Congenital pyloric atresia: clinical features, diagnosis, associated anomalies, management and outcome

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Background **Congenital pyloric atresia (CPA) is very rare and usually seen as an isolated anomaly, which has an excellent prognosis. CPA can be associated with other anomalies or familial and these are usually associated with other hereditary conditions with poor prognosis. This review is based on our experience with 20 infants with CPA.**

Patients and methods **This is a review of CPA, highlighting its clinical features; associated anomalies; and aspects of diagnosis, management and outcome.**

Results **This review is based on our experience with 20 patients with CPA (nine male and 11 female). Their mean birth weight was 2.1 kg (1.1-3.9 kg). Polyhydramnios was seen in 13 (65%) patients. Seven patients were full-term and the remaining 13 were premature. Two were brothers and four were members of the same family. Isolated CPA was seen in seven (35%) patients and 13 had associated anomalies. Epidermolysis bullosa was seen in eight (40%) patients and multiple intestinal atresias in five (25%). Three patients had associated esophageal atresia. Pyloric diaphragm was the most common and seen in 13 patients including double diaphragms in two followed by pyloric atresia with a gap in four and pyloric atresia without a gap in three. All patients did well in the early postoperative period; however, 10 died later giving an overall survival of 40%. Sepsis was the main cause of death.**

Conclusion **CPA is a very rare malformation that can be familial and inherited as an autosomal recessive. It can either occur as an isolated lesion with an excellent prognosis, or be associated with other anomalies. The overall prognosis of CPA, however, is still poor, and this is due to the frequent-and often fatal-associated anomalies.** ***Ann Pediatr Surg*** **13:188–193 © 2017 Annals of Pediatric Surgery.**

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Introduction

Gastric-outlet obstruction is divided into two types: pyloric atresia and antral webs. The first case of a patient with congenital pyloric atresia (CPA) was described by Calder in 1749. Touroff and colleagues performed the first successful operation in 1940 [1–7]. CPA is a very rare condition. The estimated incidence of CPA is 1 : 100 000 live births, and it accounts for less than 1% of all upper-gastrointestinal-tract atresias [1,4,5]. It affects male and female patients equally. CPA is known to be associated with low birth weight and polyhydramnios, both of which are reported in up to 60% of the patients [8]. Commonly, CPA occurs as an isolated lesion, which has an excellent prognosis. It can, however, also occur in association with other malformations, which can have a negative impact on the final outcome [8–16]. Carmi *et al*. [10] suggested this pathophysiology of the disorder; therefore, it is also referred to as 'Carmi syndrome'.

Aetiology and embryology

The exact aetiology of CPA is unknown. Embryologically, however, it is thought to result from developmental arrest between the 5th and 12th weeks of intrauterine life [3,14]. According to Tandler [17], CPA results from the failure of the pyloric tube to canalise during embryonic development. This is the most accepted theory for the development of CPA. In contrast, Lowe and Bernard [18] proposed a mechanical cause or vascular accident as an aetiology for CPA. Weber [19] proposed that CPA associated with epidermolysis bullosa (EB) results from an intrauterine mucosal injury within the junctional EB, with subsequent ulceration and an inflammatory scarring reaction. This is an attractive theory in CPA patients with associated EB, but does not explain the occurrence either of isolated CPA or CPA with a gap. The occurrence of CPA and EB is interesting, and appears to be more than the result of chance association, as suggested by Chang and colleagues, who also proposed that CPA in association with EB occurs secondary to an intrauterine complication of EB, in which ulceration and sloughing of the pyloric mucosa leads to fibrosis, scarring and obstruction of the pyloric canal [20,21]. The sometimes familial occurrence of CPA, with a high frequency of consanguinity and an equal sex incidence, suggest a genetic predisposition, with an autosomal recessive mode of inheritance [22,23]. The reason for the high incidence of CPA in some parts of the world is not known; however, as these patients are genetically similar, a high incidence of consanguinity in these parts of the world may be a contributing factor [8,24].

