paediatric IBD, aimed at contributing to biologic therapy, will enhance sustainability in providing this much-needed therapy to patients in developing countries. As a result, more children who qualify for biologic therapy can be readily enrolled in treatment.

Conclusion

Paediatric IBD is increasing in low-resource countries. We present four patients and the challenges of their management in Ghana. Biologic therapy improves outcomes and children's quality of

life, even in the presence of high therapy costs and a lack of therapeutic drug monitoring.

Conflict of interest

The authors declare no conflict of interest.

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