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All-Trans-Retinoic Acid (ATRA) Induced Myositis

Acute promyelocytic leukemia (APML) is a rare entity constituting 1% of all acute leukemias in the pediatric age group. All-trans-retinoic acid (ATRA) is a standard therapy used for its remission. We report a rare adverse event of severe myositis associated with tretinoin (an ATRA preparation) in a child with acute promyelocytic leukemia.

A 5-year-old girl presented with fever, skin and mucosal bleeds, and pallor. Her hemoglobin was 3.6 g/dL, total white cell count 4.5×10^3/µL and platelet count 13×10^3/µL. Peripheral smear revealed 30% blasts, confirmed as APML on bone marrow examination. Cytogenetic analysis showed the typical translocation of t(15:17) with 77% of interphase cells expressing PML:RARA gene fusion. Child was started on combination chemotherapy with etoposide (VP16), 6-thioguanine (6TG) and prednisolone. ATRA was added in the dose of 45 mg/m^2/day on day 3. On day 10 of treatment, child had severe calf muscle pain restricting her physical activity. There was no fever, joint pain, joint swelling or bleeding. However, there was a mild swelling of the limb in the region of pain. *X*-ray limbs and sonography of the calf muscles were inconclusive. Magnetic resonance imaging (MRI) of limbs done 2 days later showed edema in muscles of posterior compartment and fluid in the intermuscular planes suggestive of myositis. A diagnosis of ATRA-induced myositis was made. ATRA was discontinued and intravenous dexamethasone was given. Child improved dramatically and ATRA was restarted after 2 days in a lower dose.

The common side effects of ATRA include ATRA syndrome (in 25% of patients), hyperleucocytic syndrome (acute respiratory distress syndrome), isolated fever, weight gain, headache, pseudotumor cerebri, raised aminotransferases, hypertriglyceridemia, myalgia, hypercalcemia, erythema nodosum, fournier gangrene, Sweet syndrome and necrotizing vasculitis. Isolated muscle involvement due to ATRA therapy in APML has been rarely described(1-4). Most of the reported cases are in adults(4). Till date, to the best of our knowledge, only 2 pediatric cases of ATRA-induced myositis have been reported(4). Our patient developed muscular symptoms on day 7 of ATRA, whereas reported cases in adults had a median time of onset around 18 days (range 9-23), except in one pediatric case where the onset was within 5 days of starting ATRA(1,4). A high index of clinical suspicion coupled with modern imaging methods are required to diagnose this condition. Timely treatment is important to prevent further life threatening complications(5).

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Aeromonas hydrophila Sepsis in a Preterm Neonate

A female infant was born at 27 weeks of gestation by spontaneous vaginal delivery at home in the toilet. She was retrieved, resuscitated, commenced on intravenous antibiotics and ionotropic support. She was transferred to our level 3 neonatal intensive care unit at 8 hours of age. She received 2 doses of Curosurf® for hyaline membrane disease. Inotropes were weaned and she was extubated to CPAP on day 4 in 30% oxygen. Antibiotics were ceased at 48 hours following negative blood cultures. A patent ductus measuring 2.5 mm was detected on echocardiography on day 4 and was treated with indomethacin. On day 7, however, she suddenly deteriorated with hypotension, tachycardia, respiratory distress and abdominal distension requiring re-intubation. Full blood count, CRP and blood cultures were taken and flucloxacillin, gentamicin and metronidazole were commenced. An abdominal *X*-ray confirmed NEC with pneumatosis intestinalis and free peritoneal gas. A laparotomy was performed with primary resection of 17 cm of jejunum and anastomosis of the perforated segment of jejunum completed. Peritoneal swabs taken during surgery grew *Aeromonas hydrophila*. Hematological evidence of severe sepsis persisted. Blood cultures throughout were negative. Cranial ultrasound prior to her deterioration was normal. Following surgery, the ultrasound on day 8 revealed bilateral grade IV intraventricular hemorrhage. Given the poor prognosis and high risk of poor neurological outcome, her parents chose a palliative care management plan. She was extubated on day 9 in her parents arm and died soon after. Post mortem blood cultures and swabs from the lungs and peritoneum all grew *Aeromonas hydrophila* and *Klebsiella oxytoca*.

Aeromonas hydrophila is a gram negative aerobe found in tap water, canals, streams, sewage and rivers. It is increasingly identified as a primary pathogen in the causation of diarrhea in all age groups. However it has only been rarely implicated in children with infections of the skin, bone, joint, eye, muscle, urinary tract, lungs and meninges(1). In the neonatal period, fulminant infection with septicemia has been reported in only two cases(2,3). The source of *Aeromonas* infection is usually nosocomial and hospital water supply has been identified in nursery epidemics(4). In our case we do not believe the infection was hospital acquired as no other infant in the NICU developed septicemia or had this bacteria isolated at or near this time. We believe this infant was most likely colonised on skin, mouth and then in its bowel following delivery in the toilet at home.

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