

## Appendicitis in neonatal (AN) patients with secondary necrotizing enterocolitis (ECN) due to sepsis in the uterus: a case report

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### Abstract

Nowadays appendicitis is the leading cause of acute surgical abdomen. It occurs mainly between the first and third decade of life and is very rare in the neonatal period. The pathophysiology and clinical manifestations differ from the typical signs and symptoms, making it difficult to diagnose, which is in mostly cases at the time of surgery, and 74% of them appear with perforation and peritonitis. During the first day there were no complications; however, antibiotic therapy was initiated due to the risk of sepsis. On the next day there were changes in vital signs, fresh blood by nasogastric probe, acute abdomen data, cyanosis, and decreased tone. **Case description:** A newborn male of 34.3 weeks gestation using the Capurro method, Apgar score 8/9, obtained by emergency caesarean section, in which the maternal abdominal cavity was with copious purulent material and perforated appendix with generalized peritonitis. Surgery was determinate, where they found necrotic ileum and appendix with five perforations in total, so resection and ileostomy was performed. Intubation and dopamine support were required, but removed within a short time, beginning oral alimentation. (Gac Med Mex. 2016;152:377-81)

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### Introduction

Currently, acute appendicitis represents the main cause of surgical acute abdomen. Generally, appendicular lumen obstruction is the origin of luminal pressure increase with transmural edema and appendix distension, which causes the symptom spectrum. Peak incidence age is between the first and third decades of life, and it is rather uncommon in very young children:

an incidence of 2% has been reported in infants younger than 2 years, and the figure is even lower in newborns (0.2-0.4%)<sup>1-6</sup>.

In neonatal appendicitis (NA), both etiology and pathophysiology and symptoms differ from common presentation, since the vast majority of cases are diagnosed during surgical procedures, and up to 74% of cases are accompanied by complications (perforation and peritonitis)<sup>1-3,7</sup>.

There are two main clinical presentations: intra-abdominal (66-75%) and intraherniary (23-33%)<sup>1</sup>.

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**Figure 1.** Finding during the cesarean section procedure.

Most cases of intraherniary appendicitis are mainly associated with inguinal hernias and show inguinoscrotal inflammation, which leads to earlier diagnosis and better outcome<sup>1,8</sup>.

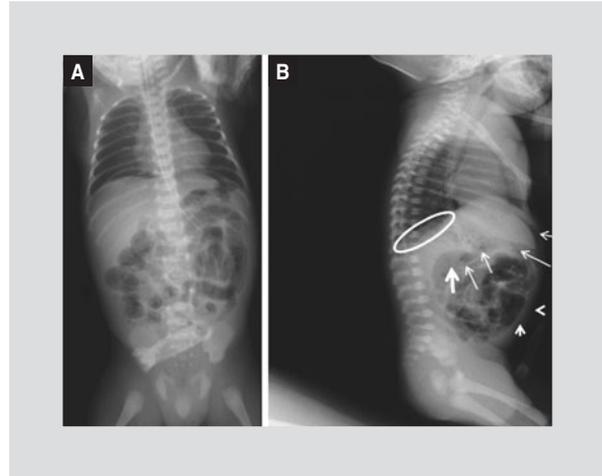
In general, it occurs in males (75%; premature males: 25-50%), mostly with concomitant conditions such as necrotizing enterocolitis (NEC), Hirschsprung disease, meconium ileus, chorioamnionitis, inguinal hernia and streptococcal sepsis, among others<sup>1-6</sup>.

### Case description

This is the case of a male newborn, preterm with 34.3 gestation weeks by Capurro, delivered by a 32-year old mother with 2 gestations and one c-section, with adequate prenatal control. He received a course of pulmonary maturation therapy. He was delivered by means of emergency c-section prompted by ultrasonographic findings of severe oligohydramnios. When the maternal cavity was opened, abundant ooze of green-yellowish-colored purulent material was found, with fetid odor originating from the parietocolic sulci, and perforated appendicitis with generalized peritonitis were found (Fig. 1).

