Full Length Research Paper

Acute abdomen, anisakidosis and surgery: Value of history, physical examination and non immunological diagnostic procedures

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> > Abstract

Anisakidosis should be taken into account in the differential diagnosis of abdominal pain. This is a cohort study involving 134 patients with acute abdominal problems. After a follow-up period, 52 patients were diagnosed as presenting anisakidosis, while in 82 anisakidosis were ruled out. In this study, raw fish ingestion, clinical manifestations, laboratory and radiology results were evaluated. Patients in the two groups differed with respect to the raw fish ingestion, presence of vomits, abdominal distension and peritonism. Eosinophilia, bowel dilatation, thickened intestinal wall and intra-abdominal free fluid were more frequent in the group with anisakidosis. In this group, 23 were operated, 4 of them undergo laparoscopy. Although some symptoms and signs, eosinophilia and the radiological and echographic findings differ between the two groups they are non-specific, but if the patient has eaten raw or marinated fish is a very suggestive diagnosis of anisakidosis. The precedent of ingestion of raw fish has a high negative predictive value and its absence rules out anisakidosis. Laparoscopy has a diagnostic-therapeutic role.

Keywords: Anisakidosis, anisakiasis, anisakis simplex, acute abdomen, Anamnesis, radiology, surgery, laparoscopy.

INTRODUCTION

Anisakis simplex is the main causal species of human anisakidosis, which is transmitted by the ingestion of contaminated raw or lightly-cooked fish (Daschner et al., 1999; Smith and Wootten, 1978), although cases have also been described following the consumption of cooked fish (Rodríguez and Cuevas, 1997). Several forms of clinical presentation have been described (Daschner et al., 1999; Smith and Wootten, 1978), including gastric, intestinal, extra-gastrointestinal, gastroallergic and hypersensitivity reactions mediated by IgE (Audicana et al., 1995). Its clinical pattern tends to be acute and self-

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limiting (Daschner et al., 1999; Verhamme and Ramboer, 1988) and its diagnosis depends mainly on anamnesis and clinical suspicion (Verhamme and Ramboer, 1988). Endoscopy can play a diagnostic-therapeutic role in accessible segments of the digestive tract (Canut et al., 1996; López et al., 1992; Zullo et al., 2010), although when the larva migrates to the intestine, surgery is often necessary (López et al., 1992, Matsuo et al., 2006; Smith and Wootten, 1978, Valle et al., 2012). Immunologic diagnosis is based on a skin test with a raw extract of *A. simplex* larva and on the determination of specific IgE against the latter (Daschner et al., 1999; Del Pozo et al., 1996).

Intestinal location is characterised by acute abdominal pain that may require the performance of an exploratory laparotomy/laparoscopy. The aim of the present study is to evaluate the anamnesis, the physical examination and the non-immunological complementary tests (laboratory, radiological, ultrasound) to distinguish between patients with anisakidosis and those with other causes of acute abdomen.

This article complements a previous earlier one which evaluated the role of immunological tests in diagnosing gastrointestinal anisakidosis (Del Rey et al., 2008).

PATIENTS AND METHODS

Patients

Cohort study, over a period of 4 years, of patients presenting acute abdominal pain and treated at the Emergency unit of our hospital. Criteria for inclusion are detailed in table 1. After a follow-up period of 1-6 months, the patients that were being included (n=134) were divided into 2 groups: A (anisakidosis, 52 patients: 23 were operated on and 29 were diagnosed after observing seroconversion against *A. simplex*); and NA (No anisakidosis, 82 patients with acute pathologies, but no anisakidosis) (table 2). The patients included in this research participated after being duly informed and giving their written consent. Another 48 patients were excluded after they failed to attend the Surgery department during the follow-up period or if they were not given the second IgE specific test against *A. simplex*.

Methods

The patients were assessed at the Emergency room, and the following items were evaluated:

A. Anamnesis: personal history of allergies, digestive disorders, the ingestion of raw or lightly-cooked fish, digestive or allergic symptoms.

