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Case report: Neonatal pancreatitis, chromosomal abnormality and duodenal stenosis in a newborn. A new syndrome?

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ABSTRACT

INTRODUCTION: Pancreatitis is a dire clinical diagnosis with variable presentation in the paediatric population. Moreover, neonatal pancreatitis has been rarely reported in the English literature.**PRESENTATION OF CASE:** A newborn, product of a poorly supervised, pre-term gestation with pre-natally diagnosed intestinal obstruction, and post-natal clinical features of jaundice, vomiting, abdominal distension, aphonation and suspected chromosomal abnormalities. There was maternal hepatitis which was untreated. Diagnosed as duodenal atresia, the baby was investigated, resuscitated and had surgery. Intra-operative findings were of an omental bubble, duodenal stenosis with annular pancreas, coagulative necrosis of the pancreas and multiple intra peritoneal cheesy deposits. Following an unfortunate demise, autopsy confirmed pancreatitis and multiple congenital abnormalities.**DISCUSSION:** Paediatric caregivers should be aware of the possibility of neonatal pancreatitis in jaundiced newborns with intestinal obstruction especially with a background of maternal viraemia.**CONCLUSION:** A constellation of unusual presentations as highlighted could be a pointer to an emerging syndrome. All paediatric caregivers should entertain a high index of suspicion of pancreatitis in such a case, investigate and expedite appropriate interventions to prevent mortality.© 2020 The Author(s). Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Pancreatitis in the paediatric population is not as common as in adults [1]. Its aetiology and clinical presentation in children also differs. Subsequent to limited reportage and under-diagnosis of the condition, it is difficult to state the true incidence. Neonatal pancreatitis is extremely rare and sparsely reported. We present a rare case of a neonate born to a hepatitis B virus infected mother, with multiple congenital anomalies and pancreatitis who was managed at our tertiary health facility. This work has been reported in line with the SCARE 2018 criteria [2].

2. Case

We present a 39-hour old female neonate of African descent delivered via emergency lower caesarean section at 34 weeks at an outside private primary care facility for premature onset of labour

in a Hepatitis positive, multiparous mother. There was an obstetric history of polyhydramnios and double bubble features in the foetal abdomen on antenatal scans done in the early 3rd trimester. No genetic screening tests were done prenatally except for 2 obstetric scans. Mother was routinely on herbal medications during pregnancy and did not register for antenatal care till the 5th month of gestation. She also took over the counter medications whose specifics could not be ascertained.

APGAR Score was queried at 7 [1] and 9 [5] with a weight of 2.1 kg and there was no history of birth trauma. The baby was brought in by the father in a rented cab from the referral facility. She presented to us at our public tertiary specialist facility with a history of weak cry, bilious vomiting and abdominal distension starting shortly after birth. Hepatitis B immunoglobulin was administered at birth. The father's perspective at presentation was that she was too ill and too small to undergo the recommended surgical review and potential intervention that they had been informed about from the referral facility. On examination, the baby had mottled skin, dysmorphic facie (occipitofrontal circumference of 32 cm), prominent forehead, slanted eyes, low set ears, flattened nasal bridge (with inter canthal distance of 2 cm) and ankyloglossia. Baby was deeply icteric, acyanosed and afebrile. Respiratory rate was 60/min with broncho-vesicular breath sounds, and a grade 3 systolic murmur on auscultation. There was significant abdominal distension which was non-tender and tympanitic to percussion, with hyper-

