Case report

Anisakiasis caused by herring in vinegar: a little known medical problem

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SUMMARY Six cases of intestinal anisakiasis, or herring worm disease, diagnosed over a two year period in a Belgian gastroenterology unit are described. They presented mainly as intestinal obstructions and larvae of this marine nematode were found in the intestinal wall of two of the four patients who were operated on. In two other patients awareness of the diagnosis permitted conservative treatment and spontaneous healing. In five patients symptoms developed after they had eaten herring marinated in vinegar, a hitherto little known source of the herring worm disease.

Anisakiasis or the herring worm disease is the infestation of man by species of marine nematode larvae belonging to the subfamily Anisakinae, which is further divided into three types: Anisakis, Contracoecum and Phocanema. The adult roundworms are intestinal parasites of marine mammals such as seals and dolphins. Ova passed in the faeces of these mammals hatch in the water, where the resulting larvae are ingested by crustaceans, which in turn are eaten by fish and squid. The larvae mature in the viscera and muscles of the fish, ultimately reaching an infective stage.

When inadequately prepared fish is eaten by man, the Anisakis larvae penetrate the mucosa of the stomach, the small intestine, or even the colon, causing an acute focal inflammation. Commonly eaten fish like herring, salmon, cod, pollack, and mackerel are frequently infected with the larvae,1,2 which are resistant to environmental changes. Anisakiasis is often diagnosed in Japan, where it is a health hazard because of Japanese culinary habits. It is remarkable that this syndrome is rarely diagnosed in most European countries except the Netherlands, and reports from North America are extremely rare.1-3

Over a two year period six presumed cases of intestinal anisakiasis were seen in our unit, five of them occurring after the patients had eaten herring commercially pickled in vinegar, a little known source of the disease.

Case reports

PATIENT 1
This 43 year old man, who had had an appendectomy, was admitted for vomiting and abdominal pain on 5 April, 1984. An x-ray examination of the abdomen suggested a small bowel obstruction; a barium enema proved normal. The white cell count was 7200. He underwent surgery on the same day. The abdomen contained dark fluid, and a bowel segment in the midileum was severely inflamed and so was resected. Pathological examination showed considerable oedema of the bowel wall along with dense infiltration with inflammatory cells and eosinophils, and some interstitial haemorrhage. In the submucosa a transverse section through a parasite consistent with Anisakis Marina larva was noted (Fig. 1). Later, the patient reported he frequently ate green herring, and two days before admission he had eaten pickled herring.

PATIENT 2
This 65 year old man, who had had surgery for an inguinal hernia, was admitted to hospital on 25 May, 1984 after a day of vomiting and abdominal cramps. The day before, he had eaten pickled herring, which
he consumed almost weekly. The white cell count was 10,300 with 3% eosinophils. An X-ray examination of the abdomen showed a bowel obstruction. Laparotomy one day later revealed the presence of serous peritoneal fluid and a acutely inflamed terminal ileum with thickening of the mesenterium. In view of the major bowel obstruction a resection of the inflamed segment was carried out. Histological examination revealed acute eosinophilic enteritis.

PATIENT 3
This 53 year old man was admitted on 7 June, 1984 with abdominal cramps and a history of passing blood in the stools. The white cell count was 10,300 with 1% eosinophils. A barium enema showed a circular stenosing mass in the caecum very suggestive of a tumour (Fig. 2). Dilated small bowel loops indicated an obstruction. When a laparotomy was done five days later the tumour seemed to have vanished, although there was still a localised thickening of the caecum wall. A right hemicolectomy was carried out and histological examination showed oedema and a predominantly eosinophilic infiltrate. Later questioning revealed that the patient was accustomed to eat herring pickled in vinegar and had done so on the day before his admission.

PATIENT 4
During a journey in South America, this 62 year old businessman ate fish in Chili and also raw salmon during a flight from Chili to Brazil. Eight hours later he suffered abdominal cramps and returned to Belgium. On admission on 27 November, 1985 a radiograph showed an obstruction of the small bowel. The white cell count was 4,900 (4% eosinophils). Conservative treatment reduced the abdominal cramps, and the radiological signs of intestinal obstruction disappeared. A barium meal five days later showed slow intestinal transit with an area of oedematous folds at the transition of a slightly dilated jejunum to a normal ileum. A repeat barium meal three weeks later was completely normal.