B. Complete physical examination.

C. Laboratory analyses: haemogram, leukocyte formula and count.

D. Specific IgE test against *A. simplex* carried out at the Emergency Dept. and at 1-6 months following the acute phase. Carried out by radio-immunoblot assay (CAP system: Unicap Specific IgE, Pharmacia, Uppsala, Sweden). Results >0.35 kU/L were considered positive. The presence of seroconversion was determined after performing a second test to classify patients into one group or the other (see criteria for inclusion in Table 1).

E. Abdominal plain X-ray and ultrasound according to symptoms presented, clinical signs and preliminary diagnosis. CT abdominal scan was not performed routinely in patients with abdominal pain in the first two years of the study.

Statistical analysis. Carried out using EPIINFO 3.3.2. and EPIDAT 3.1. For quantitative variables, the Student *t* test was used, and for the qualitative ones, Pearson's chi-squared test. Multivariate analyses were carried out for all the variables with statistical significance.

RESULTS

The mean age in group A (42.9 ± 12 years) and NA (47.1 ± 20) did not vary significantly (p=0.281), neither had the gender a significant effect (p=0.354), although a higher proportion of men could be noticed (55.8%).

There was a seasonal trend in the presentation of the patients in group A: in the spring there were 28 cases (53.8%), comparing with 12 in the summer (23.1%) and 6 in the winter (11.5%) and autumn (11.5%), respectively. In group NA, the distribution was equitable throughout the year.

All the patients in group A except one (51/52) confirmed the ingestion of raw fish, mainly anchovies in vinegar, and in one case, raw sardines. In group NA, 21 patients (25.6%) had also consumed raw fish (table 2). With respect to this variable, the differences between the two groups were significant (p<0.001). The predictive values of this variable are shown in table 3.

No significant differences were found regarding the past history of intrinsic allergy (p=0.07), extrinsic allergy (p=0.33), peptic ulcer (p=0.15), gastroesophageal reflux (p=0.55) or gastric surgery (p=0.66).

The mean time interval between fish intake and the onset of symptoms in groups A and NA was 36.3 ± 25 hours (range: 4–150) and 86.4 ± 55 (range: 12-168), respectively (p=0.01). In group A, the duration of symptoms in non-operated patients ranged from 2 to 8 days and the abdominal pain was colicky and intense or continuous. Among the digestive symptoms, only the vomits presented significant differences. Allergic symptoms were observed in 4 patients in group A (7.7%), in 3 of them appeared after the digestive symptoms, and in 1 concurrently (table 4).

Among the patients in group A, the abdominal pain was the main clinical sign reported during the physical examination, and was located in the right lower quadrant (34.6%) or was diffuse (28.8%). Abdominal distension and peritonism were significantly different between the groups (table 4).

63.5% and 45.7% of the patients in groups A and NA presented leukocytosis, respectively. Eosinophilia (>500/mL) was observed in 4 patients (7.7%) in group A, and in none in group NA (p=0.02).

The radiologic and echographic findings were as follows: dilated intestinal loops, the presence of intraabdominal free fluid and thickened intestinal wall (figure. 1 and 2), and these were significantly more frequent in group A (table 5). The presence of free fluid was the only variable that presented statistical significance in the univariate and multivariate analysis of the data came from the physical and complementary examination.

A gastroscopy was performed on 4 patients in group

Table 1. Inclusion criteria for groups Anisakidosis and No-Anisakidosis.

Group Anisakidosis	Group No-Anisakidosis				
Abdominal pain	Abdominal pain				
• Surgical and/or anatomopathologic findings of eosinophilic enteritis with or without the presence of the anisakis larva, and/or	• Radiologic, surgical or anatomopathologic findings related to different from eosinophilic enteritis and/or				
• Specific seroconversion: change of class of the values of specific IgE against <i>A. simplex</i> in serial measurements up to 6 months following the acute phase of the illness.	• Absence of seroconversion in the titre of specific IgE against <i>A. simplex</i> .				

Table 2. Diagnoses of patients in group No-Anisakidosis: number (percentage in the group), ingestion of raw fish and high values of specific IgE against *A. simplex*.

