

Response to the Editor and Reviewers

Reviewer(s)' Comments to Author:

Reviewer: 1

The case of isolated histoplasmosis in a pediatric patient with Crohn's disease presented by the authors is of clinical importance. It is critical to rule out any infection, including fungal infection, in patients with IBD before starting immunosuppressive therapy. The case is well described and illustrated by the authors. The advantage of the manuscript is the Reports of histoplasmosis mimicking IBD in pediatric immunocompetent patients (Table 1) and the List of infectious diseases mimics of IBD that should be excluded in IBD patients (Table 2), which can be used in real clinical practice. Cited references are relevant, up-to-date, and without self-citation. The manuscript is certainly recommended for publication without any revision.

Thank you for your very careful review of our paper and for the comments.

Reviewer(s)' Comments to Author:

Reviewer: 2

The authors report a case of Gastrointestinal Histoplasmosis Complicating Pediatric Crohn's Disease. This case is rare and of value for reporting. There is one question that needs to be answered. The relevant signs were not obvious under HE staining. GMS and Periodic acid-Schiff stain is not a routine test at this time. Why would the authors prescribe such a test to the patient here? Does the patient have a history of relevant travel?

Thank you for your very careful review of our paper and for the comments that ensued. Below we address the questions posed by the review.

Response: Fungal infections are becoming more frequent because of expansion of at-risk populations. Although histopathologic examination detects fungal invasion of tissues, there are few instances where the morphological characteristics of fungi are specific. Therefore, histopathologic diagnosis is primarily descriptive of the fungus and includes the presence or absence of tissue invasion and the host reaction to the infection (i.e., granulomatous inflammation). Grocott-Gomori methenamine silver (GMS) and periodic acid-Schiff (PAS) special stains represent two of the most commonly used ancillary tests that serve as adjunctive tests beyond routine hematoxylin and eosin in histopathology practice. Both tests are used predominantly for their detection of fungal infections. These stains help to distinguish fungi based on morphologic characteristics such as size, type of budding, presence of hyphae, and branching. Histoplasma are characterized as 2–4 µm in size with round to oval uninucleate yeast cells that may show narrow-based budding, usually intracellular, and clustered within the histiocytes. Other yeast forms of similar size may be difficult to discriminate from one another (i.e., Histoplasma may be confused with capsule deficient Cryptococcus neoformans, Sporothrix schenckii, the small form of Blastomyces dermatitidis and endospores of Coccidioides spp).

The patient has no history of travel, but resides in an area considered endemic for Histoplasmosis.