Treatment of *Stronglyoides* Hyperinfection with Subcutaneous Ivermectin in an Immunocompromised Patient

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Background:
Ivermectin is an effective treatment for strongyloidiasis. However, it's use is limited in the malabsorptive state. Subcutaneous administration is supported in the literature, however, it is only licenced *per os* in Ireland.

Case report:
A 52-year-old man presented to hospital in April 2022 with chronic diarrhoea. He has a past medical history of atrial fibrillation, eosinophilic cardiomyopathy, and he has experienced housing instability for five years. He had a distant history of travel to Asia and South America. Investigation revealed anaemia (11.3g/dL) and hypereosinophilia ($1.13x10^9$/L). He was hypogammaglobulinemic, presumed secondary to gastrointestinal losses, but subsequently received a diagnosis of possible common variable immunodeficiency (CVID) following specialist immunology input. CT imaging showed colitis and mesenteric lymphadenopathy. Endoscopic evaluation showed features of intestinal inflammation, both colitis and enteritis (image 1,2), and biopsies showed histological evidence of eosinophilic inflammatory changes with parasitic organisms suspected to be strongyloidiasis (image 3,4). *Strongyloides* serology was negative and repeated stool samples revealed no ova or parasites. He was treated with oral albendazole and ivermectin and commenced on intravenous immunoglobulin replacement. He was discharged and, in the intervening months, received immunoglobulin therapy and several further courses of oral ivermectin for recurrence of diarrhoea. Months later he was re-admitted with macrocytic anaemia and persistent diarrhoea. He was folate and iron deficient. Intravenous vitamin and nutrient replacement was commenced. Further stool samples revealed rhabditiform larvae of *Strongyloides* stercoralis. Following a complex procurement process, he was treated with subcutaneous veterinary ivermectin,. Treatment regimen was initiated as once weekly dosing (200mcg/kg) in order to reduce the risk of central nervous system toxicity, as has previously been reported in the literature.
This resulted in rapid improvement of diarrhoea and fatigue, clearance of strongyloides from his stool, and reduction in peripheral eosinophilia.

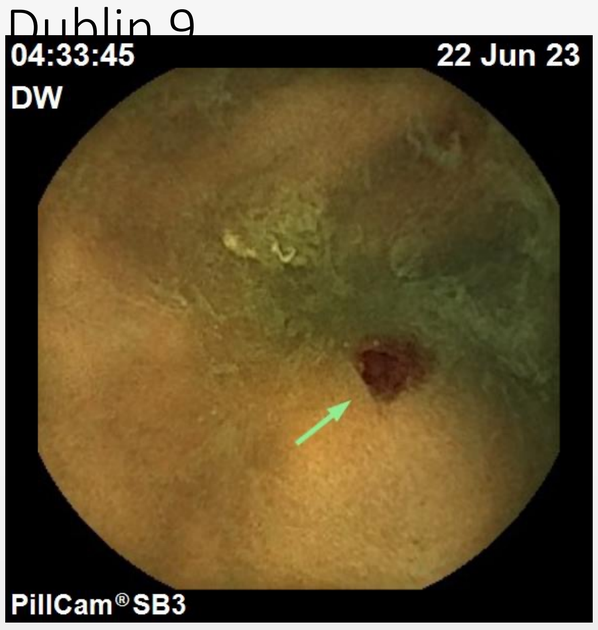


Image 1. Inflammation and ulceration as visualized on capsule endoscopy

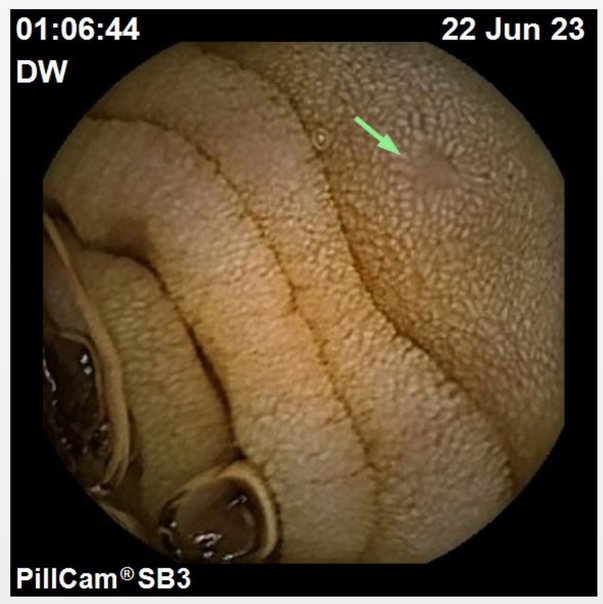


Image 2. Ulceration as visualized on capsule endoscopy.