Diagnosis	Number (%)	Ingestion of raw fish	High IgE–AS*
Acute appendicitis	8 (9.8)	1	3
Carcinomatosis	1 (1.2)	1	-
Acute cholecystitis	8 (9.8)	2	-
Acute diverticulitis	7 (8.5)	1	2
Non-specific abdominal pain	29 (35.4)	8	1
Non-specific enteritis	10 (12.2)	6	-
Epiploic infarction	1 (1.2)	-	-
Intestinal ischaemia	5 (6.1)	-	-
Blank laparotomy	2 (2.4)	-	-
Pneumonia	1 (1.2)	-	-
Intestinal obstruction	4 (4.9)	1	-
Ruptured ovarian cyst	2 (2.4)	-	-
Food-borne infection	2 (2.4)	-	-
Peptic ulcer	2 (2.4)	1	-
Total	82	21	6

* High IgE-AS: High specific IgE against A. simplex

Table 3. Predictive values of raw fish ingestion.

Raw fish ingestion	Value (95% CI)	
Sensitivity	98% (96-100)	
Specificity	74% (67-82)	
Positive predictive value	71% (63-79)	
Negative predictive value	98% (96-100)	
Positive probability quotient	3.83	
Negative probability quotient	0.03	

Table 4. Abdominal and allergic symptoms and signs: number of individuals affected (percentage in the group)

	Vomits	Constipation	Diarrhoea	Urticaria	Exanthema	Angio-oedem	a Abd. Mass	Abdominal distension	Peritonism	Abd. defence
Group	21	3	6	4	3	1	2	14	25	8
Anisakidosis	(40.4)	(5.8)	(11.5)	(7.7)	(5.8)	(1.9)	(3.8)	(26.9)	(48.1)	(15.4)
Group No-	18	9	15	1	1			9	24	10
Anisakidosis	(22.0)	(11.0)	(18.3)	(1.2)	(1.2)	-	-	(11.0)	(29.3)	(12.2)
Statistical										
significance (p value)	0.036	n.s.s.	n.s.s.	n.s.s.	n.s.s.	n.s.s.	n.s.s.	0.03	0.04	n.s.s.

Abd: abdominal

n.s.s.: value not statistically significant



Figure 1. Abdominal plain X-ray film in patient with anisakidosis: dilatation of intestinal loops with air-fluid levels.



Figure 2. Abdominal ultrasound in patient with anisakidosis: dilatation of intestinal loops, thickening of folds and the presence of small amounts of free fluid among the loops.

Table 5. Findings of abdominal radiography and ultrasound.

	Plain X-ray film: thickened or dilated loops	Ultrasound: free intra abdominal fluid	a- Ultrasound: thickened intestinal wall
Group Anisakidosis	27/52 (51.9%)	16/22 (72.7%)	11/22 (50%)
Group No-Anisakidosis	18/70 (25.7%)	10/35 (28.6%)	3/35 (8.6%)
Statistical significance (p value)	0.005	0.002	0.001

A, all of whom presented pathological signs (gastric ulcer and gastritis) but without the presence of parasite. A plain X-ray of the abdomen revealed 3 of these patients to have dilated intestinal loops and 1 to have pneumoperitoneum, so this patient was operated.

In group A, 23 patients were operated, mostly in the first two years of study, with the following preoperative diagnoses: small bowel obstruction (39.1%), acute

appendicitis (34.8%), non-specific acute abdomen (21.7%) and pneumoperitoneum (4.3%). The area of digestive tract affected, the presence of intestinal perforation and parasite are detailed in table 6. In one patient, the parasite was extracted alive and highly active inserted within the intestinal mucosa (figure. 3 and 4), it was in the moulting phase to L4; in the remaining patients it was found within the intestinal wall (figure. 5). In every

Table 6. Location,	length of the	affected seg	ment, presence	e of perforatio	n and of	parasite in	operated	patients
with anisakidosis.								

Location	Number (%)	Length*	Perforation	Presence of parasite
Stomach	1 (4.3)		1	
Jejunum	6 (26.1)	9-40		1
lleum	9 (39.1)	3-20	2	4
Right colon	7 (30.4)	2-20	1	
Transverse colon	1** (4.3)	6		

%: percentage in operated patients in group A. * Length of the affected segment (in centimetres).