On day 1 physical examination (PE), the following data were obtained: length: 44 cm; weight: 2,000 g; HC: 32 cm; CC: 28 cm; AC: 27 cm; HR: 154 bpm; RR: 56 breaths per minute; temperature: 36 °C; Apgar score: 8/9. Rest of PE was normal.

Given the birth conditions, initiating antibiotic therapy was decided (ampicillin and amikacin) and isolation owing to the risk for sepsis.



**Figure 2. A:** erect position X-ray where scarce air is observed in the pelvic cavity, with bowel dilatation and generalized polyhedral images, which indicates it is intramural gas (pneumatosis intestinalis), accompanied by right scoliosis and increased inter-loop space (edema). **B:** tangential x-ray showing subdiaphragmatic free air (oval), pneumobilia with abdominal distension (arrows) and abdominal wall thickening (arrowheads). In this case, portal venous gas appears as radiolucencies spreading from the porta to the liver periphery.

On the second day of extrauterine life, the following data were found on PE: 168 bpm, 60 breaths per minute, 37.2 °C, BP of 81/46 mmHg, uresis of 2.8 ml/kg/h, negative balance of 113 ml, capillary blood glucose at 124 mg/dl. The patient was awake, reactive to stimuli, with good hydration status, with slight jaundice coloration (Kramer I), with soft and depressible non-tender abdomen, and with presence of peristalsis. There was slight coffee ground gastric residue (4 cm<sup>3</sup>), with meconium stools, which prompted oral route discontinuation.

Laboratory results were the following: hemoglobin: 18.8 g/dl; hematocrit: 52.2%; platelets: 259 x 10<sup>3</sup>/μl; leukocytes: 11.1 x 10<sup>3</sup>/μl; neutrophils: 47%; lymphocytes: 35.1%; sodium: 141 mmol/l; potassium: 4 mmol/l; chlorine: 109 mmol/l; calcium: 7.3 mg/dl.

A few hours later he had an unfavorable evolution: fresh blood was observed by means of orogastric tube drainage, distended abdomen with 3-cm augmentation, palpable bowel loop, presence of muscular resistance at superficial palpation and absent peristalsis, in addition to 2-s capillary refill, signs of cyanosis and decreased tone. It was not possible to determine if there was visceral enlargement and, therefore, tangential and erect position X-ray radiographs were obtained, where free air in the abdominal cavity and pneumobilia was observed (Fig. 2). At the respiratory level, the patient showed a shallow breathing pattern

with apnea, which warranted ventilatory support (FiO<sub>2</sub>: 80%; PIP/PEEP: 13/4; HR: 60 bpm).

Assessment of the patient was requested to the Pediatric Surgery department, which determined emergency surgical intervention for suspected NEC.

After surgery, purulent, brown-colored, fetid fluid abundant outflow was reported, with necrotic bowel loops from the ileum to the ileocecal valve, accompanied by 4 perforations at 15, 20, 35 and 40-cm distance of it, as well as appendix perforation and necrosis. A 45-cm resection of the distal ileum, appendectomy and ileostomy were carried out; in addition, antibiotic treatment was started with cefotaxime, metronidazole and amikacin.

During the postoperative period, the patient received dopaminergic support (8 mcg/kg/min, and the following vital signs were found: HR: 164 bpm; RR: 35 breaths/min; temperature: 36.5 °C; BP: 59/38; AC: 25 cm; uresis: 2.5 ml/kg/h; capillary blood glucose: 108 mg/dl; capillary refill: 2-3 s. Ventilatory support: FiO<sub>2</sub>: 50%; PIP/PEEP: 9/4; orogastric tube: 3-cm<sup>3</sup> drainage with biliary characteristics; surgical wound with well approximated, erythematous edges; violet-colored ileostomy with minimal serohematic material drainage; absent peristalsis.

