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RESEARCH ARTICLE

SICKLE CELL DISEASE-INDUCED OGILVIE'S SYNDROME IN A CHILD TREATED PHARMACOLOGICALLY WITH NEOSTIGMINE: A CASE REPORT.

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Abstract

Abdominal manifestations of vaso-occlusive crises of patient with sickle cell disease are pain and gut hypotonia as a result of ischemia of the abdominal viscera. Acute colonic pseudoobstruction is a rare, unexplained abdominal manifestation of sickle cell disease. The diagnosis needs high index of suspicion after ruling out other etiologies of similar presentation. Although there is no guideline recommendations for the optimal management, recognition and early management of this complication is important as this can avoid unnecessary surgical intervention and alters patient outcome. Here we describe a 2-years child, known to has sickle cell disease who presented with acute colonic pseudo-obstruction and was treated successfully by neostigmine. To our knowledge, this is the second such reported case in the literature.

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Introduction:-

Acute colonic pseudo-obstruction (ACPO) is also known as an Ogilvie's syndrome after Sir William H Ogilvie, in 1948, observed and reported the condition (Ogilvie, 1948). It is a poorly understood syndrome, characterized by symptoms, signs and radiological pattern of the large bowel obstruction with no evidence of mechanical obstruction (De Giorgio et al., 2001; Singh et al., 2005). Typically ACPO occurs in patients with serious illnesses, surgical interventions, infections, burns, trauma and narcotic administration (Gmora et al., 2002). An extremely less well known and potentially misinterpreted abdominal manifestation of sickle cell disease (SCD) is an acute colonic pseudoobstruction, or Ogilvie's syndrome. It has been described in adults (Hsiao et al., 2005; Knox-Macaulay et al., 2003) with only one reported case in pediatric populations (Khosla and Ponsky, 2008). Here we present the case of a 2 year-old boy with SCD, presented with evidence of bowel obstruction, who was ultimately diagnosed with ACPO and was successfully managed nonsurgically with neostigmine. To our knowledge, this is the second such reported case in the literature.

Case report:-

Our patient was a 2-year-old boy presented to the pediatric emergency department with complaints of one day history of abdominal pain, mild abdominal distention with constipation, mild shortness of breath and back pain. There was no complaint of vomiting or fever. This patient is a known case of sickle cell disease and had twice presented to pediatric department with vaso-occlusive crises in past. There was no history of opioid use for analgesia. On clinical examination his pulse was 115 beats per minute, blood pressure was 90/44, Oxygen saturation was 100% on room air, respiratory rate 28 per minute, body weight was 10 kg and temperature was normal. His abdomen was soft, distended, non tender with sluggish bowel sounds. He was admitted by pediatrician with suspicion of vaso-occlusive crisis secondary to sickle cell disease. His laboratory investigations revealed hemoglobin 7.5 gm/ dl, white blood cells (WBCs) 10.4×10^3 , platelets 123.000, hematocrit 24.7% and normal electrolytes, renal and liver function tests. Chest x-ray was normal. He was given intravenous fluids, non-steroidal anti-inflammatory analgesics and broad-spectrum parenteral antibiotics with no blood transfusion.

On reassessment the backache had settled but there was persistent constipation with increasing distention and shortness of breath secondary to abdominal distention. At this stage surgical consultation was sorted. On clinical examination his pulse was 120 beats per minute (tachycardia), respiratory rate 29 per minute, Oxygen saturation 99%, temperature was 37.7°C with non toxic look but visibly uncomfortable. His abdomen was grossly distended, soft, non tender, no organomegaly or palpable lump and tympanitic with no bowel sounds. His rectal examination showed empty rectum without any evidence of blood, palpable lump and normal anal tone. An abdominal x-ray showed pattern of a bowel obstruction with what appeared to be a hugely dilated colon, measuring 5.7 cm (Fig. 1) with rectum and cecum appeared loaded with stool with no air fluid levels on erect film. His repeated complete blood picture showed slight increase in WBCs to 13.6×10^3 with no hemoglobin drop, normal urea, electrolytes, normal arterial blood gases with PH of 7.44 and bicarbonate 22.6 mmol/l. Child was given a trial of conservative management as he was kept nil by mouth, nasogastric tube was placed and 200 cc of gastric fluid drained and fleet enema was given and although he passed scanty stools but his abdominal distention persisted. Abdominal ultrasound was ordered to rule out appendicitis or free intraperitoneal fluid which was only suggestive of excessive gases in gut loops.



Figure 1:- Plain x- ray abdomen showing distended colon loaded with fecal matter.

Repeated chest radiograph showed right peribronchial and perihilar thickening, oxygen saturation was 91% on room air with increase of body's temperature where it was 38.6°C with more tachycardia (pulse was 144 beats per minute) and his respiratory rate was 34 per minute with shallow breathing. The intensive care unit team on duty was contacted and they advised intermittent oxygen via nasal cannula and more intravenous fluids with close follow-up. As the patient's abdominal condition remains unchanged with the supportive measures for the vaso-occlusive crises and the conservative management for abdominal condition, so urgent gastrograffin enema was done to exclude any mechanical large bowel obstruction or perforation and it showed grossly dilated colon up to caecum with no evidence of mechanical obstruction or gastrograffin leakage. In view of non toxic generally stable condition of patient, absence of signs peritoneal irritation or bowel ischemia and the fact that radiological findings suggestive absence of mechanical obstruction or bowel perforation, diagnosis of acute pseudo colonic obstruction (ACPO) secondary to sickle cell disease was made and the patient was not responding to conservative management. Medical therapy with neostigmine was planned. Patient was given single intramuscular dose of neostigmine (0.1mg/kg body weight) with continuous heart rate monitoring and readily available atropine in order to treat severe bradycardia. Patient had slight return of bowel movements after 30 to 35 minutes and he passed small amount of flatus and watery stools.