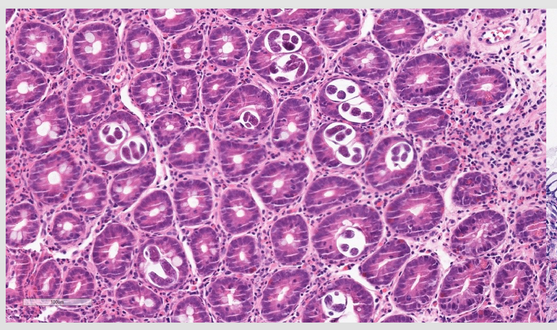


Image 3. Duodenal mucosa showing organisms within crypts

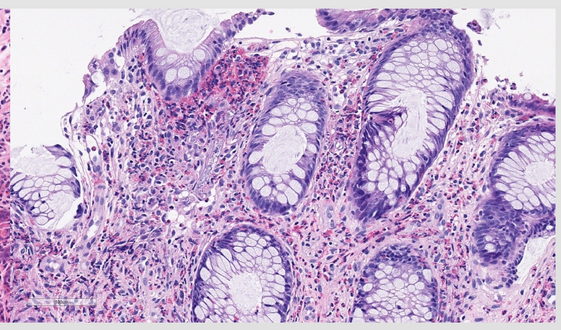
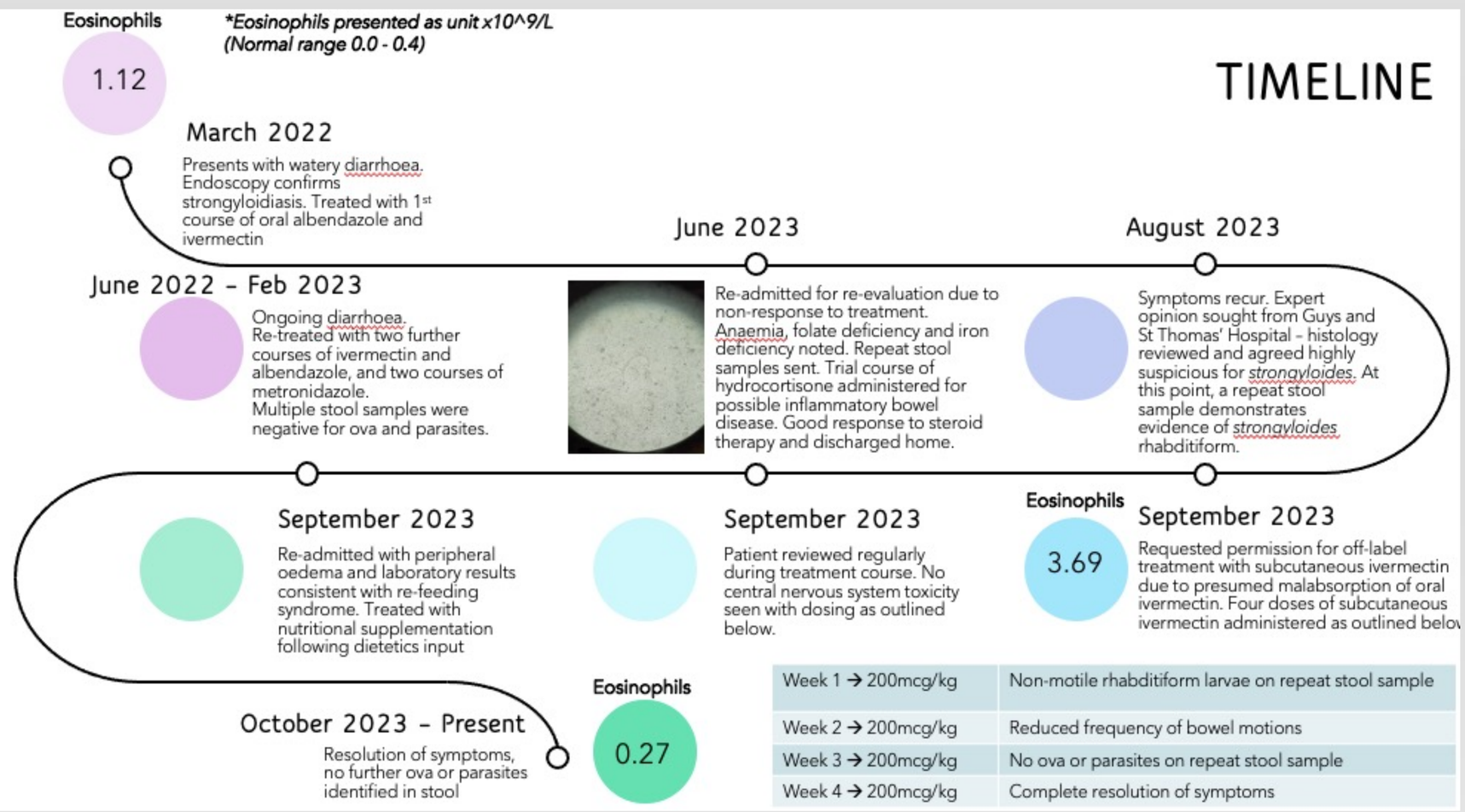