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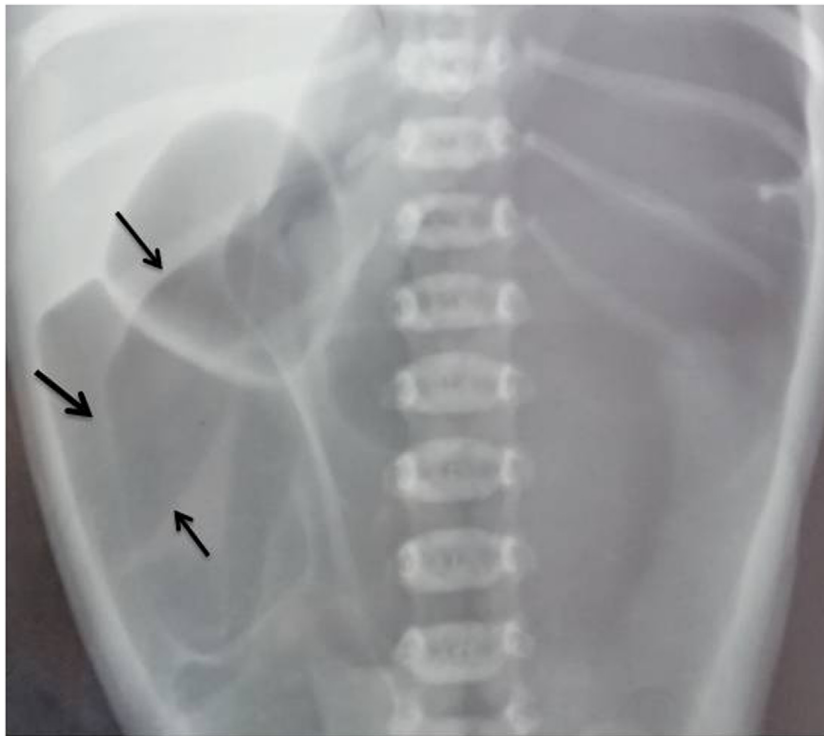


Fig. 1. X-ray showing pneumoperitoneum with positive Rigler's sign (arrows).

active bowel sounds. The anus was normally sited and genitalia was normal. Grünwald sign was negative and there was no Grey Turner or Cullen's sign. We also observed that she was grimacing but made no sounds (despite noxious stimuli), reminiscent of silent wailing. There was some muscular rigidity but no spasms or paraplegia. We made a diagnosis of neonatal intestinal obstruction secondary to duodenal atresia, keeping in view a perforated viscus from necrotizing enterocolitis on a background of? Trisomy 21 in compensated shock.

On admission, we passed a nasogastric tube (which drained coffee grounds effluent), catheterized, obtained blood for chemistry, requested an echocardiogram (which could not be done immediately because of the COVID-19 associated scale down of services), plain babygram (erect and supine) and administered 10% DW (105mls) + 0.9% Normal saline (65mls), 2 mg IV Vit.K, Astymin (30mls), proton pump inhibitor (Ranitidine, 2 mg/kg/dose, 8hourly), antibiotics (Cefotaxime 100 mg 12hrly, Amikacin 15 mg 12hourly) and maintenance electrolytes (potassium chloride and bicarbonate) over 24 hours. Fluids and electrolytes were reviewed daily and adjusted as investigation results became available. She was commenced on phototherapy for elevated unconjugated bilirubin fraction. Electrolyte results showed severe hyponatremia of 120 mmol/l but haemoglobin and platelets were adequate. Vital signs improved with resuscitation.

The babygram showed multiple large bubbles and positive Riglers' sign (Fig. 1) suggestive of pneumoperitoneum though free air under the diaphragm could not be demonstrated despite the large volume of air.

She was scheduled for and had an exploratory laparotomy performed by the surgical team, led by the attending paediatric surgeon on call, on day 4 following presentation. Aim of surgery was to relieve intestinal obstruction and decompress potential pneumoperitoneum. Delay in intervention was partly due to parental financial constraints and unavailability of type specific blood for the planned procedure as well as shortage of hospital staff due to the COVID-19 pandemic and lockdown. Intra-operatively, under gen-

eral anaesthesia and in the supine position, intra-abdominal access was through a right transverse supraumbilical incision. Intraoperative findings were of a grossly distended abdomen, significant pneumoperitoneum with the air trapped inside the omentum similar to a helium balloon (Fig. 2a), cheesy deposits between the leaves of the omentum, the anterior abdominal wall, lesser sac, anterior to and behind the mobilized second part of the duodenum, in the peripancreatic region and on the rest of the bowel loops (Fig. 2b). There was annular pancreas with moderately dilated duodenum up to D2, a normally sited DJ junction, and there was no malrotation. There was necrotic debris in the lesser omentum and liquefactive necrosis of the head of the pancreas, grossly hypoplastic small bowel, and curiously no significant peritoneal fluid was encountered. The rest of the pancreas (body) looked grossly normal. The liver and gall bladder were grossly normal. The aspirated jejunum contained bile. After difficulty with advancing fluid past the dilated duodenum freely, we made an intraoperative diagnosis of annular pancreas with peri-natal pancreatic injury, fat saponification and duodenal stenosis. A Diamond duodeno - jejunostomy was done. Intraoperative time was 67 min and estimated blood loss was 20mls. She was infused with warmed lactated ringers and 40mls of whole blood intraoperatively.

