

# Neonatal appendicitis: how many sides does this coin have?

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## ABSTRACT

Neonatal appendicitis is a very rare entity associated with immune, vascular, hypoxic, and obstructive factors. We present two cases of neonatal appendicitis with different characteristics.

The first case is a 15-day-old newborn with congenital hypothyroidism who had abdominal distension and sepsis data. An appendicular plastron was found. Hirschsprung's disease was ruled out through biopsies. The second case is a 27-week-old preterm newborn with history of necrotizing enterocolitis who presented an incarcerated inguinal hernia consistent with Amyand's hernia.

The prognosis of neonatal appendicitis varies according to how fast diagnosis is achieved, since it is associated with high mortality rates in the first hours. Although appendicitis is the condition best known to the pediatric surgeon, it represents a diagnostic challenge in newborns as a result of its extreme rarity and how likely it is to present comorbidities.

**KEY WORDS:** Neonatal appendicitis; Congenital hypothyroidism; Amyand's hernia.

## APENDICITIS NEONATAL, ¿CUÁNTAS CARAS TIENE ESTA MONEDA?

### RESUMEN

La apendicitis neonatal es una entidad infrecuente que asocia factores inmunes, vasculares, hipóxicos y obstructivos. Presentamos dos casos de apendicitis neonatal con diferentes características.

El primer caso es un neonato de 15 días de vida con hipotiroidismo congénito. Presentaba distensión abdominal y datos de sepsis. Se halló un plastrón apendicular y se descartó enfermedad de Hirschsprung mediante biopsias. El segundo caso es un prematuro de 27 semanas, con antecedente de enterocolitis necrotizante, que a los 53 días de vida presentó una hernia inguinal incarcerada compatible con hernia de Amyand.

El pronóstico de la apendicitis neonatal va unido a la celeridad del diagnóstico, ya que supone una importante mortalidad en las primeras horas. Aunque la apendicitis es el cuadro más conocido por el cirujano pediátrico, a edad neonatal es un reto diagnóstico por su extrema rareza y probable comorbilidad.

**PALABRAS CLAVE:** Apendicitis neonatal; Hipotiroidismo congénito; Hernia de Amyand.

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## INTRODUCTION

Neonatal appendicitis (NA) is a rare condition associated with high mortality rates – up to 28%<sup>(1)</sup> according to the most recent studies – in the first 24 hours following symptom onset. The first case was described in 1905 in a 30-day-old newborn who died as a result of peritonitis. Three years later, the first case of a newborn who survived appendicitis at the age of 3 weeks was reported<sup>(2)</sup>. Appendicitis has an estimated incidence of 0.04%-0.2% in patients under 30 days of age, and of 0.38% in patients under 1 year of age. Patients are predominantly male, in a 3:1 proportion. Abdominal distension is the most common presentation, but some unspecific symptoms such as irritability, breastfeeding refusal, vomit, increased gastric remnants, lethargy, or fever can also occur. Over the decades, risk factors associated with NA have been searched for. Some associations described include prematurity, Hirschsprung's disease, chorioamnionitis, necrotizing enterocolitis (NEC), and cystic fibrosis. Similarly, anatomical and dietary protective factors typical of newborns have also been described – cone-shaped appendix, little follicular hyperplasia, breastfeeding, and decubitus position. None of the predisposing or protective factors are supported by scientific evidence today.

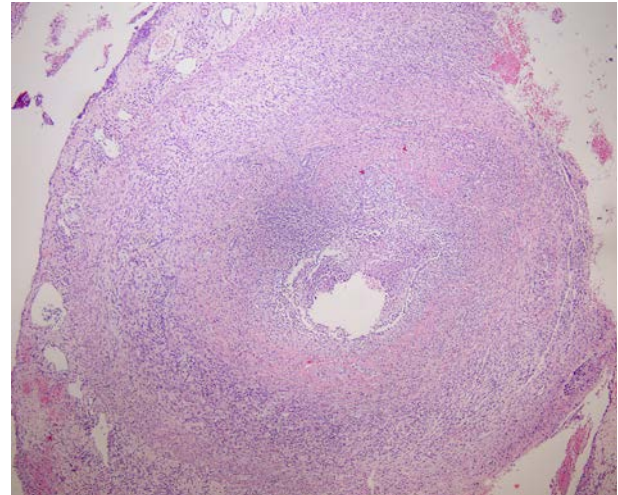
We present two cases of neonatal appendicitis, each of which had its own characteristics, with very few things in common. Appendicitis – which is the oldest surgical condition – in the neonatal period remains a diagnostic challenge for pediatric specialists.