** Associated with infected cecum.



Figure 3. Surgical specimen of anisakiasis of the small intestine (ileum): visible are mucous oedema and erythematous area in the centre, with a live larva affixed to the wall.



Figure 4. Detailed picture of the larva penetrate the intestinal mucosa in the figure 3.



Figure 5. Transversal section of the larva of *A. simplex* within the intestinal wall: i: intestine; **Ic**: lateral cords; **ec**: excretor cell; **m**: muscle.

case, the parasite involved was *A. simplex*. No extra gastrointestinal locations were found.

The following types of surgery were performed: (i) intestinal resection (16 patients) -segmental when the lesion was located in the small intestine and right hemicolectomy for colonic involvement-, (ii) suture of the gastric perforation (1 patient) and (iii) exploratory surgery without resection (6 patients). The surgical approach depends on the pre-operatory diagnosis; in our cases, in general, a median laparotomy or McBurney incision was performed. In 4 cases, a minimally invasive approach was applied: in one of them, to suture a gastric perforation; in two patients, after confirming the findings, it was decided not resection of the affected area; and in the fourth case, a mini laparotomy was included to extirpate the affected intestine and to perform a primary anastomosis.

At present, the number of cases has decreased to a current 1-2 yearly and no surgical interventions are required. We have only observed one relapse of intestinal involvement, following the ingestion of anchovies in vinegar, and this patient recovered with symptomatic treatment.

DISCUSSION

The diagnosis of anisakidosis may be difficult (Repiso et al., 2003; Smith and Wootten, 1978). Due to the non-specific nature of its symptoms, it is probably underdiagnosed (Toro et al., 2004), and thus if the background of the prior consumption of raw fish is not taken into account, it may fail to be diagnosed. Moreover, the patient may not remember this fact (Smith and Wootten, 1978), as in one of our patients; who was operated to be suspected of acute appendicitis, but the surgical findings were ileal inflammation. It should taken into account that the high level of consumption of raw fish among the spanish population (Del Rey et al., 2006, González et al., 2005) means that this factor has a low positive predictive power (71%) and a high negative one (98%); in other words, the importance of being aware of this background in a patient with acute abdomen is that it may enable us to exclude this disease as a cause of the symptoms presented.

Abdominal pain is the predominant symptom of this disease, it is colic and intense, although it may also be continuous, due to abdominal distension, and mainly located in the right lower quadrant or diffuse (Navarro et al., 2005). On comparing the frequency of the symptoms in groups A and NA, only the presence of vomits was associated with significant differences (table 3), although this cannot serve as a diagnostic criterion due to its non specificity. Among our patients, allergic symptoms and eosinophilia were recorded among only 7.7% of those with anisakidosis; and this finding is of limited practical use, due to their low frequency (0-7%) (Alonso et al, 2004; Domínguez et al., 2003; Matsuo et al., 2006; Navarro et al., 2005; Olveira et al., 1999). In the gastric and gastroallergic forms, the presence of eosinophilia is more common, and may range from 0-40% (Alonso et al., 2004; Olveira et al., 1999; Smith and Wootten, 1978), but the problem is that this only tends to appear after 7-10 days of the acute phase of the illness (Daschner et al., 2000; Olveira et al., 1999).

Although peritonism and abdominal distension

presented significant differences between the two groups, the findings of the physical examination –like those for the symptoms– were non-specific and of no assistance for establishing the diagnosis of this illness. Furthermore, the statistical differences measured are probably due to the variety of pathologies contained within the group NA.

Because most of the patients with anisakidosis examined at our hospital presented intestinal location, endoscopy had a limited utility. Sometimes, an accurate diagnosis is not made because these patients often present only mild-moderate symptoms, or because those with epigastralgia are examined by non-surgical medical practitioners and are prescribed pharmaceutical treatment (Ortega et al., 2005).