She recovered fully from anaesthesia and was transferred to the neonatal general ward on supplemental oxygen. Post-operatively, treatment regime was continued as in the pre-operative period, with the addition of analgesics and a change of infusion from normal saline to lactated ringers. Urine output was adequate but blood tinged. On the post-operative day 2, she was observed to be bleeding from puncture sites and passing blood stained urine. She also suffered an episode of witnessed apnoea. Blood sugar was found to be 28 mg/dl (hypoglycemia) despite being on 220mls of IV fluids (160mls of 10%DW and 60mls lactated ringers). She was resuscitated successfully and her saturation improved to the high 90 s. She was continued on post-operative plans including Vit. K, blood chemistry, platelet transfusion, an echocardiogram, an ENT review (due to a suspicion of a laryngeal web) and endocrinology

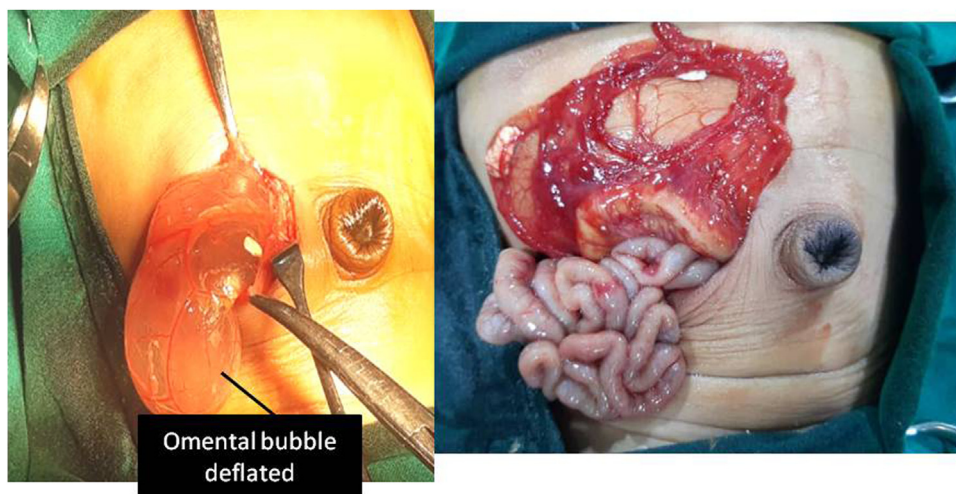


Fig. 2. Intraoperative picture showing omental bubble and cheesy deposits on the omentum.

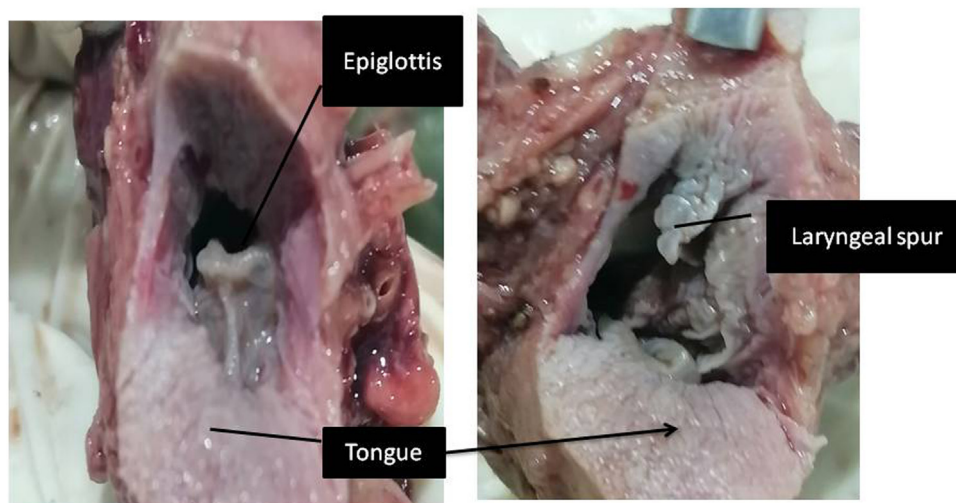


Fig. 3. (a) and (b) showing normal epiglottis and a laryngeal spur adjacent to it.

review. She however developed a fatal cardiac arrest about 8 hours later.