Patient's abdominal distention though decreased, was persisting and he passed flatus and watery stools twice and this was considered as an initial good and encouraging response to continue neostigmine therapy. So dose of

neostigmine was repeated in the next day. Patient's normal bowel movements returned and he started passing copious amount of well formed stool and flatus resulting in settling of abdominal distention and decrease in abdominal girth with no signs or symptoms of acidosis, bowel ischemia or perforation.

His follow up abdominal radiographs showed progressive return of colonic diameter to normal (Fig. 2) and he tolerated oral fluid and advanced regularly. The child was discharged on day 7 of admission, after tolerating his oral diet and after treatment of his chest infection with instructions to keep the supportive measure to avoid recurrence of the vaso-occlusive crises of the SCD.



Figure 2:- Plain x- ray abdomen showing colon with normal diameter.

Discussion:-

The most frequent and debilitating problem seen in patients with SCD are vaso-occlusive crises which often lead to severe organ dysfunction due to microvascular occlusion (Platt et al., 1994). The incidence of these occlusive crises range between 0.8 and 1 episode per patient per year (Platt et al., 1994; Platt et al., 1991). Abdominal pain and bowel hypotonia are commonest manifestations of an abdominal crisis. Although abdominal complications of SCD rarely involve the colon, there have been reports of ischemic colitis (Karim et al., 2002; Gage and Gagnier 1983), necrotizing colitis (van der Neut et al., 1993), nonspecific ulcerative colitis (Terry et al., 1987) in an adult and pseudomembranous colitis in a child (Baruchel et al., 1992). The pathogenesis of these complications seems to be due to end-organ ischemia.

Acute colonic pseudo obstruction or Ogilvie's syndrome is a less well known and potentially misinterpreted manifestation of patients with SCD. Although there have been rare case reports in adults, to our knowledge, there is only one reported pediatric case in the literature (Khosla and Ponsky, 2008). Here we described the second report of sickle cell-induced acute colonic pseudo obstruction in a 2-years child.

In this patient, the suspicion of acute colonic pseudo obstruction was high because there was acute dilation of the colon with no intestinal air fluid levels or detectable mechanical obstruction, moreover there was no evidence suggesting generalized peritonitis or acute appendicitis. Although acute appendicitis often mimics bowel obstruction and may be the inciting event of a sickle cell crisis, it is low on the differential diagnosis because it has been recognized that acute appendicitis is rarer in sickle cell disease patients (Antal et al., 1998).

The pathogenesis of Ogilvie's syndrome or ACPO has been explained by Abnormalities of the autonomic nervous system, particularly dysfunction of parasympathetic system and the underlying pathophysiology, whatever the cause, is an early motor disturbance followed by complete impairment of gut peristalsis with progressive dilatation (De Giorgio et al., 2001). However, the pathogenesis of ACPO in patients with SCD is unclear, this is because not only previous studies have shown no evidence of gut ischemia, micro vascular or macro vascular occlusion in these

patients but also the disorders associated with acute colonic pseudo obstruction have been ruled out in studied patients and all investigations failed to clarify a cause for this manifestation (Knox-Macaulay et al., 2003).

The most feared but fortunately rare complication of Ogilvie's syndrome is caecal perforation, which is reported only in 1-3% of patients (Trevisani et al., 2000). The duration of distension, evidence of bowel compromise and the diameter of the colon are important factors in determining the need for colonoscopic decompression or surgical intervention. Patients with ACPO are usually given a trial of conservative management provided caecal distension is less than 12 cm and they are not exhibiting any evidence of ischemia or bowel perforation (MacColl et al., 1990). Conservative management involves bowel rest, nasogastric tube decompression, and/or rectal tube placement and is usually for 48-72 hours with treatment of underlying infection and correction of electrolyte imbalances.

Our patient presented by colonic distention for one day duration without evidence of perforated or ischemic bowel and the diameter of the colon in abdominal radiograph was 5.7 cm. So we started our management by conservative trial. Although successful resolution usually achieved in 83-96% of patients within 2-6 days of initiating the conservative therapy (MacColl et al., 1990), our patient did not improve.

Medical treatment is commenced when conservative measure failed or when the patient demonstrates clinical deterioration. This is usually directed at counteracting the parasympathetic-sympathetic imbalance associated with Ogilvie's syndrome to increase the parasympathetic tone. The best evidence for medical treatment is available for neostigmine (De Giorgio et al., 2001) which is a reversible acetyl cholinesterase inhibitor so, indirectly stimulates the muscarinic receptors and increases the colonic motility (Saunders and Kimmey, 2004). Neostigmine may be repeated for patients with incomplete response. Recent studies proved the effectiveness of neostigmine with successful outcome in adult patients with ACPO (Aghadavoudi et al., 2013; Mehta et al., 2006; Ponc et al., 1999; Stephenson et al., 1995), in a pediatric patient with Ogilvie's syndrome secondary to other causes (Gmora et al., 2002) and in 3- years-old girl with ACPO as a manifestation of SCD (Khosla and Ponsky, 2008). Our patients showed initial response with the first dose of neostigmine therapy and this encourage us to continue the pharmacological treatment for another one day till the colonic motility returned to its normal pattern

Conclusion:-

Ogilvie's syndrome or ACPO is a rare manifestation in the sickle cell disease in the pediatric populations and this report introduces the successful treatment of sickle cell- induced Ogilvie's syndrome with neostigmine in a child. Medical management is usually sufficient. Considering our patient and previous reports; thus, unnecessary more aggressive measures as colonoscopic decompression or surgical exploration can be avoided, hence reduce morbidity and mortality.

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