

Original Article

Intestinal anisakidosis: Histopathological findings and differential diagnosis



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ARTICLE INFO

Article history:

Received 6 May 2014

Received in revised form 6 June 2014

Accepted 19 June 2014

Keywords:

Anisakidosis

Crohn's disease

Eosinophilic enteritis

Anisakis

ABSTRACT

Anisakidosis is a human zoonotic disease caused by the ingestion of raw or undercooked or not adequately salted, pickled, or smoked fish containing larval nematodes of the *Anisakis* species. The incidence of this infection is higher in geographical zones with traditional consumption of raw fish. However, in the last years, prevalence raised in low risk zones due to the increase popularity of Asian cuisine. According to where the larvae settle in the gastrointestinal tract, anisakidosis may have different clinical symptoms. In particular, intestinal anisakidosis may mimic several surgical conditions, including appendicitis, ileitis, diverticulitis or inflammatory bowel disease. For this reason, diagnosis is often histopathological. In the present paper, we describe the clinico-pathological findings of six novel cases of intestinal anisakidosis occurred in southern Italy, and provide clues for the differential diagnosis toward Crohn's disease and eosinophilic enteritis, which have similar histopathological characteristics. Awareness of the existence of intestinal anisakidosis may facilitate its recognition and correct diagnosis, which is of fundamental importance for appropriate therapeutic approach.

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Introduction

Anisakidosis is a human infection caused by the ingestion of raw, undercooked or not adequately salted, pickled, or smoked fish containing larval nematodes of the *Anisakis* species [1–4].

Following ingestion, *Anisakis* larvae migrate to the human digestive tract, invade the gut wall, and cause various symptoms depending on where they settle. The stomach is involved in most of the cases, while intestinal anisakidosis represents only 4% of the cases [5–7]. Clinically, gastric anisakidosis is characterized by a sudden onset of severe abdominal pain, nausea, and vomiting 1–8 h after the ingestion of raw fish containing *Anisakis* larvae [7]. In these cases, diagnosis can be accomplished by endoscopy, which shows the presence of the worm in the stomach wall [8]. In contrast, intestinal anisakidosis develops within few days (from 1 to 5 days) after ingestion of the larvae, and presents with severe abdominal pain, ileus-like symptoms, or diarrhea with blood or mucus [4,9]. Intestinal complications include small bowel

obstruction, ileal stenosis, intussusception, intestinal perforation, and pneumoperitoneum [10]. Due to the vague symptoms [8,12], enteric anisakidosis may simulate several surgical conditions such as appendicitis, ileitis, diverticulitis or inflammatory bowel disease [4,5,10,12]. For this reason, the first diagnosis is often performed by the surgical pathologist. The histopathological diagnosis of intestinal anisakidosis is based on the identification of the parasite and inflammatory infiltrate rich in eosinophils [7,11]. However, in countries where the incidence of this disease is low and in the absence of a detailed clinical history, intestinal anisakidosis may be misdiagnosed with other entities, such as Crohn's disease or eosinophilic enteritis, with relevant disadvantages for the quality of life of patients [13].

In the present paper we describe six novel cases of anisakidosis occurred in southern Italy (Campania and Sicily) and discuss the histopathological differential diagnosis. The clinico-pathological findings observed in all of the cases are resumed in the table.

Case 1

A 20-year old man referred to our hospital because of abdominal pain and vomiting. Laboratory tests revealed an increased neutrophil count table. Ultrasonographic (US) examination showed a

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globous appendix with intraluminal coprolites, and an anechoic peri-appendicular fluid collection. The patient was submitted to the surgical resection of the ileum, in the suspicion of intestinal perforation associated with Chron's disease. The gross examination of the surgical specimen revealed two linear lesions extending from the mucosa to the muscularis propria and showing sharp borders and hemorrhagic areas. The histological examination with conventional hematoxylin and eosin (H&E) stain showed ulcerative lesions, interstitial edema and inflammatory infiltrate with predominance of eosinophils within the mucosa and the submucosa. Eosinophils formed microabscesses and granulomas around well-preserved helminthic larva with the morphology of *Anisakis* (Fig. 1a). Diagnostic morphologic characteristics of the parasite included an unpaired excretory gland, Y-shaped lateral epidermal cords, no apparent reproductive system, and a ventriculus (glandular esophagus) (Fig. 1b). Granulomas composed of a central core of eosinophils surrounded by a dense cuff of histiocytes and chronic inflammatory cells were also found around fragments of the parasite cuticle (Fig. 1c) were also seen around fragments. Based on the histopathological findings, intestinal anisakidosis was diagnosed. Neutrophil count fell to normal values immediately after surgery. In addition, a targeted study of the patient's history showed that he had eaten raw fish (marinated anchovies) about 7 days before the onset of the clinical symptoms.