## CLINICAL CASE 1

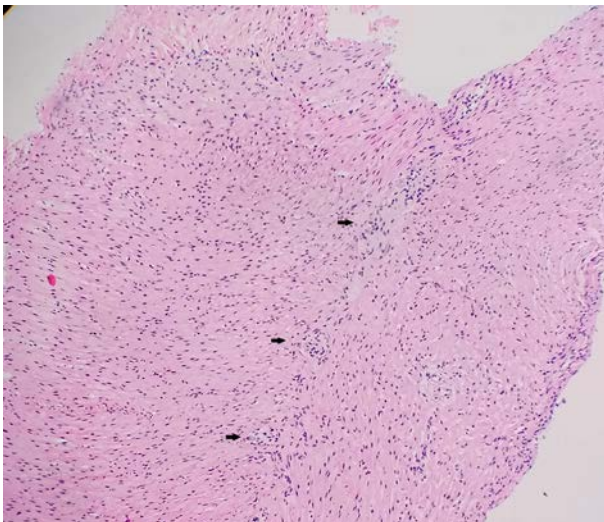
Full-term female newborn – born at gestational week 39+2 – presenting with acute abdomen at the age of 15 days. At gestational week 32, she had had mild polyhydramnios. At birth, she was diagnosed with congenital hypothyroidism as a result of thyroid agenesis. At the initial exploration, the patient had a relatively poor general condi-



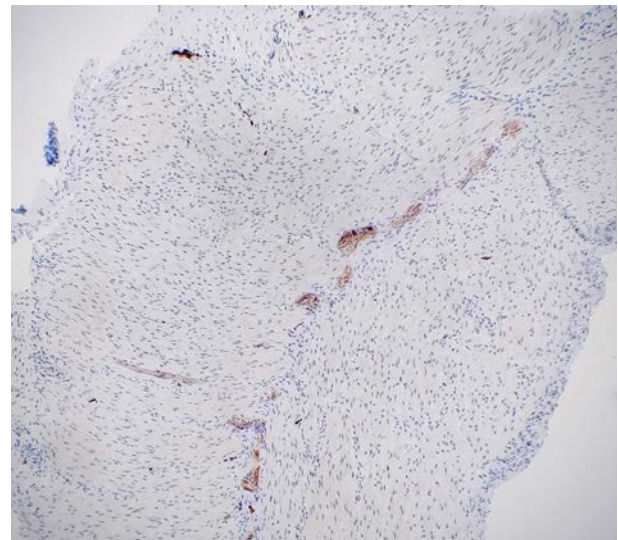
**Figure 1.** Abdominal ultrasonography using a linear transducer. Two tubular structures are identified – one with circumferential wall thickening (*upper arrow*) and the other being a lateral, 6 mm diameter one (*lower arrow*). Local and regional fat around both structures is hyperechogenic.



**Figure 2.** Histological image of the appendix with mucosal ulceration and an intense transmural polymorphonuclear inflammatory infiltrate (hematoxylin-eosin, 40x).



**Figure 3.** Histological image of the muscularis propria with presence of myenteric plexus (*arrows*) (hematoxylin-eosin, 100x), which allows Hirschsprung's disease to be ruled out.



**Figure 4.** Immunohistochemical confirmation (calretinin, 100x) of the presence of ganglion cells.

tion with reticular skin, septic aspect, distended abdomen painful to palpation, and right iliac fossa guarding and tenderness. Remarkable blood count levels included 12.9 g/dl hemoglobin,  $3.54 \times 10^6$  erythrocytes, 38.7% hematocrit, 7.55 mg/dl CRP, and 586 mg/dl fibrinogen. Leukocyte count, renal function, and electrolytes were normal. Emergency ultrasonography identified two tubular structures adjacent to the cecum – one of them slightly medial with circumferential wall thickening at its base and a diameter of 10 mm, and the other one lateral with a maxi-

imum diameter of 6 mm. These images were interpreted to be suggestive of complicated Meckel's diverticulum and inflammation of the cecal appendix as a result of its proximity (Fig. 1). Emergency transverse laparotomy was decided upon, which demonstrated an appendicular plastron with perforated appendix in the middle third. Colonic wall biopsies including the cecum, the hepatic and splenic flexures, and the sigmoid colon were performed. Pathological examination showed the appendix had mucosal ulceration and an intense inflammatory infiltrate (Fig. 2). Hirschsprung's disease was ruled out, since the myenteric plexus was present in the muscularis propria, which was immunohistochemically confirmed (Figs. 3 and 4). The



**Figure 5.** Anterolateral X-ray demonstrating a dilated loop with a “coffee bean” sign at the level of the scrotum.

patient initiated oral feeding 24 hours later and had a favorable progression. The postoperative period was uneventful.

