# Clinical case

# Acute Pancreatitis secondary to gallstones in a girl with Down Syndrome

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## Abstract

Gallstones are infrequent in children, and usually asymptomatic. However, complications can be severe if pancreatitis ensues. Recent reports indicate above-average prevalence of cholelithiasis in Down syndrome. We report the successfully treated case of a 7-year-old girl with Down syndrome who developed pancreatitis secondary to cholelithiasis.

**Keywords:** Gallstones. Cholelithiasis. Pancreatitis. Down syndrome.

## Introduction

Gallstones are uncommon in children, with a prevalence of no more than 0.5% (1). They are usually asymptomatic, although potentially serious if secondary cholecystitis or pancreatitis occurs. Juvenile gallstones have traditionally been linked to parenteral nutrition or conditions such as sepsis, hypercholesterolemia, dehydration, prematurity and obesity, among others. Recently published studies indicate a higher prevalence of gallstones in children with Down syndrome (DS). We describe the case of a DS girl with acute pancreatitis secondary to gallstones.

## Case Presentation

The patient was a 7-year-old girl with double trisomy - trisomy 21 and triple X (48,XXX,+21) - with a presenting complaint of abdominal pain starting two weeks prior to the visit and worsening shortly before she came in, accompanied by vomiting. She had no fever and showed no changes in frequency of bowel movements and consistency of stool. Her family history included a maternal great-aunt with gallstones. Three years prior she had an abdominal ultrasound scan because of significantly elevated alkaline phosphatase (1,483 U/L; normal values, 25-600 U/L), which revealed gallstones without dilation of the common bile duct or any other signs of cholestasis.

When the girl came in she was in good overall condition, without jaundice and with slight dryness of the oral mucosa. Her abdomen was soft and depressible, with no organomegaly, with tenderness of the epigastric region and right hypochondrium. Blood tests showed elevated amylase and lipase (Table I). We suspected acute pancreatitis, and she was examined with abdominal ultrasound, which revealed slight dilation of the bile ducts. A CT scan of the abdomen showed a calcium-density deposit about 7 mm in diameter at the distal end of the common bile duct and findings compatible with grade-E

pancreatitis, without necrosis. She was hospitalized after fasting and treated with intravenous fluids and analgesics. Antibiotic therapy was started 24 hours later with piperacillin/tazobactam after elevated inflammatory parameters were detected (C-reactive protein [CRP] of 87.3 mg/L).

Clinical and analytical improvement was seen within four days and an ultrasound scan showed no lithiasis or common-bile-duct dilation. We therefore decided to gradually begin nasogastric feeding, to which the patient responded well. A week later she was placed on an oral fat-free diet, which she tolerated well. She was released within two weeks, following magnetic resonance (MR) cholangiopancreatography which showed no calculi in the biliary tract, only signs of mild papillitis, and excellent improvement in the biological pancreatitis parameters (Table 1). Deferred cholecystectomy was scheduled in view of the patient's satisfactory progress with conservative treatment.

## Discussion

Gallstones are uncommon in children, with a prevalence of no more than 0.5%. The etiopathogenic factors traditionally related to gallstones in children are sepsis, parenteral nutrition, intestinal resection, obesity, hypercholesterolemia, hemolytic anemia, dehydration, premature birth, cholestasis, and certain drugs (cytostatics, diuretics, analgesics). There are studies that also identify a family history of gallstones and female gender as risk factors (1).

The patient described in this report had a family history of gallstones, female gender, and a slight tendency to obesity (BMI: 24) as factors predisposing to biliary calculi. It is doubtful whether the DS factor increased the likelihood of developing gallstones.

**Table I.**
Main biochemical results at diagnosis and on release

| | At diagnosis | On release | Normal values |
|---|---|---|---|
| Amylase (U/L) | 2435 | 95 | *30-122* |
| Lipase (U/L) | 9823 | 359 | *114-286* |
| ALT (U/L) | 929 | 22 | *10-45* |

Although there are numerous references to gastrointestinal malformations clearly associated with DS, such as duodenal atresia, annular pancreas and anal atresia, among others, until a short time ago a clear relation between gallstones and DS was unknown. Studies published in the last few years report an increased prevalence of gallstones in DS children (2, 3, 4). Llerena (2) examined 145 pediatric patients with DS with abdominal ultrasound and found that 7% of them had asymptomatic gallstones. A prospective study comparing the prevalence of cholelithiasis in children with and without DS revealed gallstones in 4.5% of the DS cases, as compared to only 0.2% in the controls (3).

Various factors have been posited to explain the higher incidence of gallstones in DS children. One theory is based on the hypomotility of the gall bladder in DS patients (5), which slows biliary flow and may explain the higher prevalence of gallstones. It has also been observed that blood triglycerides are higher in DS patients than in the general population (5). Bocconi (6) studied lipid metabolism in DS and demonstrated that trisomy 21 is associated with hypercholesterolemia during intrauterine life. The assumption is that this relative hypercholesterolemia and hypertriglyceridemia would enhance the formation of cholesterol calculi in these children. It is also known that the prevalence of obesity in DS is significantly higher than in controls, which in itself is a known risk factor for developing gallstones.

Whereas cholesterol calculi predominate in the adult population (78%), gallstones in children are composed predominantly of pigment (calcium bilirubinate in 48%); 24% consist of calcium carbonate and only 21% are cholesterol (7). Furthermore, cholesterol calculi are very common in the subpopulation of overweight adolescent girls with a family history of gallstones, a group that included our patient (7).

Pancreatitis is found among the complications secondary to gallstones. Acute pancreatitis is rare in childhood but important because of its significant morbidity and mortality, although the prognosis is good in most pediatric cases. Among the most common etiologies of pancreatitis are idiopathic, traumatic and toxic factors, congenital

abnormalities, and diseases of the biliary tract. Our patient's pancreatitis can be considered a predictable complication of her gallstones. Treatment was started immediately with digestive rest, fluid therapy, analgesia and antibiotics; the patient progressed favorably and no invasive methods such as endoscopic retrograde cholangiopancreatography were required. We decided to start nasogastric feeding early because it has been shown to reduce the inflammatory response and severity of acute pancreatitis as compared to parenteral nutrition (8). Our patient's excellent tolerance of enteral feeding and her highly favorable progress corroborated this theory.

A complex chromosome anomaly with double trisomy (48,XXX,+21) is an exceptional situation, rarely reported, and it is unknown whether it may bear some relation to the clinical picture described in this article.

## Conclusion

Pediatricians should be alert to the enhanced risk of gallstones in children with DS and their possible complications, such as acute pancreatitis. Treatment should be started as soon as pancreatitis is diagnosed, with appropriate hydroelectrolytic and nutritional support, and antibiotics if necessary. More studies are needed to determine the pathophysiological mechanisms that link DS to gallstones.

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