Classification and associated anomalies

CPA is classified anatomically and also clinically [8]. CPA is classified, depending on the presence or absence of associated anomalies, into three groups:

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Isolated CPA [1]

In these patients, CPA occurs in isolation without other anomalies. These patients have an excellent prognosis.

CPA associated with other genetic disorders like EB and aplasia cutis congenita (ACC) [6,9–11,25–30]

Patients with this combination have the worst prognosis. Although CPA commonly occurs in isolation, it is frequently reported in association with other anomalies, which are commonly seen in 30–45% of the patients. Ilce *et al*. [4] reported associated anomalies in 43.8% of their patients. This study has reported associated anomalies in 54.5% of the patients [8]. EB and intestinal atresias are the most common associated anomalies. EB in association with CPA was first described by Swinbume and Kohler [31]. It is believed that CPA in association with EB results from the intrauterine sloughing of the mucous membrane, with subsequent healing by fibrous tissue, leading to the obliteration of the pylorus lumen [21]. This is supported by the occasional occurrence of atresias in other parts of the gastrointestinal tract, such as the oesophagus, larynx and anus. The occurrence of acquired pyloric atresia in association with EB is another supporting factor [32–36]. Although this can explain the occurrence of the pyloric membrane, it does not explain the occurrence of CPA with a gap between the two ends [24]. A more acceptable theory is that both conditions are genetically determined, and their occurrence together is due either to the pleiotropic expression of a single gene, or the action of two closely related genes. This is also the case with ACC, which is seen in association with CPA. More commonly, all three conditions may occur in the same patient [10,11,35]. ACC is also a hereditary condition, and this study proposes that the occurrence of CPA, together with EB and ACC, is the result of closely linked abnormal genes.

EB consists of a group of hereditary bullous skin disorders. On the basis of histology, it is divided into three types: EB simplex, junctional EB and dystrophic EB. All three types have been reported in association with CPA, although junctional EB is the most frequently reported. Evidence suggests that the CPA–EB association is a distinct clinical entity, which is now referred to as the CPA–EB syndrome. This clinical entity may result from a mutation in one of the integrin genes. The absence of detectable α-6 integrin, but not β-4 integrin, in these patients raises the possibility that α-6 integrin or its ligands are responsible for the CPA–junctional EB association [20–22,37]. In eight of the patients, CPA was associated with EB, four being from the same family. One of them also had associated ACC [8].

CPA associated with other intestinal atresias [8,12,13,38–41]

The associated intestinal atresias are usually multiple, and can form part of the hereditary multiple intestinal atresias (HMIA) [4,5,14,15]. These atresias can affect any part of the gastrointestinal tract, from the stomach to the rectum. The presence of these associated anomalies is a contributing factor for the reported high mortality in these patients [8]. The possibility of associated intestinal atresias must always be kept in mind, and, to exclude or locate associated colonic atresia, a preoperative barium enema is advocated. The presence of calcification on plain abdominal radiography should raise the possibility of associated HMIA [42]. Intraoperatively, it is also important to check the patency of the remaining intestines, using a catheter that is passed distally and injecting saline, to exclude associated intestinal atresias, which are often multiple. HMIA is a very rare condition transmitted as an autosomal recessive inheritance. The atresias can affect any part of the gastrointestinal tract, from the oesophagus to the rectum. Although the atresias are multiple, there are variations in the affected parts of the gastrointestinal tract among the reported patients, even among affected brothers [5,12,13]. This may be attributed either to gene mutations or to incomplete gene penetration. Lambrecht and Kluth [43] collected 35 well-documented patients of HMIA from the literature. An interesting finding in some of these patients is the occurrence of CPA with distal duodenal atresia. This occurrence forms a closed duodenal loop, in which biliary and pancreatic secretions accumulate, leading to a massive distention of the duodenum. This distention increases the danger of perforation, or of the secretions refluxing back into the biliary tree and leading to its dilatation [7,12–14]. The presence of associated pure oesophageal atresia makes the preoperative diagnosis of associated CPA impossible. It is important to exclude this at the time of gastrostomy. This, however, is not the case in patients presenting with associated oesophageal atresia and tracheoesophageal fistula. In the latter two conditions, a plain abdominal radiography shows the stomach to be dilated, with no air seen distally [8]. Other reported associated anomalies with CPA include Down's syndrome, Meckel's diverticulum, ureterovesical-junction obstruction, pelviureteric-junction obstruction, agenesis of the gallbladder and malrotation, high anorectal agenesis, congenital heart disease, cleft palate and pylorocholedochal fistula [7,36,41,44,45].

