CASE REPORT

Ileal iterative spontaneous perforation from foreign body granuloma: problems of histopathologic diagnosis

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Abstract
Spontaneous ileal perforation is a very rare cause of peritonitis. It occurs, in most of the cases, as a complication of Crohn’s disease or intestinal tuberculosis. We present the case of a 23-year-old female patient with multiple surgical interventions during the last year, for iterative ileal spontaneous perforation with generalized peritonitis of which cause was initially assigned to intestinal tuberculosis. Actual episode of generalized peritonitis was determined once again by an ileal perforation of 5 mm at 70 cm from the ileo-cecal valve situated on a suture scar. Distally, a bowel stricture and a non-complicated Meckel’s diverticulum were also noted. We performed an enterectomy including all three aforementioned lesions with end-to-end anastomosis. The histopathologic report revealed granulomatous giant-cellular inflammation in the margins of the perforation. The tuberculous etiology was questioned because of the negativity of the PCR-test and multiple recidives of perforation under specific anti-tuberculous medical therapy. The discovery of some rests of non-resorbable suturing material in a granuloma on an ancient enterorraphy scar in the resected specimen, finally established the cause. The granulomatous giant-cellular inflammation of foreign body is a rare cause of ileal perforation. The histopathologic differential diagnosis is difficult needing correlation with clinical data. Usage of resorbable suture material avoids that risk.

Keywords: tuberculosis, Crohn’s disease, ileal perforation, granuloma, foreign body.

Introduction
Ileal spontaneous perforation is a rare cause of peritonitis, most of the time occurring as a complication of Crohn’s disease or intestinal tuberculosis [1].

We will present the case of a female patient with multiple surgical interventions in the last year, with the diagnosis of generalized peritonitis from ileal iterative spontaneous perforation.

Initial diagnosis was intestinal tuberculosis based on macroscopic intraoperative findings and histopathologic finding of granuloma.

The real cause of the perforations was established only recently – granulomatous inflammation of foreign body determined by the non-resorbable suture material.

Patient, Methods and Results
We present the case of a female patient, 23-year-old, with multiple surgical interventions in the last year for “generalized peritonitis from perforated ileal tuberculosis”.

Each intervention consisted in closure of the perforation, peritoneal lavage and multiple drainages. Postoperative course was simple.

Her medical history included also a lumbar spondylodiscitis L4–L5 operated on and a surgical intervention for a gynecologic problem that the patient cannot clearly indicate and from which she kept no record at all.

The patient was admitted once again, this time in our surgical unit, with the same clinical picture of generalized peritonitis and septic shock. The abdominal and pelvic computer tomographic scan confirmed the diagnosis and the patient was operated on, when the vital functions were stable.

The peritoneal cavity contained approximately 3000 mL of pus mixed with intestinal content. In the inframesocolic compartment, there was intensive perivisceritis.

After viscerolysis, we identified a perforation orifice of 5 mm at 70 cm from Bauhin’s valve, with sharp edges. Distally, at 50 cm from Bauhin’s valve we also noticed a stricture reducing the bowel lumen at 1 cm and, at 40 cm, a Meckel’s diverticulum that seemed not complicated. The loops of the small bowel presented such an aspect of “creeping fat” suggestive for Crohn’s disease.

An enterectomy, including all three aforementioned lesions with end-to-end anastomosis, was then decided; the perforation was excised and sent separately to histopathologic examination; lymph nodes were harvested from mesentery and sent separately to...
pathology; peritoneal lavage was done with more than 10 liters of warmed saline solution; multiple drains were placed in the peritoneal cavity; the incisional hernia was repaired with the excision of the old scar.

Specimens for histopathologic analysis included: ileal segment with perforation, stricture and Meckel’s diverticulum, lymph nodes and margins of the perforation.

The postoperative course was simple; the patient was discharged at 13th postoperative day, with the wound healed.