Autopsy findings were of central and peripheral cyanosis, low set ears, a well formed tongue with a spur or valve like structure extending from the larynx but no choanal atresia or tracheo-oesophageal fistula (Fig. 3). There was cerebral oedema and she had a large membranous VSD (1 cm in diameter), subtotal lung collapse with bronchopneumonia, annular pancreas, duodenal stenosis in D2, patent anastomosis of D1 to jejunum, cheesy infiltrates within the peritoneum and in the splenic area at the tail of the pancreas (Fig. 4). There was also congestion in the kidneys. Histology of the cheesy deposits was reported as necrotic tissue with fat necrosis and mixed inflammatory cells comprised of neutrophilic and histiocytic infiltrate (Fig. 5). Also seen were dead fatty tissue without calcifications. Histology of the pancreas showed necrotic pancreatic tissue in the area of the annular pancreas with fat necrosis, areas of fibrosis and inflammatory infiltrate consisting of histiocytes and polymorphonuclear cells. The body of the pancreas was otherwise normal with some areas of autolytic changes and vascular congestion (Figs. 6 and 7). There were cystic spaces in the liver and hypertrophy of the muscularis propria at the stenotic duodenum (Fig. 8). Cause of death was ruled as bronchopneumonia with subtotal lung collapse in a background of multiple congenital anomalies and prematurity.

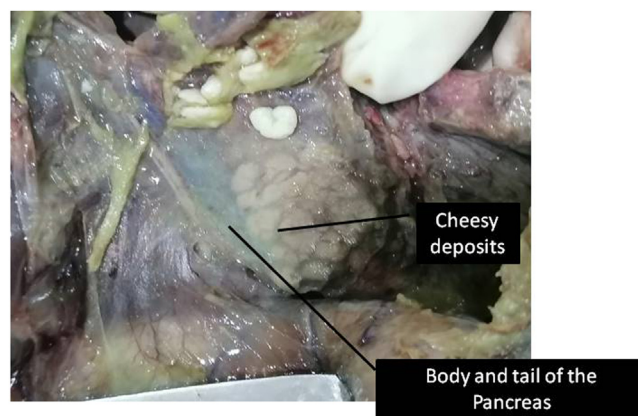


Fig. 4. Autopsy picture showing cheesy deposits in the peri-splenic area.

3. Discussion

Pancreatitis, acute or chronic, is a clinical entity that is not as common in the paediatric age group as in adults [3]. Occurring clinically and histologically as a spectrum both in duration and severity, inflammation of the pancreas is often attended by acinar