A review of the literature in 1989 reported 125 patients of CPA, three of whom presented with associated oesophageal atresia, and 18 with EB [1]. The researchers in this study treated 20 newborn babies with CPA, in seven (35%) of whom, CPA occurred in isolation; in eight (40%) of whom, it was associated with EB; and in five (25%) of whom, it was associated with other gastrointestinal atresias [8].

CPA is also classified anatomically into three types [5,8,24]:

Type 1: pyloric membrane (57%), which may be multiple.
Type 2: pyloric atresia without a gap (34%).
Type 3: pyloric atresia with a gap between the stomach and the duodenum (9%).

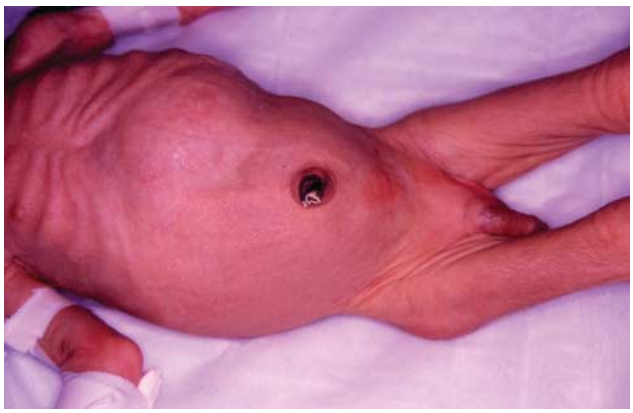
Moore [1] proposed a pathophysiological classification of congenital gastric-outlet obstruction due to pyloric atresia or gastric antral web. In most patients of CPA, the defect consists of a mucosal or submucosal membrane, without a muscular component (pyloric membrane or diaphragm). Intraoperatively, it is important to make sure that only one pyloric diaphragm is present, as there

may be multiple occurrences [8]. Less frequently, the pylorus is a fibrous string; else, a complete segmental defect may be present. CPA with a gap is the least common type.

Clinical features

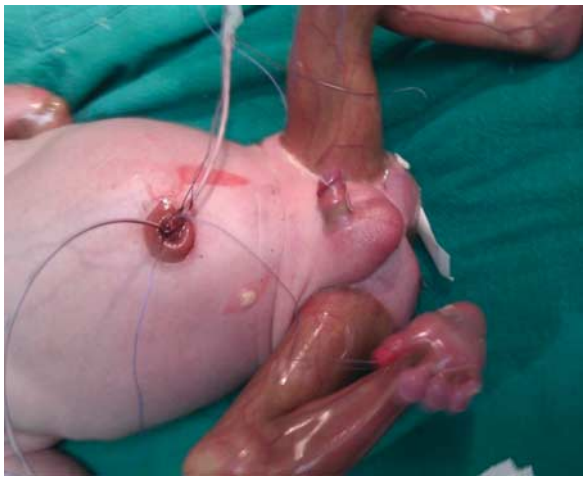
Infants with CPA usually present with nonbilious vomiting soon after birth, feeding difficulties and, sometimes, upper-abdominal distention. The upper-abdominal distention is secondary to the dilated stomach (Fig. 1). A history of polyhydramnios is present in the majority of these patients. A delayed diagnosis may lead to pulmonary aspiration, severe metabolic derangement and gastric perforation, all of which can be fatal. The presence of associated anomalies is a contributing factor for delayed diagnosis [8]. This must be kept in mind. Clinically, the presence of EB and or ACC can be detected. This evidence should raise the possibility of associated CPA, in those who present with nonbilious vomiting (Fig. 2). In patients with associated pure oesophageal atresia, the preoperative diagnosis of CPA is difficult, as there is no gastrointestinal air. This must be kept in mind at the time of gastrostomy [8]. In patients with oesophageal atresia and distal tracheo-oesophageal fistula, the stomach appears dilated on plain abdominal radiography, with no air distally (Fig. 3). Patients with CPA and intestinal atresia involving the duodenojejunal junction have been reported [12,13]. This forms a closed duodenal loop that can dilate as a result of accumulation of pancreaticobiliary secretions and, sometimes, perforate. The diagnosis in these patients is usually made intraoperatively.