Histopathologic report:

- 15 cm of ileal loop with a perforation of 1.5 cm, presenting on the mesenteric edge a surgical suture of 5 cm length;
- fragment from the perforation – microscopic structure of small bowel with inflammatory giant-cellular reaction in subserosa and granulation tissue;
- fragment of 1.5 cm of small bowel with central ulceration – microscopic structure of small bowel with ulcerated mucosa, perforation of the entire wall and non-specific foreign body granulomatous inflammatory reaction at the serosa;
- fragment of 2/3/1 cm with diverticular appearance – microscopic aspect of diverticulum walled with ileal type mucosa and submucous edema;
- mesenteric lymph node of 0.5 cm – microscopic structure of lymph node with reactive center;
- fragment from the intestinal suture – microscopic structure of small bowel presenting at the level of the muscular layer a foreign body giant-cellular granulomatous inflammation.

The microscopic aspect of the lesions was a tuberculoid giant-epithelial lesion with giant atypical cells (small number of nuclei or centrally situated) (Figures 1 and 2).

At the first surgical intervention for peritonitis, the intraoperative aspect suggested intestinal tuberculosis. Histopathologic examination in the Pathology Department revealed a giant-epithelioid granuloma with crystalloid inclusion in the giant cell (Figures 3 and 4) – the diagnosis remained uncertain.

There was enhancing for beta-globin (testing of the successful extraction) in the studied case which was then re-tested for PCR to infirm the diagnosis of tuberculosis. The result was in assertion with previous testing, 100% negative for IS620 sequence (Figure 5).
\section*{Discussion}

Establishing the cause of a free distal ileal perforation may be very challenging for both surgeons, during the operation, and pathologists.

Non-traumatic ileal perforation is still common in the developing world, as cause for peritonitis.

The causes of spontaneous ileal perforations may be very different: intestinal tuberculosis \cite{2}, Crohn’s disease, foreign bodies, perforated diverticula or radiation enteritis \cite{3}.

Intestinal tuberculosis is still a major problem in many regions of the world, underdeveloped or in development. There is noted also a rising in incidence in Western countries due to immigration from Third World countries and human immunodeficiency virus infection \cite{2}.

Tuberculosis can involve the entire gastrointestinal tract including the peritoneum and the pancreatobiliary system \cite{4}. The common sites of involvement in the gastrointestinal tract are the ileum and the ileo-cecal region \cite{5}. Perforation is not a common complication of intestinal tuberculosis, reported incidence ranging from 1–15\% \cite{6}. It is usually single and proximal to a stricture \cite{7}, but it may be also multiple. It occurs most frequently in the distal ileum \cite{6}.

Together with the increase of morbidity through tuberculosis, it was noticed the multiplying of histopathologic atypical forms of the granulomatous inflammation. Therefore, there are more and more cases with tuberculoid inflammation, in which \textit{Mycobacterium tuberculosis} (MT) cannot be identified, through neither histochemistry nor cultures, nor PCR-reaction. The only available modality of diagnosis remains the therapeutic essay. The atypical morphology of the tuberculous inflammation (the diminishing or absence of the epithelioid cells, the onset of abnormal forms of giant cells, absence of the caseum necrosis, infiltration on polymorphonuclears, eosinophils or plasmocytes) are frequently associated with a negative histochemical Ziehl–Nielsen reaction.

In the reported case, at the first surgical intervention for peritonitis, the intraoperative aspect suggested intestinal tuberculosis. Histopathologic examination in the Pathology Department revealed a giant-epithelioid granuloma with crystalloid inclusion in the giant cell (Figures 3 and 4) but the diagnosis remained uncertain.

There was enhancing for beta-globin (testing of the successful extraction) in the studied case which was then re-tested for PCR to infirm the diagnosis of tuberculosis. The result was in assertion with previous testing, 100\% negative for IS620 sequence (Figure 5).

Because those methods do not have a negative predictive value of 100\% for tuberculosis, a therapeutic test was also performed by specific anti-tuberculosis therapy after the first operation. After three months, she was again operated on for the same problem, the diagnosis being once again intestinal tuberculosis. At eight months from the second operation, the patient was admitted in our clinic and re-operated.