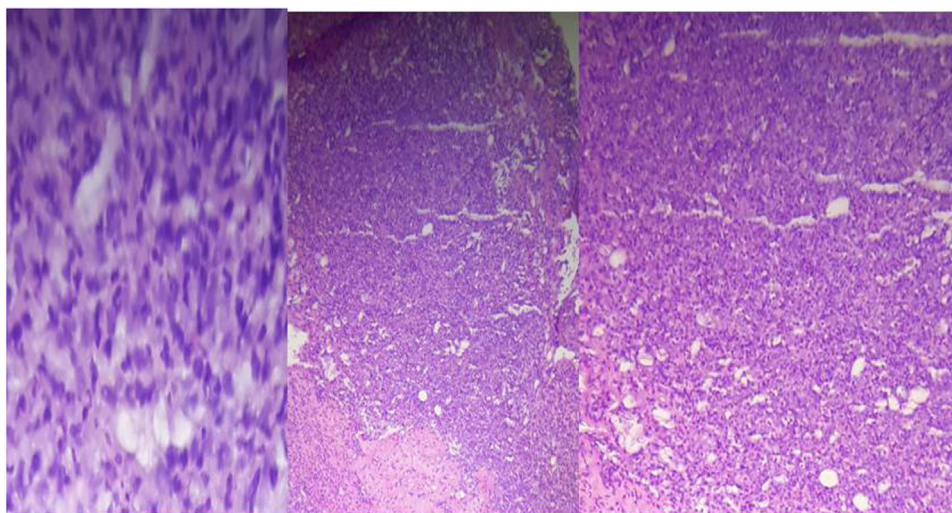


Fig. 5. Micrographs (a) ($\times 400$) and (b), (c) ($\times 40$). Cheesy granules showing necrotic pancreatic tissue with fat necrosis and inflammatory cell infiltrate consisting of histiocytes, polymorphonuclear cells and areas of fibrosis.

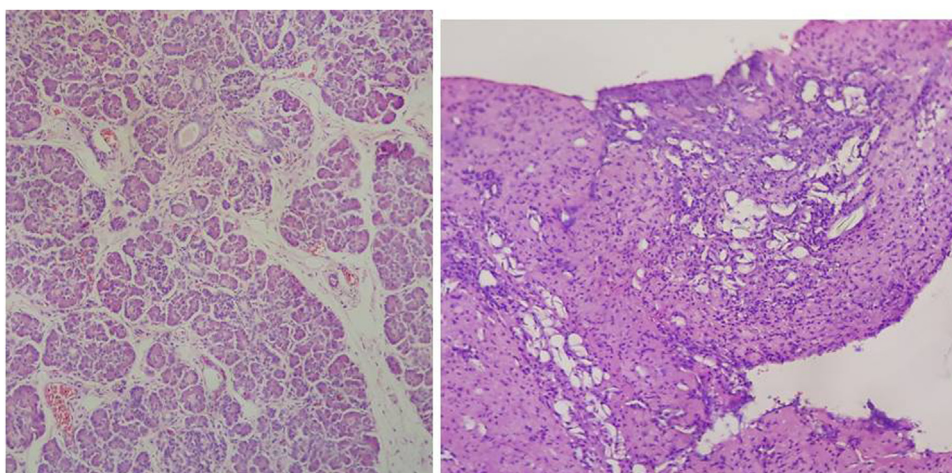


Fig. 6. (a) Dilated pancreatic acini with inspissated secretions, oedema of the interstitial tissue and congested bloody vessels; (b) Section of the peritoneal deposit (globule) showing fat necrosis with inflammatory cell infiltrate consisting mainly of neutrophils.

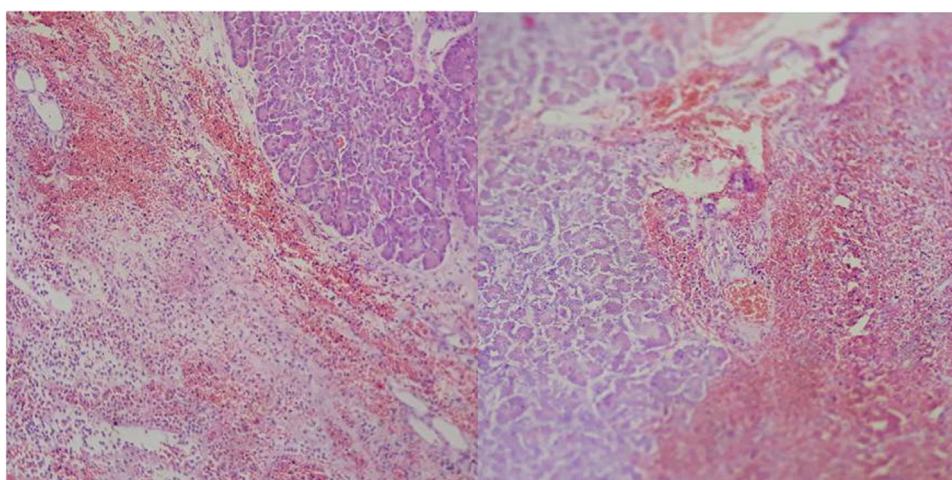


Fig. 7. (a) and (b) Haemorrhage and inflammation in peri-pancreatic tissue.