PATIENT 5
This 44 year old man complained of abdominal cramps some 12 hours after eating herring pickled in vinegar. He was admitted on 20 January, 1986, and radiograph showed an obstruction of the small bowel. The white-cell count was 11,100 (2% eosinophils). In view of the anamnestic data, a conservative approach was selected with prednisolone intravenously 50 mg/day. A barium enema showed no abnormalities, and a barium meal...
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Fig. 3 Transverse section through an Anisakis marina larva found in the wall of the terminal ileum of patient 6.

four days later revealed only a slight dilatation of some small bowel loops. He made an uneventful recovery.

**Patient 6**
This 56 year old woman ate herring pickled in vinegar on 6 and 7 February, 1986. A few hours later she complained of diffuse abdominal pain. On admission the next day there was a marked tenderness of the right iliac fossa, and a white cell count of 9500. As an acute appendicitis was suspected she was operated on. An inflammation of the ileocaecal valve and caecum was found and a limited resection of this area was carried out. Pathological examination revealed an acute inflammatory and eosinophilic infiltrate together with the presence of a worm larva in the ileum mucosa, which was considered an *Anisakis marina* larva (Fig. 3).

**Discussion**

Anisakiasis or the herring worm disease is perhaps an uncommon but possibly also an underestimated disease in Belgium and in most European countries. Documented reports from Belgium,\(^7\) the United Kingdom,\(^9,11\) France,\(^12-14\) and North America\(^1,5,15\) are few and usually give only one case. Anisakiasis is a common problem in Japan\(^16-18\) and one could expect an increasing incidence in the West as enthusiasm for raw fish is growing, reflected in the popularity of Japanese restaurants with their uncooked seafood and the so-called ‘sushi-bars’.\(^1,19\)

Before 1968, it was a common problem in the Netherlands largely because of the consumption of green herring (‘maatjes’) which is only lightly salted.\(^20-24\) Since then, compulsory freezing to \(-20^\circ\)C of all fish before marketing has virtually eradicated anisakiasis in this country. The infective larvae are killed by freezing at \(-17^\circ\)C to \(-20^\circ\)C for 24 hours and also by heating at \(60^\circ\)C for a few minutes.\(^25,26\) They are, however, quite resistant to the environment and are unaffected by salting, smoking, or pickling in vinegar.\(^1,25,26\) Early evisceration of the fish immediately after being caught, once thought to be useful, is probably of little value in preventing infection in man as most fish have larvae in the muscles as well as in the visera.

Most cases of anisakiasis occur after ingestion of raw or undercooked fish. As far as we know, there have been no documented case reports of anisakiasis caused by herring pickled in vinegar. Although we did not examine pickled herring for the presence of larvae, living larvae of *Anisakis marina* were recently recovered from pickled herring in The Netherlands.\(^27\) During the course of two years we dealt with six cases of anisakiasis, five of which occurred after eating of herring commercially pickled in vinegar. One case occurred after eating raw fish in South America.

Experimental studies in rabbits\(^28-29\) have shown the following pathological sequence: penetration of the
larvae into the mucosa and submucosa provokes edema, followed some 24 to 48 hours later by infiltration with predominantly eosinophilic granulocytes, and, after about 96 hours, local necrosis and haemorrhage and the death of the larvae. This histological picture of acute eosinophilic phlegmon was found in all our operated patients. Some reports describe granuloma formation, but this was not seen in our patients, perhaps because the time between the initial manifestation and surgery was rather short.

To explain the discrepancy between a probably considerable consumption of larvae bearing fish and the seemingly low incidence of clinical anisakiasis, the hypothesis of ‘the double strike’ was developed based on experiments in rabbits.26-28 The initial penetration of the mucosa usually provokes only a minor reaction, but leaves a local hypersensitivity that gives rise to intense inflammation when a new penetration occurs. This reaction would then be worse the closer the two penetrations are in time and distance. Most of our patients were, indeed, regular consumers of herring. A first penetration, however, might also provoke a florid inflammation.29