Fig. 1



A clinical photograph showing upper-abdominal distention, as a result of gastric dilatation in a patient with congenital pyloric atresia.

Fig. 2

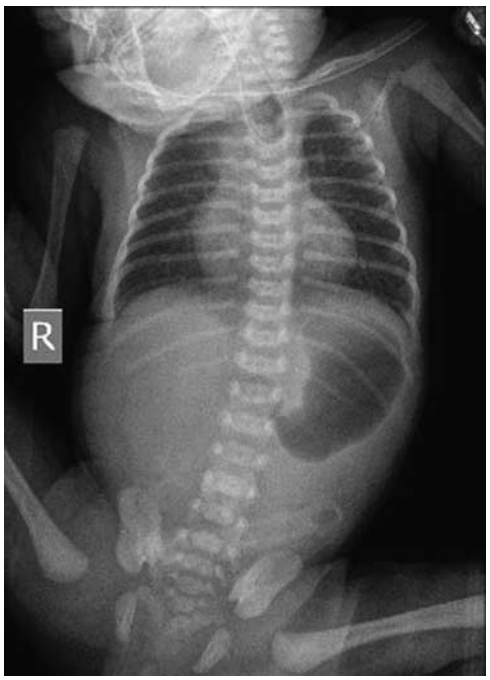


Clinical photographs showing a newborn baby with epidermolysis bullosa and asplasia cutis congenita, associated with congenital pyloric atresia.

Diagnosis

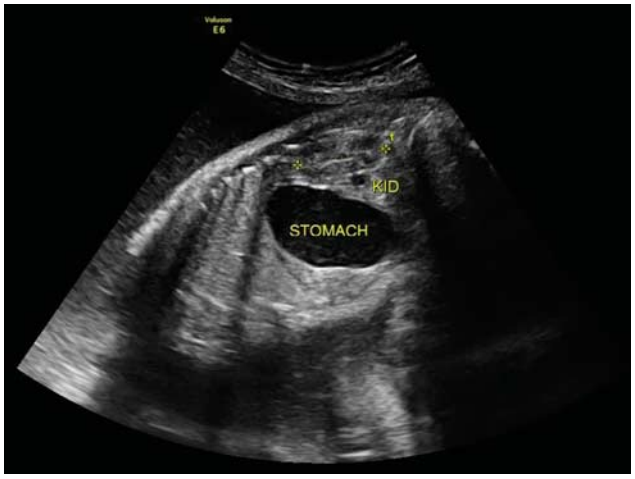
Congenital anomalies of the gastrointestinal tract are relatively common, but CPA is extremely rare, constituting less than 1% of all upper gastrointestinal atresias [1–5]. Commonly, it occurs as an isolated lesion, which presents with upper-abdominal distention and nonbilious vomiting. The familial occurrence of isolated CPA supports an autosomal recessive mode of inheritance [46,47]. CPA can be diagnosed antenatally by an ultrasound in the second trimester, which can show the presence of polyhydramnios, associated with a dilated stomach (single air-bubble) [11,48,49] (Fig. 4). The diagnosis of CPA is simple and can be made with a plain abdominal radiography. This classically shows a single large gastric air-bubble, and a gasless nondistended abdomen distally (single air-bubble) (Fig. 5). The diagnosis can be confirmed by a barium meal, although it is often not necessary (Fig. 6). Reports of perforated pyloric webs are available. These show scanty gas distally in the gastrointestinal tract [50]. These are not simple to diagnose, and contrast enema or endoscopy may be