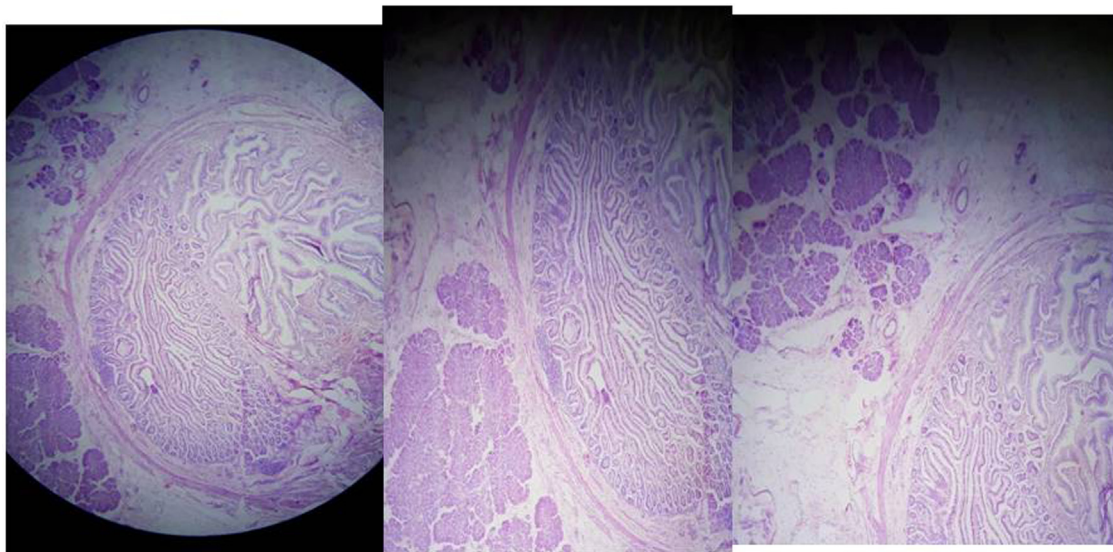


Fig. 8. (a) (b) and (c) Micrographs ($\times 40$) Pancreatic tissue surrounding the duodendum (annular pancreas) with fibrosis of the intestinal wall and occlusion of its lumen.

cell injury which eventually culminates in enzymatic necrosis facilitated by inappropriately activated pancreatic enzymes [4]. Three possible pathways have been postulated; pancreatic duct obstruction, primary acinar cell injury (i.e from viruses, drugs ischaemia or trauma) and lastly, defective intracellular transport of proenzymes within the acinar cells. The causes in children are myriad and include abdominal trauma (23%), use of hyperalimentation, medications, metabolic abnormalities (14%), pancreaticobiliary junction malformation (15%), viruses (10%), drugs and toxins (12%) to name a few [5]. Another entity is hereditary pancreatitis, a rare, genetic disease that leads to recurrent episodes of acute pancreatitis and is associated with carriers of the cystic fibrosis (CTFR) gene [6,7]. Autoimmune pancreatitis is characterized by autoimmune inflammation of the pancreas and can occur alone or in association with other autoimmune diseases [8]. In about 30% of cases, however, a cause cannot be found. Acute pancreatitis may present symptoms attributable to a cytokine storm causing an explosive activation of the systemic inflammatory response resulting in fluid sequestration, hemolysis (jaundice) DIC (coagulopathy), fat necrosis (cheesy deposits), acute renal tubular necrosis (haematuria). Symptoms in older children include abdominal pain (87%), jaundice, abdominal distension, vomiting (67%), fever. GI haemorrhage and coma have also been reported though presentation in children vary widely.

Its clinical features are characterized by a mix of signs and symptoms coupled with elevated digestive enzymes in the blood analysis. It can be fatal without prompt and effective intervention [3,5]. It is known that these cascade of events may cause localized collections of pancreatic fluid which then become walled off by granulation or fibrous tissue to become a pseudocyst seen within the peripancreatic region. What is not documented in the English literature is the occurrence of such a capsule, thus formed, containing only air as seen in our patient where the omentum became a thin glistening capsule of air reminiscent of an air filled balloon. Also rare, is the report of pancreatitis in a neonate.