Image 4. Rectal mucosa showing strongyloides elements

Discussion:
This cases describes the use of subcutaneous ivermectin in the treatment of strongyloidiasis hyperinfection in a patient with suspected CVID, with good clinical response. Hyperinfection describes acceleration of the life cycle of *strongyloides* in the human host, with increased parasitic burden and a more severe clinical course than classic strongyloidiasis. While subcutaneous ivermectin has been identified as a 'promising therapeutic approach' (1), it has not been licensed for subcutaneous use in humans. A number of case reports describe its off-license use in complex cases of strongyloidiasis, such as hyperinfection. This is reported in patients with immunocompromised states included transplant recipients and people living with HIV with good effect (2,3). This is, to our knowledge, the first description of its use in a patient with suspected CVID. CVID is a clinical syndrome characterized by B-cell dysfunction, hypogammaglobulinemia, and recurrent infections (4). It is distinct from secondary hypogammaglobulinemia, which can arise from myriad conditions, including protein-losing enteropathy (5). One of the challenges in this case was determining whether the patient had underlying CVID, thus predisposing him to strongyloidiasis, or whether hypogammaglobulinemia developed as a result of protein malabsorption secondary to chronic strongyloidiasis.
The case also highlights the diagnostic challenges in identifying strongyloidiasis, particularly in a low-prevalence country like Ireland. The patient had multiple stool samples in which ova and parasites were not detected. Furthermore, due to his underlying B-cell dysfunction, serological testing was unhelpful. Definitive diagnosis required collaboration between physicians, microbiologists, histopathologists, and laboratory scientists over a period of months to ensure an accurate diagnosis was reached.



References:
1. Crump A. Ivermectin: enigmatic multifaceted 'wonder' drug continues to surprise and exceed expectations. J Antibiot (Tokyo). 2017 May;70(5):495-505.
2. Barrett J, Broderick C, Soulsby H, Wade P, Newsholme W. Subcutaneous ivermectin use in the treatment of severe Strongyloides stercoralis infection: two case reports and a discussion of the literature. J Antimicrob Chemother. 2016 Jan;71(1):220-5.
3. Zeitler K, Jariwala R, Restrepo-Jaramillo R, Kapadia S, Casanas B, Alrabaa S, Sriaroon C. Successful use of subcutaneous ivermectin for the treatment of *Strongyloides stercoralis* hyperinfection in the setting of small bowel obstruction and paralytic ileus in the immunocompromised population. BMJ Case Rep. 2018 Jun 4;2018:bcr2017223138.
4. Tam JS, Routes JM. Common variable immunodeficiency. Am J Rhinol Allergy. 2013 Jul-Aug;27(4):260-5.
5. Franco-Parades C. Infectious Syndromes Associated with Immunodeficiencies. Core Concepts in Clinical Infectious Diseases. 2016.