With respect to the value of specific IgE (data not shown), we observed that this may be less than 0.35 kU/L at the onset of this parasitosis, probably due to a first infestation (Del Rey et al., 2008); alternatively, the value may be high without the parasitosis being present. due to a high seroprevalence in the healthy population against A. simplex (11-21%) (Del Rey et al., 2006; Puente et al., 2008), related to the ingestion of raw. smoked or marinated fish (González et al., 2005; Puente et al., 2008) [13,21]. The use of purified excretedsecreted antigens (Ani s 1, Ani s 4, Ani s 7, Ani s 10) (Anadón et al., 2009, 2010; Caballero et al., 2011; Moneo et al., 2000; Rodríguez et al., 2007) may facilitate its diagnosis, especially for allergic forms. Circulating antigens of A. simplex have been detected in experimental anisakiasis in rats (Campos et al., 2004); the extrapolation of this to humans might enable us to achieve a diagnosis in the acute phase of this disease.

In the intestinal localization of this illness, a plain Xray film of the abdomen shows dilatation of small bowel loops with thickening of the folds and the presence of airfluid levels (Canut et al., 1996; Matsuo et al., 2006; Navarro et al., 2005), in our patients was observed in 51.9%. Abdominal ultrasound is sensitive for the detection of bowel wall thickening (>4mm) and the presence of free fluid, detecting these in 33-100% of cases (Castán et al., 2002; Ido et al., 1998). Among our patients, these were observed in 72.7% and 50% of cases, respectively. It is important to note that although these findings are not specific, their concomitance with the ingestion of raw or marinated fish is very suggestive of the diagnosis of anisakidosis. Nakaji has published a case of a patient with intestinal anisakiasis diagnosed by capsule endoscopy (Najaki, 2009).

We performed abdominal computed tomography (CT) scan only in cases in which etiology was not suspected or in those who had poor outcome. Probably a greater use of CT could have avoided surgery, but we must take into account that most were operated due to unresolved bowel obstruction or abdominal pain with defense, and four patients had gastric or intestinal perforation; this is in accordance with previous reports (Alonso et al., 2004; López et al., 1992; Marzocca et al., 2009; Matsuo et al.,

2006; Navarro et al., 2005; Olveira et al., 1999; Ortega et al., 2005; Valle et al., 2012). Only 4 out of the last 24 patients in group A underwent surgery, all exploratory laparoscopy. As occurs in other abdominal pathologies requiring surgery, the use of a laparoscopic approach reduces the aggression to the patient, and may constitute a valid diagnostic-therapeutic method (Biondi et al., 2008; Sugita et al., 2008).

In the intestinal involvement of this parasitosis, the ileum is reported to be the most commonly affected segment (66-73%), followed by the jejunum (4-27%) and the colon (8%) (Alonso et al., 2004; Daschner et al., 2000; Domínguez et al., 2003; Ido et al., 1998; Ortega et al., 2005), although in our study the areas most commonly affected were the ileum (39.1%) and the right colon (30.4%), which is in accordance with the cases described by Ortega et al. (2005). This fact might be accounted by a fast transit through the small intestine, by the ingestion of a more fibre-rich diet, or by a smaller loss of larval vitality (Matsumoto et al., 1992).

In our health area the number of cases of anisakidosis has decreased in recent years from an annual incidence between 10 and 16, to 0-2 cases at present, probably due to public-health education.

It may be said that the clinical findings and those of the routine complementary examinations carried out in the Emergency department can provide guidance towards an accurate diagnosis; this is especially so in the case of bowel wall thickening and free intra-abdominal fluid. This disease may remain undetected if the ingestion of raw or lightly cooked fish is not taken into account. With a very high rate of accuracy (98%), the absence of this ingestion rejects the presence of anisakidosis. Minimally invasive surgery is useful in diagnosis and treatment of patients with suspected anisakidosis and poor outcome.

ACKNOWLEDGEMENTS

We thank doctors Adela Valero and Josefa Lozano, at the Parasitology Department of the School of Pharmacy of Granada University, for their encouragement in carrying out this study and for their work in the identification of larvae.

This article has been financed by the funds of the "Asociación Jornadas Quirúrgicas de Antequera" (Málaga). Spain.

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