## CLINICAL CASE 2

Preterm 1,016 g male newborn – born at gestational week 27 – who developed respiratory distress immediately post-birth following emergency Cesarean section as a result of HELLP (*Hemolysis Elevated Liver Enzymes Low Platelets*) syndrome. At 24 hours of age, general condition worsening, abdominal distension, and uncomplicated reducible bilateral inguinal hernia were evidenced. Blood count demonstrated  $13.9 \times 10^3/\text{ml}$  leukocyte and 8.3 mg/dl CRP levels, the remaining parameters being normal. Lateral X-ray showed the presence of subdiaphragmatic gas, consistent with pneumoperitoneum. Midline laparotomy media was performed, which found an ileal perforation 35 cm away from the ileocecal valve and lesions consistent with localized necrotizing enterocolitis. The loop involved was resected, and an end-to-end anastomosis was carried out. The patient had a favorable progression and initiated oral feeding on postoperative day 6, which was successful. At the age of 53 days, the right inguinal hernia became



**Figure 6.** Amyand’s hernia: gangrenous appendicitis covered with fibrin exteriorized from the inguinal hernia sac.

incarcerated, with the anterolateral X-ray showing a dilated intestinal loop and a “coffee bean” sign at the level of the scrotum (Fig. 5). A right inguinal incision was performed, which allowed the hernia sac to be identified. The content within was the ileocecal appendix covered with fibrin, consistent with Amyand’s hernia (Fig. 6). Histological findings confirmed a 2.5 cm ileocecal appendix with a dull serosa and signs of gangrenous appendicitis

## DISCUSSION

The etiology of NA remains an issue of discussion, with various hypotheses available – a limited form of necrotizing enterocolitis, an obstruction secondary to Hirschsprung’s disease, meconium ileus, cystic fibrosis, and incarcerated hernia<sup>(1)</sup>. However, primary neonatal appendicitis cannot be histologically distinguished from isolated NEC in the appendix, which means its causes remain unclear<sup>(4)</sup>. Some authors even consider NA and appendicitis at a later age to be different entities, based on NA’s association with ischemic factors similar to those found in NEC<sup>(5)</sup>.

On the other hand, the low incidence of appendicitis at this early age can be explained by the morphology of the neonatal vermiform appendix, which has a cone shape with a wide base, thus making it less prone to obstruction. Other protective factors of newborns include soft diet, breastfeeding, decubitus position, and the low incidence of gastrointestinal and respiratory infections in the perinatal period<sup>(6-7)</sup>.

In the diagnosis of appendicitis, blood count results are less useful in the neonatal period than in older patients<sup>(8)</sup>. Ultrasonography is superior to X-ray when it comes to detecting intra-abdominal liquid, abdominal wall thickening, and intestinal perfusion, but there are no specific criteria in terms of NA. The high position of the appendix at the right hemiabdomen or at the subhepatic level is the only distinct characteristic<sup>(9)</sup>.

The first case features an unprecedented pathological association – congenital hypothyroidism and appendicitis. Similarities with Hirschsprung’s disease could be found in terms of motility disorder. Tahan described the case of a 1-year-old child with abdominal distension, chronic constipation, delayed weight gain, and bradycardia at X-ray imaging and even anorectal manometry, which were consistent with Hirschsprung’s disease. However, the patient was diagnosed with hypothyroidism, and levothyroxine treatment allowed the condition to be healed<sup>(10)</sup>. Constipation occurs in 12% of children with congenital hypothyroidism, and nearly 2.5% of the children undergoing constipation and delayed growth assessment are diagnosed with hypothyroidism<sup>(11)</sup>. Various studies establish a link between thyroid hormone and gastrointestinal motility<sup>(12)</sup>, with some authors suggesting thyroid hormone deficit could alter cranio-caudal neuroblast migration in the first stages of Hirschsprung’s disease<sup>(13)</sup>. Kotar presented a case directly associating hypothyroidism with Hirschsprung’s disease and tried to explain this coincidence<sup>(14)</sup>. However, this did not occur in our first case, where the absence of Hirschsprung’s disease could be demonstrated. Our objective was to report the potential association of hypothyroidism with NA, but considering it was a single case, no causal link should be established.

In 1735, Claudius Amyand described the combination of incarcerated inguino-cruural hernia and appendicitis in an 11-year-old child. In the late 20<sup>th</sup> century, one of the first series in newborns under 30 days of age was published. It considered this type of appendicitis as a more favorable one than intra-abdominal appendicitis<sup>(15)</sup>. Amyand’s hernia represents 1% of all inguinal hernias. Appendicitis in incarcerated hernia is caused by the vascular compromise occurring as a result of the compression at the level of the hernia ring, which sparks off inflammation and bacterial overgrowth<sup>(16)</sup>. This type of appendicitis can occur in different forms, with perforated appendicitis being the least likely one<sup>(17,18)</sup>. This is in contrast to NA-related perforation rates, which can reach 75-85%. According to some authors, Amyand’s hernia should be included as a differential diagnosis when assessing neonatal testicular torsion, since they both have the same clinical signs<sup>(19)</sup>. In our second case, no prophylactic appendectomy in the NEC-related perforation surgery was carried out, since there is no scientific evidence of this indication. In addition, functional disorders could not be ruled out at first, so decision was made to preserve the appendix as it could prove useful as a diversion pathway.

In short, there are four types of NA-related factors: immune, vascular, hypoxic, and obstructive factors. However, regardless of the factors found, and given the high mortality rates involved and how vulnerable neonatal patients are, it should be regarded as a surgical emergency, which means it should not be put off. Understanding the associations described is key to the diagnosis of these

children, since some of the associated pathologies have significant morbidity and require long-term follow-up.

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