Red blood cell concentrate and fresh plasma transfusion was indicated owing to the presence of fresh bleeding, with slight hemodynamical improvement.

After 3 days' postoperative period, dobutamine dose was reduced (5 mcg/kg/min) and parenteral nutrition was discontinued due to a persistent state of hyperglycemia, prolonged capillary refill and thrombocytopenia. Within the antibiotic therapy, there was a change of amikacin for vancomycin. Proximal stoma with adequate coloration and meconium outflow was observed, as well as violet-colored distal stoma with no output.

At the fifth day post-surgery, the patient had 10 x 10<sup>3</sup>/μl platelets and overt bleeding through tube, stoma and feces and therefore he was transfused red blood cell and platelet concentrates.

On the eighth postoperative day, the patient was extubated owing to cardiorespiratory system improvement. The following was observed on PE: HR: 144 bpm; RR: 40 breaths/min; temperature: 36.5 °C; MBP: 55 mmHg; blood glucose: 104 mg/dl; uresis: 5 ml/kg/h; balance: +43; capillary refill: 3 s, with no orogastric tube-output, colostomy: 0.30 ml/kg/h; SaO<sub>2</sub>: 94%; AC: 27 cm. Surgical wound showed a dehiscent stitch on the skin and subcutaneous cellular tissue, with traces of fibrin, and there were no data of local or systemic infection.

**Table 1. Comparison between NEC and NA clinical characteristics**

Sign/symptom	NEC	NA
Abdominal distension	85%	78%
Vomiting	28%	63%
Blood in stool	28%	17%
Lethargy	9%	24%
Abdominal mass	5%	13%
Abdominal erythema	24%	22%

*Adapted from Arora et al.<sup>16</sup>*

The next day, a dairy formula with protein hydrolysate (12.5 ml/kg/h) was initiated, which the patient tolerated adequately. Soon after, the dopaminergic support was withdrawn.

## Discussion

In current medical literature, there are a little more than 120 NA cases, and less than 5 that have taken place in Mexico, since this is an extremely rare entity, perhaps owing to the anatomical shape of the newborn's appendix (funnel-shaped with a wide opening at the cecum), which hinders intraluminal obstruction<sup>1-3,9</sup>. In addition, there are factors that act as protectors; for example, the lack of coprolith formation due to a liquid diet, continuous decubitus position and relative infrequency of lymphatic hyperplasia at the periappendicular region prevent the mechanical pathogenesis of the disease<sup>10,11</sup>. Generally, it is an intraoperative finding that entails complications (perforation and sepsis) and, therefore, it has an elevated rate of morbidity and mortality, which ranges from 85 to 90%<sup>1-6</sup>.

Although NA signs and symptoms are quite varied and have some similarity with NEC clinical presentation (Table 1), most reports (isolated cases and series) indicate that abdominal distension, fever and oral route rejection accompanied by vomiting and abdominal mass on the right iliac fossa are its main clinical manifestations<sup>1-7,9,10</sup>. The patient may also display irritability, respiratory distress and signs of peritoneal irritation<sup>3-6</sup>.

In spite of its poor usefulness at early stages, plain abdominal X-ray is enough for suspicion. Radiologic findings considered to be suggestive of NA include hydroaereal levels pattern, pneumoperitoneum, abdominal wall thickening, right scoliosis and obliteration of the psoas margin<sup>1-3,8,9</sup>.

**Table 2. Factors associated with appendicular perforation predisposition**

- Thin wall with low vascular irrigation
- Small and immature omentum
- Lack of wall elasticity
- Hollow viscus large mesentery
- Small abdominal cavity
- Low resistance to infection

*Adapted from Guzmán-Reyes et al.<sup>1</sup>.*

Laboratory tests usually reveal hydroelectrolytic imbalance, leukocytosis with polymorphonuclear predominance and, in more advanced stages, leucopenia and thrombocytopenia<sup>3</sup>.