Case 2

A 52-year old woman was admitted to our hospital because of abdominal pain, vomiting, diarrhea and fever. An increased neutrophil count was evidenced by laboratory tests. In addition, US examination and computed tomography (CT) scan showed diffuse meteorism and the distension of the jejunum and ileum with air-fluid levels and intra-peritoneal effusion. In the suspicion of neoplastic intestinal obstruction, the patient underwent resection of the ileum. Gross examination of the surgical specimen revealed a 2 cm in size ulcerative lesion in the mucosa, which was centered by a whitish filamentous structure 2 cm in length (Fig. 2). Microscopic examination of the formalin-fixed and paraffin embedded samples of the ileum showed an ulcerative lesion involving the mucosa and submucosa, interstitial edema and a trans-mural chronic inflammatory infiltrate with a high percentage of eosinophils. Eosinophils were organized in granulomas and micro-abscesses. The histological examination of the filamentous structure revealed that it was a parasitic nematode with morphological characteristics corresponding to *Anisakis*. On this evidence, intestinal anisakidosis was diagnosed. Immediately after surgery, neutrophil count fell to normal levels. Finally, a close and targeted study of the patient's history showed that she had eaten raw fish (marinated anchovies) a couple of days before the onset of the clinical symptoms.

Case 3

A 36-year old woman referred to our institution because of diffuse abdominal pain. Laboratory tests revealed an increased neutrophil count. US examination showed thickening of the wall of right colon. Findings were confirmed by CT scan which revealed a concentrically thickening of the wall of the ascending colon, suggestive for intussusception. Hence, the patient underwent surgical resection of the right colon and terminal ileum. Macroscopically, the colonic mucosa showed absence of normal plicae and edema, while ileocecal valve, appendix, and terminal ileum were spared. A filamentous structure 2 cm in length lied on the mucosal surface of the colon. Histological examination of the right colon showed interstitial edema in the submucosa and a transmural inflammatory infiltrate with a high amount of eosinophils. Inflammatory infiltrate

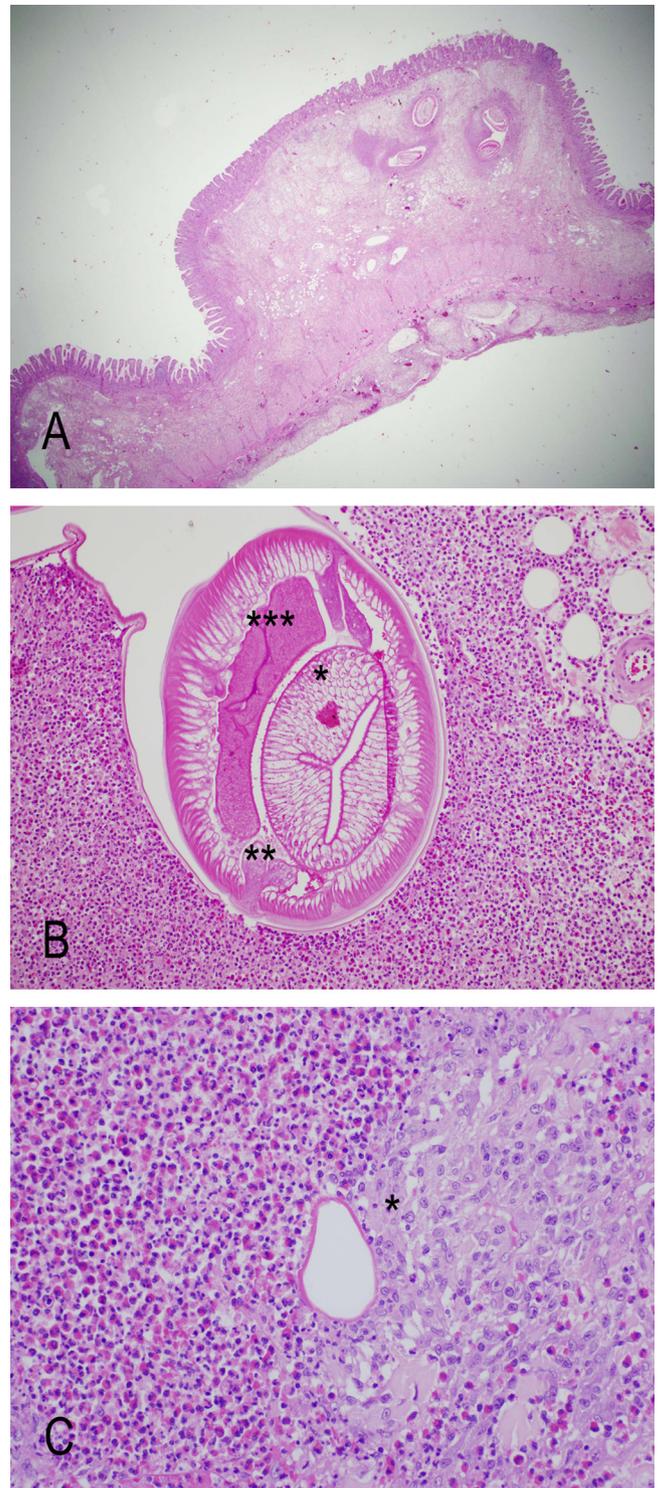


Fig. 1. (a) Panoramic view of ileum showing interstitial edema, inflammation in the mucosa and submucosa and granulomas around *Anisakis* larvae (hematoxylin and eosin stain; original magnification, 12 \times). (b) Higher magnification showed that the parasite larva was surrounded by a thick cuff of acute inflammatory cells with numerous eosinophils. The larva had a central digestive tract (*), Y-shaped lateral epidermal cords (**) and an unpaired excretory gland (***) (hematoxylin and eosin stain; original magnification, 400 \times). (c) Granuloma composed of eosinophils surrounded by a cuff of histiocytes around a fragment of the parasite cuticle (*) (hematoxylin and eosin stain; original magnification, 400 \times).

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