Neonatal Appendicitis with Cow Milk Protein Allergy

Appendicitis is rare in the neonatal period. A 6-week-old baby presented with fulminant appendicitis. At the age of 6 months, the infant was diagnosed with Cow milk protein allergy. Association between CMPA and appendicitis was a rare association in our case, showing that CMPA can have a wide spectrum of gastrointestinal involvement.

Keywords: *Mesenteric abscess, Neonatal sepsis*.

Appendicitis is rare in the neonatal or post neonatal period with incidence reported as 0.04% to 0.2 % in premature males [2]. A 6-week-old baby presented with complaints of frank blood in stool, diarrhea, and fever since 7 days. The child was afebrile, feeding well and was occasionally irritable but consolable on carrying and feeding. Abdominal examination was normal. Stool routine examination done on day 2 showed 8-10 red blood cells and 6-8 pus cells, and stool culture had no growth. Ultrasonography (USG) abdomen done on day 2 was normal. Child was started on oral cefixime, but as symptoms persisted, child was admitted and treated with intravenous ceftriaxone and amikacin. On day 7, child developed fever and three episodes of bilious vomiting. Hemoglobin was 7 g/dL and total leucocyte count was 39000 per mm^3 with 90 % neutrophils and CRP of 162 µg/dL. Repeat USG of the abdomen now showed four liver abscesses, largest measuring 1.9×1.1cm and remaining small, subcentimeter sized. Ultrasonography showed a doubtful mass in the pelvis without vascularity and mixed echogenicity, measuring 5×4.3×3.1 cm, which was confirmed on computed tomography of abdomen to be a mesenteric collection measuring 4.9×2.6×2.4 cm with irregular margin, in close proximity to the ileum with air speckles inside suggesting possibility of intestinal perforation and mesenteric abscess.

Surgical exploration revealed that appendix was badly inflamed and infected, tip had sloughed off with perforation. The ileal loop which was close to the appendix was stuck to its wall and had also perforated with a mesenteric abscess. Appendectomy was done with resection anastomoses of the inflamed ileal loop. The remaining intestine was normal and there was no Meckel diverticulum. Histopathology showed appendicitis and ileal serosal inflammation. The Nitroblue-tetrazolium (NBT) test for chronic granulomatous disease and Lymphocyte subset assay were normal.

The intra-operative findings were considered to be not commonly associated with the symptom of frank blood in stool. Hence, possibility of coexisting pathologies like Cow milk protein allergy (CMPA), polyp, and early inflammatory bowel disease (IBD) was kept in mind. The child recovered well after surgery. Feeds (soy protein formula) were started on day 3 and gradually increased to full feeds by day 6. Complete blood count on day 7 was normal. Day 10 USG showed complete resolution of liver abscesses and normal abdominal findings. Child was discharged on day 10 on soy-based milk formula and there was no recurrence of symptoms till 6 months age.

At 6 months, two weeks after introduction of weaning food (containing milk protein), child started passing fresh blood in stool again. On elimination of this food the symptoms disappeared in one week. IgE specific for cow's milk was reported negative. Fecal calprotectin was 423 mg/kg (normal ≤50). However, it is a non- specific marker of inflammation in the intestine and may be elevated in IBD as well as CMPA. It has also been used to evaluate efficacy of elimination diet in CMPA [1]. Hence, a colonoscopy/ biopsy was planned to confirm etiology. Colonoscopy showed scattered nodules all over colon and terminal ileum, no sites of bleed and no signs of IBD like ulcers or skip lesions. Microscopy revealed many eosinophils in the lamina propria suggesting CMPA. Thus, the diagnosis of non IgE-mediated CMPA was confirmed. At 9 months of age, off cow's milk in any form, child is doing well.

In the neonatal or post-natal period, appendicitis presents as irritability, bilious vomiting, fever, leukocytosis like non-specific signs and symptoms. It is generally not known to cause frank blood in stools. So we assume that the symptom of frank blood in stools seen in our case was because of the underlying CMPA, which was confirmed later at 6 months of age as the criteria needed for making the diagnosis was met *i.e.*, through allergen elimination and challenge.

CMPA has a wide spectrum of gastrointestinal involvement. The alarm symptoms are macroscopic blood loss in stool causing anemia, failure to thrive, breathing difficulty, anaphylaxis, and severe exudative urticaria. If any of these symptoms occur and cannot be explained by another cause, CMPA may be considered a potential

diagnosis. In most cases with suspected CMPA, the diagnosis needs to be confirmed or excluded by an allergen elimination and challenge procedure [3]. This can be performed as open, single-, or double-blind challenge. Seum specific IgE, skin prick test and radio-alergosorbent assay are some of the tests available for IgE mediated CMPA. No confirmatory laboratory test is available for non IgE-mediated CMPA. Nevertheless, an oral challenge test is necessary in most cases to confirm an adverse reaction to cow's milk protein and then to make a diagnosis of CMPA. A biopsy is not needed to confirm the diagnosis unless there are very severe or overlapping symptoms.

Non IgE-mediated food allergies are known to be associated with enterocolitis syndrome (Food protein-induced enterocolitis), enteropathy, enteritis, proctitis and proctocolitis [4]. Neonatal appendicitis, as noted in this child, is a rare finding, and needs to be recognized as another manifestation of the wide spectrum of presentation of CMPA.

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Consumptive Hypothyroidism Due to Diffuse Hepatic Hemangiomas Treated With Propranolol Therapy

Infantile hepatic hemangioma (IHH)-related consumptive hypothyroidism is rare and occurs as a result of excess thyroid hormone inactivating enzyme, type-3 iodothyronine deiodinase. We present an infant with IHH-related hypothyroidism, in whom treatment with propranolol led to regression of tumor and subsequent euthyroid status.

Keywords: *Liothyronine, Management, Type 3 deiodinase.*

Consumptive hypothyroidism is a complication of infantile hepatic hemangioma (IHH) caused by increased expression of type-3 deiodinase enzyme in the tumor tissue. This enzyme causes increased degradation of T4 and T3 to reverse T3 (inactive metabolite). When this exceeds the rate of synthesis of these hormones, a state of hypothyroidism ensues. Definitive therapy for the hemangioma and reduction in tumor burden leads to resolution of hypothyroidism. We describe a child who presented with severe hypothyroidism secondary to consumption by an IHH.

A 3-month-old female baby presented with severe constipation for the past one month. Parents also complained of dullness, poor cry and abdominal distention. There was no history of poor feeding, umbilical hernia or jaundice. The child had been born at term to a primigravida mother with a birth-weight of 2.2 kg. Her weight at presentation was 4.5 kg –2 SD) and length 55 cm (–2 to –3 SD). Physical examination revealed pallor, depressed nasal bridge and macroglossia. Her abdomen was distended and liver palpable 6 cm below the costal margin. She had an ejection systolic murmur. The thyroid gland was normally palpable.

An abdominal ultrasound revealed multiple hypoechoic lesions in the liver. Contrast-enhanced CT scan showed these lesions to have early enhancement with persistence in delayed phase consistent with a diagnosis of IHH (***Fig.* 1 a**). The child was not found to have any cutaneous hemangiomas. Thyroid function tests showed high TSH >75 mIU/L (0.57–5.54), low-normal FT4 14.6 pmol/L (60-160) and low T3 <0.62 nmol/L (1.3-2.8) (***Web Table* I**). Thyroid ultrasound showed a eutopicaly located gland and thyroid scan showed normal radionuclide uptake. Reverse T3 levels were raised (607 ng/dL, normal range 10-50) pointing towards peripheral consumption of thyroid hormone. She was