The microscopic aspect of the lesions was a tuberculoid giant-epithelial lesion with giant atypical cells (small number of nuclei or centrally situated) (Figure 1).

The perforations recurred under anti-tuberculosis treatment, which may be a strong argument against the diagnosis of intestinal tuberculosis.

However, there are reports about intestinal tuberculosis perforations that occurred after the commencement of anti-tuberculosis drug therapy in an interval between two days and four months. This is possibly due to progression of the disease or reduced inflammatory local response impairing the healing of intestinal ulceration and reinforcement of mesentery. Another possible explanation, especially in the situations where there is initial favorable clinical course under drug therapy, is a so-called paradoxical response. Its pathogenesis may be explained by a raise in the host’s delayed hypersensitivity response and increased exposure to antigens released from many destroyed bacilli. Anyway, this phenomenon should be taken into account only after an eventual drug resistance is excluded \cite{8}.

The diagnosis of Crohn’s disease was also considered based on the aspect of “creeping fat” seen intraoperatively and the microscopic identification of granuloma. Free intestinal perforation from Crohn’s disease is encountered in surgical series with a frequency of 15.6\%. It may be the first sign of the disease in 23\% of cases \cite{6}.

One of the most characteristic macroscopic findings in Crohn’s disease is the presence of \textit{fat wrapping}. This finding is highly characteristic of the disease and refers to the “creeping” of mesenteric fat onto the serosal surface of the bowel. It was for long time considered a reliable indicator of the presence of diseased tissue. The hypertrophy of the mesenteric adipose tissue and the creeping fat are identified early in the course of disease at laparotomy or laparoscopy. At a local level, fat wrapping correlates with the presence of underlying acute and chronic inflammation, as well as transmural inflammation in the form of lymphoid

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure5.png}
\caption{From the left to the right: PCR IS6110 sample 1 – negative control (water), sample 2 – positive control, samples 3–6 – tested samples performed by Dr. Florin Andrei, “Victor Babes” National Institute for Research and Development in Pathology and Biomedical Sciences, Bucharest.}
\end{figure}
aggregates [9]. The presence of granulomas is highly characteristic of Crohn’s disease but is neither unique to Crohn’s disease nor universally found [10]. Free perforation is a rare event in this disease [11], occurs most frequently in the ileum, on the side attached to the mesentery. Distal intestinal strictures are present in almost 83% of cases [12]. Histological findings generate the hypothesis that free perforation occurs because of proximal intraluminal high-pressure and local circulatory disturbances [11].

A perforation from an ingested foreign-body was also suspected. In emergency departments, ingestion of foreign bodies is a common clinical problem, perforations of the bowel occurring in less than 1% of cases. Generally, chicken bones seem to be the most frequent cause, but fish bones are predominant in other series, indicating that the dietary habits of the population are of most importance. The site of the perforation is regularly the distal ileum [13]. Unfortunately, neither the anamnesis nor the intraoperative exploration, were successful in identifying elements in favor of that diagnosis.

Finally, the histopathologic examination managed to identify the presence in the intestinal wall of some granulomas including non-resorbable suture material, which must have leaded to perforation through abscess-forming process.

The granuloma of foreign body is common in the skin and subcuticular layer. The suture is a foreign material that causes local irritation and tissular necrosis. The monofilament and resorbable sutures have a lower risk for infection. Usually the non-resorbable sutures on the bowel are eliminated inside the lumen. This case must be an exceptional one, in which the sutures were infected, developed a local abscess in the bowel wall that erupted into the peritoneal cavity.

The only remaining question was: how did the first perforation occur? The most probable answer is that during a surgical intervention in the gynecologic area there was some accidental lesion of the small bowel sutured with non-absorbable material.

During the last intervention, all sutures were performed with slowly resorbable material. This is common attitude nowadays for sutures on the bowel wall.

Conclusions

Foreign-body granulomatous inflammation is a very rare cause of spontaneous ileal perforation. The diagnosis is set upon histopathologic examination, correlated with PCR, but the most important aspect by far is the response to adequate therapy. The risk is avoided by using for intestinal sutures only slowly resorbable materials.

References


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