

Though the stool culture was negative, purulent discharge culture revealed *Klebsiella oxytoca* and *Proteus mirabilis* and the culture of perianal skin revealed *Klebsiella oxytoca*, *Enterobacter cloacae* and *Escherichia coli*. The patient was seronegative for HSV 1 and 2. Rectosigmoidoscopy was unremarkable and pathology did not reveal any evidence of underlying inflammatory bowel disease; colonic biopsy revealed only moderate alterations suggestive of active focal erosive proctitis. Additional investigations with polymerase chain-reaction in the blood, skin lesion and rectal tissue for Herpes viruses (HSV1, HSV2, VZV, EBV, CMV) were also negative. Empiric antimicrobial treatment with cefotaxime, clindamycin, metronidazole and acyclovir was initiated and continued for 14 days. The clinical course was favorable with complete clinical resolution (**Fig. 1b**). In the follow-up period for next two years, child continued to remain well with no stool incontinence.

We report this unusual case because of the clinical presentation mimicking lesions associated with sexual abuse, as stellate lacerations were present. We elected to treat with broad spectrum antibiotics and provide antiviral treatment. The complete resolution of his lesions and anal incompetence was remarkable. Since the investigation did not identify any underlying disease, we concluded that the most likely pathogenetic cause was the development of severe neutropenia post viral infection. This highlights the importance of a complete blood count and a peripheral blood smear in the initial evaluation of perianal abscess upon presentation. Moreover, although his family history strongly suggested possible phagocytic dysfunction, the investigation failed to diagnose such an immune deficiency.

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Early Onset Predominantly Diffuse Lung Disease in an Infant of Combined Methylmalonic Acidemia With Hyperhomocysteinemia Cobalamin C Type

Elevated blood methylmalonic acid (MMA) levels combined with elevated homocysteine is called combined methylmalonic acidemia with hyperhomocysteinemia [1,2]. It is found that MMA may damage the central nervous system, retina, liver, kidneys and blood cells. It also causes macular coloboma, thrombotic microangiopathy [3], and sometimes pulmonary arterial hypertension (PAH) [4,5], but an association between combined methylmalonic acidemia with hyper-

homocysteinemia and diffuse lung disease (DLD) has rarely been reported in infants [6].

A 7-month-old boy was admitted with complaints of pallor for 30 days. It was followed by cough 8-10 days later. Personal history showed delayed motor development. The child was hospitalized in a local hospital for respiratory distress. Investigations showed white blood cell count of $9.78 \times 10^9/L$, hemoglobin of 6 g/L, platelet count $319 \times 10^9/L$, and reticulocytes of 9%. High resolution computed tomography (HRCT) scan of the lungs revealed diffuse lesions in both lungs. Cytomegalovirus DNA detection revealed 5.08×10^5 copies/mL in sputum. Injection meropenem, azithromycin, voriconazole and ganciclovir were administered. In spite of the above treatment, child continued to have progressively worsening respiratory difficulty. He was intubated transferred to our hospital.

We added trimethoprim-sulfamethoxazole with a possibility of *Pneumocystis carinii* infection. Further investigations were non-contributory for bacterial, fungal and tuberculosis infection, and liver and renal function tests were

within normal limits. Serum erythropoietin level was >750.0 mIU/mL, vitamin B12 >1000 pg/mL and folic acid >24.0 ng/mL. The morphology of red blood cell of the peripheral blood, and bone marrow aspiration had no abnormalities. Thoracoscopic lung biopsy was performed and pathology showed alveolar septum widened with local atelectasis and pulmonary arteriolar thickening. Further blood tests and tandem mass spectrometry revealed increased homocysteine levels (95.9 μ mol/L; normal: 10-40 μ mol/L) and highly elevated MMA (0.2598; normal levels: 0.001). We performed a whole exome sequencing and confirmed a compound heterozygosity in *MMACHC* gene, with c.80 A>G (p.Gln27Arg) and c.609 G>A (p.Trp203Term) sequence variants. Therefore, the child was considered to be combined methylmalonic acidemia with hyperhomocysteinemia cobalamin C type (MMACHC). The patient was treated with folic acid 5 mg twice daily orally, vitamin B12 (cyanocobalamin) 1 mg daily intramuscularly, betaine 500 mg three times daily orally, and L-carnitine 100 mg/kg/d intravenously. After two weeks of further treatment, there was some clinical and radiological improvement. Ventilator setting was decreased but the child could not be weaned off completely. Due to poor prognosis and high costs, parents decided to discontinue treatment and left against medical advice. The child subsequently died.

The baby had a brother admitted to our hospital three years ago who was aged 5 months. The chief complaint was paleness for 4 months, repeated cough for 22 days, and diarrhea for 18 days. He was diagnosed with cytomegalovirus pneumonia, severe anemia, brain dysplasia, enterogenous acrodermatitis, and possible metabolic disease. Pulmonary CT suggested diffuse lesions in both lungs along with brain atrophy on CT head. After admission, child was started on antibiotics and supportive treatment but as the patient did not show any improvement, patients discontinued with the treatment.

In this study, we suggest that there may be a relationship between MMACHC and DLD in infants. No other causes of DLD such as connective tissue disease, Langerhans cell histiocytosis, idiopathic pulmonary hemosiderosis, alveolar hemorrhage syndromes, pulmonary vasculitis, hypersensitivity pneumonitis or drug induced interstitial pneumonia were detected in these siblings. Thus, we think that it is possible that DLD was caused by MMACHC in this case. The occurrence of DLD in MMACHC may be related to the abnormal proliferation of vascular smooth muscle cells and pulmonary interstitial cells caused by abnormal accumulation of metabolites [6]. The specific cellular and molecular mechanisms need to be further studied.

Our patient presented with early and progressed rapidly, though literature review shows a history of several months or even years without significant respiratory failure [6]. We propose that one of the reasons that the condition was too severe and it was too late to start treatment, so the pathological changes of the tissues could not be reverted [2]. Early onset disease also suggests a more serious metabolic

enzyme deficiency and greater accumulation of metabolic waste adding to a poor prognosis and higher mortality [3]. Treatment with hydroxycobalamin and betaine has been shown to be efficient in MMACHC. Hydroxycobalamin is considered to be the only form of cobalamin to be beneficial in patients with MMACHC [1]. A possible reason of slow improvement could be non-availability of hydroxycobalamin; however, beneficial effect with cyanocobalamin is also reported [6].

MMA patients have been reported to have pulmonary vascular embolism [6]. Our patient also had hematologic abnormalities; however, there was no obvious abnormality in the peripheral blood smear, and no micro-thrombotic change in the lung biopsy. Although the elder brother did not have a definite diagnosis, MMACHC was the most likely candidate considering his medical history and his brother's final diagnosis suggesting that genetic background plays an important role in the age of onset and phenotype of the disease.

In summary, our report suggests that MMACHC should be considered as a potential cause of DLD. Early recognition, diagnosis and treatment of MMACHC defect are important, especially in early-onset cases.

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