The case we presented can be regarded as a typical NA clinical presentation, since the above-mentioned data were almost entirely the main manifestations. Likewise, preoperatively considered diagnosis was NEC and, therefore, NA corresponds to an entirely intraoperative finding.

In contrast with other pediatric and adult age stages, appendicolith has never been reported in NA cases, without this being the exception<sup>1-7</sup>.

The incidence of perforation is extremely high (> 80%), not only due to the vague clinical manifestations together with low rates of suspicion, but because certain factors that make the neonate appendix more susceptible to sustain perforation have been documented<sup>1-6</sup> (Table 2).

Saeki et al. mention that the state of prematurity and other states of seriousness can cause vascular insufficiency at the appendix, leading to easy perforation<sup>12</sup>.

As previously mentioned, NA is not usually an isolated entity. Some authors consider it to be a secondary condition, developed as a consequence of an underlying pathology (e.g., NEC, Hirschsprung's disease, meconium ileus, etc.)<sup>1-7,9-12</sup>. Likewise, Gil et al.<sup>13</sup> indicate that conditions such as perinatal asphyxia, cardiac anomalies and other states of hypoxia are risk factors for NA.

There are theories that consider NA as a localized form of NEC limited to the appendix<sup>1,13</sup>. According to Guzmán et al.<sup>1</sup>, an associated underlying condition should be initially suspected; if there isn't any, NA is a form of NEC limited to the appendix.

In our case, it is impossible for this theory to be evidenced, owing to the multiple perforated zones and the subject's state of immaturity, which are suggestive

of an underlying disease, such as stage IIIB NEC, according to Bell's classification.

Hirschsprung's disease-related NA should be suspected when severe periappendicular involvement, with no inflammation of the appendix and minimal infiltration of the mucosa is intraoperatively observed; in these cases, corroborating the diagnosis is recommended by means of colon and rectum biopsies<sup>1,14</sup>. In our patient, owing to the findings during the surgical procedure, as well as to the histopathological report, which demonstrated inflammation, Hirschsprung's disease was ruled out.

Systemic infection has been considered as a possible cause of NA (chorioamnionitis, streptococcal sepsis, etc.); in our case, as a consequence of the intraoperative finding during the c-section, it is impossible for maternal infection to be ruled out as the origin of the NA<sup>1-3,13,15</sup>.

As in the report described by Gil et al.<sup>13</sup>, we can speculate with that the fact that the mother received antibiotic treatment during the c-section might explain why there were no data of disease in the beginning, i.e., we can infer that, although the newborn's infection was not prevented by the initial antibiotic treatment, the inflammatory process that led to appendix-localized infection was minimized.

Acute appendicitis diagnosis in the neonatal period requires a high degree of suspicion and should be considered in the acute abdomen differential diagnosis in this age group. In the past, most cases were diagnosed after necropsy (56%), and the rest was established by exploratory laparotomy. However, currently, even cases whose treatment has been carried out by means of laparoscopic surgery thanks to the knowledge on this entity have been reported<sup>16</sup>.

When there are no data suggestive of Hirschsprung's disease and perforation, the treatment of choice is appendectomy with surgical lavage of the peritoneal cavity; however, if perforation is suspected, an exploratory laparoscopy has to be performed to directly visualize the cavity and this way rule out possible complications<sup>1-6,17</sup>.

According to Saeki et al.<sup>12</sup>, three cases of laparoscopic appendectomy have been reported with transumbilical visualization being used as diagnostic and treatment method, and it has been useful and with major advantages (e.g., single umbilical incision); however, this method has no use in case of multiple adhesions.

In our case, owing to the suspicion of perforation as a consequence of serious NEC, practicing an exploratory laparotomy was decided.

In spite of multiple complications, the patient had a favorable evolution; he required over one-month hospitalization and multiple readmissions. After a period of little more than one year, intestinal reconnection was performed with favorable results. Currently, the subject has an adequate quality of life, and has no complications associated with the surgical procedure.

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