Fig. 3



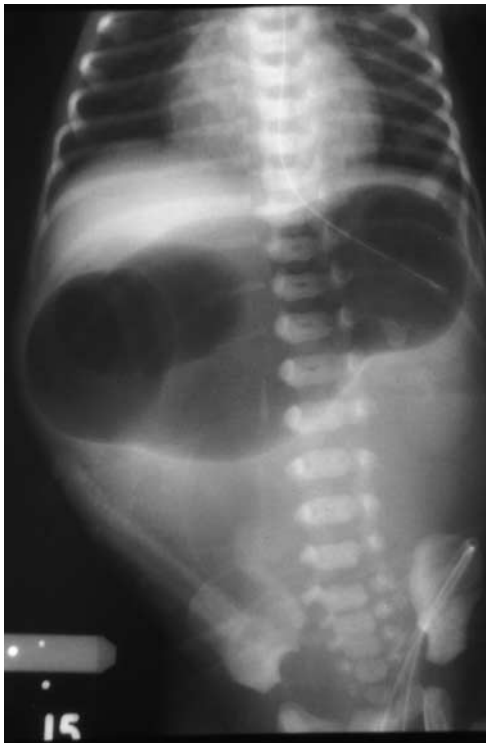
Preoperative abdominal radiography showing congenital oesophageal atresia with tracheo-oesophageal fistula and congenital pyloric atresia. Note the coiled nasogastric tube in the upper-oesophageal pouch and the dilated stomach, with no air distally.

Fig. 4



An antenatal ultrasound showing a dilated stomach associated with polyhydramnios, suggestive of congenital pyloric atresia.

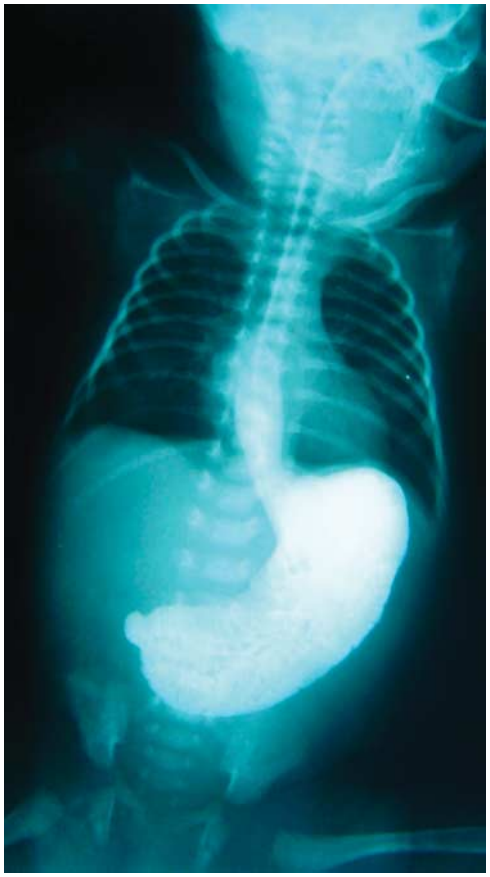
Fig. 5



Plain abdominal radiography showing a single large gastric air-bubble, with no air distally, diagnostic of congenital pyloric atresia.

necessary to confirm the diagnosis. In patients who are suspected to have associated multiple intestinal atresias, a contrast enema is done to locate or roll out associated colonic atresia. The presence of calcification in plain abdominal radiography should alert the physician to the possibility of associated multiple intestinal atresias [42,43]. It is important to inspect the whole intestines intraoperatively, to roll out associated intestinal atresia. The physician needs to ensure the patency of the remaining intestines through distally injected saline, also

Fig. 6



Upper contrast studies showing congenital pyloric atresia. Note the dilated stomach, with no contrast passing distally.

known as a saline test. The presence or absence of associated oesophageal atresia can be confirmed by passing a nasogastric tube. Neonatal gastric perforation is also a rare and unusual presentation of CPA, and these patients present with pneumoperitoneum.