The site of the penetration (stomach, jejunum, ileum or colon) determines the clinical form. All our patients presented acute abdominal pain together with an intestinal obstruction or an appendicitis like syndrome. Four were operated on, partially because we were unfamiliar with the syndrome but also to exclude either other causes of intestinal obstruction (patients 1, 2, 3) or acute appendicitis (patient 6). We did not see a gastric form of anisakiasis, in which it happens to find penetrating larvae and to remove them by gastroscopy, thereby making a correct diagnosis and at the same time providing an effective therapy.13-14 Few cases of gastric anisakiasis have been described in Europe, whereas in Japan it seems to be the predominant form.10 It has been suggested that a relatively high frequency of gastric achlorhydria or hypochlorhydria in Japan could play a predisposing role.15 These gastric cases present acute epigastric pain, nausea, and vomiting a few hours after ingestion of infected fish. A more chronic form with granuloma formation and a more indolent symptomatology is also known.26-30 Gastric anisakiasis can be misdiagnosed as peptic ulcer, acute gastritis, food poisoning, polyps, or neoplasia.

In Europeans, the intestine seems to be the most common site of anisakiasis. The symptoms may include diffuse abdominal tenderness or colicky abdominal pain, nausea, and vomiting. The syndrome is often incorrectly diagnosed as acute appendicitis or regional ileitis. Further differential diagnosis includes intussusception, ileus, diverticulitis, and neoplasia. Especially the colonic form, which is infrequent, may simulate a tumour of the colon as was the case in patient 3. In rare cases the larvae migrate into the mesentery and even migration into the liver, pancreas, greater omentum of gall bladder has been described.

It is usually stated that the symptoms occur within seven days after the ingestion of the infected fish, but all our patients had symptoms within two days. Although an abdominal condition requiring surgery is often simulated, the natural course of intestinal anisakiasis is usually good in the absence of perforation and peritonitis. On the other hand, the diagnosis is difficult to make clinically and is dependent upon an accurate history, an appropriate degree of suspicion and a close follow up of the patient. Radiological investigations are useful in excluding other conditions. The white cell count and blood eosinophilia do not help in making the diagnosis and serological tests are of limited value.31 Most commonly the final diagnosis hinges upon surgical resection and the pathologist’s search for larval fragments within the inflamed tissue, this being the final proof of the diagnosis (see patients 1 and 6). Larvae cannot always be found in resected specimens,32 however, as they may disappear by migration, desintegration, and resorption. So the pathognomonic presence of the larvae can not be a claim for the diagnosis of anisakiasis. We therefore suggest that the combination of an acute regional eosinophilic enteritis, along with a history of recent ingestion of potentially infected fish, should allow the diagnosis (our patients 2, 3). In a Japanese series of 1351 cases of acute and chronic regional enteritis, it was suggested on re-examination of the histologic preparation half of the cases might have been anisakiasis.17 Furthermore surgery is usually unnecessary as most cases resolve spontaneously. So, the paradox of anisakiasis is that the medical treatment is the treatment of choice for a condition that can only be definitely diagnosed by finding larvae in a resected specimen. We propose, however, that in the absence of dramatic abdominal signs and in the presence of a suggestive history (recent ingestion of infected fish) the diagnosis of anisakiasis is acceptable and a conservative treatment should be followed. We are aware that in these cases the diagnosis is rather speculative but one may avoid unnecessary surgery, as in our patients 4 and 5. In the latter the disappearance of inflammation seems to have been accelerated by the administration of corticosteroids which may well be a helpful adjuvant therapy. Penetration of the larvae through the intestinal wall indeed provokes a florid inflammatory reaction that is usually self-limiting and results in the death of the parasite. A short anti-inflammatory treatment thus seems justified instead of anti-helmintic agents which are ineffective.
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In conclusion, we suggest that anisakiasis might be more common than expected, as only the worst cases are admitted into the hospital, and even then only some are properly diagnosed. It seems likely that only the tip of the iceberg is seen and that many of the less severe cases remain undiagnosed, the condition being considered transient gastroenteritis. Patients with recent abdominal pain or intestinal obstruction should always be asked about the intake of herring or other uncooked fish. In this way, unnecessary surgical procedures may be prevented. The disease is completely preventable either by proper preparation of the fish or by general measures such as prolonged freezing of the fish before marketing.

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References