Duodenal atresia has an incidence of 1 in 2500 live births and is associated with Down's Syndrome in up to 40% of cases. Polyhydramnios is documented in half of the cases and over 30% result in premature births [5]. Neonates may have blood stained vomitus from gastritis. Our patient was born prematurely with a background of polyhydramnios, had dysmorphic facial features, and also duodenal stenosis. A review of 115 patients with duodenal obstruction treated over a 44 year period at the Red Cross Children's Hospital in Cape Town noted maternal polyhydramnios in 12.5% of cases

with duodenal stenosis and in 65% of cases with atresia. 32% of the babies had Downs syndrome and 19 of them had Congenital Heart Defects [5]. An 11 year retrospective review of 131 cases of paediatric acute pancreatitis in an Australian study developed laboratory parameters (the biliary pancreatitis triad) that may predict acute biliary pancreatitis in a child [6]. These 3 tests were not carried out in our patient because there was no suspicion of pancreatitis and only a serum bilirubin assay was requested. The decision to do a duodeno-jejunostomy in this case and not the standard duodeno-duodenostomy was because we could not delineate the particular cut off area of the stenosis in the duodenum beyond the area of the annular pancreas nor could we mobilize the distal duodenum (D3) without risking further pancreatic injury.

Our patient's mother had Hepatitis B which was untreated. It is unclear whether she had any vaccine in pregnancy as most of the pregnancy was managed at home and obstetric history is sparse. She took alcohol containing locally concocted herbal mixes generously. A causative relationship has been established between hepatitis B virus infection and acute pancreatitis, however, there is no documentation of mother to child transmission of the virus resulting in a fulminant pancreatitis in the newborn as was the case with our patient [9–11]. The parents reported that the baby had a weak cry since birth but we never heard a sound from her till demise. It is unclear whether the laryngeal spur seen at autopsy acted like a valve to prevent phonation. The presence of muscle rigidity could be a pointer to a cerebral event like palsy which may be supported by the autopsy finding of cerebral oedema. The association of cerebral oedema in cerebral palsy however has only been poorly demonstrated. Our patient also had ankyloglossia but this is unlikely to have been obstructive to phonation. The key take away messages of this report is that neonatal pancreatitis is a possible differential in babies presenting with evidence of gastrointestinal obstruction and jaundice and thus should be actively investigated. Children's surgery providers should have a high index of suspicion and therefore ensure appropriate investigation and institute management rapidly and aggressively. It is unlikely that we could have done anything more in our facility because of resource constraints and the services access problems that accompanied the COVID-19 pandemic lockdown. However, we have learnt from this case the need to extend our investigation panel to include serum amylase/lipase, further imaging (Ultrasound/CT) as well as aggressive pain control keeping in mind a need for closely monitored glucose levels. The baby would also have benefited from immediate post-

operative care in a NICU as well as parenteral nutrition which were not available. In a resource constrained setting, we would recommend a feeding jejunostomy or a trans-anastomotic nasojejunal tube insertion to facilitate early feeding. There needs to be a consensus guideline for the management of pancreatitis in the paediatric age group as recommended by Abu-El-Haija et al. [12], the adaptation of which may improve outcomes even in low resource settings like ours.

4. Conclusion

Neonatal pancreatitis is rare. An association between maternal hepatitis infection and neonatal pancreatitis is poorly reported in literature. A compedium of chromosomal abnormality, duodenal stenosis and pancreatitis may be an emerging syndrome.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

This study/case report is exempt from ethical approval in our institution because there are no patient identifiers in the manuscript, pictures or figures.

Consent

Written informed consent was obtained from the patient's father for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Ladipo-Ajayi: Surgical intervention, Conceptualization, Investigation, Writing (original draft, review and editing), visualization.

Ihediwa: Surgical intervention, investigation, data collection.

Akinjo: Performed autopsy, provided micrographs, investigation, resources.

Awolola: Performed autopsy, investigation.

Elebute: Conceptualization.

Ademuyiwa: Conceptualization.

Registration of research studies

Not applicable.

Guarantor

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