Treatment

The treatment of CPA involves surgical correction, and this depends on the type of pyloric atresia. Different procedures are followed, depending on the anatomic type. Pyloric atresias of types 1 and 2 include pyloric diaphragms and pyloric atresias without a gap. These are treated by the excision of the membrane and Heineke-Mikulicz or Finney pyloroplasty. Intraoperatively, it is important to make sure that only one pyloric diaphragm is present, as these manifestations can be multiple [8]. It is also important to check for the patency of the remaining intestines using saline injection, to exclude associated intestinal atresias, which are often multiple. For those with pyloric atresia with a gap, the treatment is pyloroduodenostomy. Dessanti *et al.* [51] describe pyloric-sphincter reconstruction for patients having CPA without a gap. Gastrojejunostomy should be avoided, as it is associated with high morbidity, including anastomotic ulcers. Gastrostomy should not be part of the operative treatment, but can be carried out in those with associated pure oesophageal atresia.

The association of CPA and EB has almost fatal outcomes. In consequence, surgeons advocate no surgical intervention for CPA in these patients [27]. Others feel that the association of CPA with EB should not preclude surgical treatment, as, recently, encouraging reports of survivors have surfaced, and new treatments of EB are being developed [25,45,52]. These patients usually die because of fatal infections with sepsis and severe electrolyte imbalance. The CPA–EB syndrome is a hereditary condition, which carries a 25% risk of recurrence in future siblings. This is important, and parents should undergo genetic counselling. This is specially so in this era, in which a prenatal diagnosis of CPA can be made as early as 10 weeks of gestation, and EB can be diagnosed by the electron microscopy of a foetoscopic skin biopsy [11,48,49].

Prognosis

The prognosis of CPA is variable, depending on the presence or absence of severe associated anomalies [8,53]. The overall mortality is very high, exceeding 50%, but this is due to the high incidence of severe, and often fatal, associated anomalies. The prognosis of isolated pyloric atresia, and of pyloric atresia associated with other non-hereditary intestinal atresias, is excellent. Early diagnosis and surgery, together with neonatal supportive care, have significantly improved the survival rate in these patients. CPA associated with HMIA has a poor prognosis, and some of these patients may have an associated combined immunodeficiency syndrome. Recently a combined immunodeficiency syndrome was reported in patients with HMIA [38–40]. CPA, in association with HMIA, is universally fatal, as so far none of the reported patients have survived [7,13]. The cause of death in the majority of them was sepsis. The association of CPA and EB has a poor prognosis, and the majority of these patients die because of sepsis and dehydration. EB is generally a fatal disease, and the cause of death is sepsis and fluid loss. As a result of this, some surgeons advocate non-surgical intervention in those with EB associated with CPA [27]. Okoye *et al*. [16] and others feel that the association of CPA with EB should not preclude surgical treatment [16]. Recently, the use of steroids and phenytoin has been reported to give favourable results [20,35,52]. Prenatally, it is now possible to diagnose CPA on ultrasound, as early as 10 weeks, and EB can be also diagnosed by the electron microscopy of a foetal-skin biopsy, carried out at 19 weeks' gestation [11,48,49]. The decision regarding the prognosis and the continuance of that pregnancy, as well as future pregnancies, should be discussed with the parents, considering both the 25% risk of recurrence and the encouraging results with EB, using phenytoin and steroids.

In conclusion, CPA is a very rare malformation that can be familial and inherited as an autosomal recessive. It can either occur as an isolated lesion with an excellent prognosis, or be associated with other genetically determined conditions, such as EB and/or ACC. Its occurrence in association with other intestinal atresias is interesting and must be kept in mind. These atresias can affect any part of the gastrointestinal tract, from the oesophagus to the rectum. Whereas the managemnet of CPA is simple, the managment of associated intestinal atresias is more complex. Every case should be managed individually. The overall prognosis of CPA, however, is still poor, and this is due to the frequent – and often fatal – associated anomalies.

Conflicts of interest

There are no conflicts of interest.

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