

Idiopathic Intracranial Hypertension due to Intralesional Triamcenolone Acetate

Systemic corticosteroid therapy and its withdrawal is one of the causes of idiopathic intracranial hypertension. Intralesional steroids have not been reported as a cause.

A 3-year-old boy presented with complaints of irritability for one month, nonprojectile vomiting for 4 days and medial deviation of both eyes for 3 days. There was no history of fever, headache, seizures or neck stiffness during this period. The child had scalds over 75% of the body surface area one year previously. For the hypertrophic scar due to scald, the child was receiving intralesional injections of triamcenolone every month for last 7 months. Magnetic resonance imaging (MRI) of brain showed buckling of bilateral intra-orbital optic nerve with partial empty sella turcica, without dilatation of ventricles, and without any structural abnormality or meningeal enhancement. Magnetic resource venography was also normal. He was treated with intravenous mannitol, oral glycerol and oral acetazolamide. His complete blood counts were within normal limits. His lumbar puncture done on 3rd day of admission, revealed normal CSF pressure. CSF gram staining, cytology and biochemistry were normal.

Although the lumbar puncture and CSF pressure recording was not done at the time of acute episode but the acute presentation of vomiting, papilledema, medial deviation of both eyes with normal blood pressure, and MRI findings makes the diagnosis of idiopathic intracranial hypertension likely. Triamcenolone acetonide is a fluorinated prednisolone derivative, with four times the potency of hydrocortisone [1]. Due to fluoridation, it is less soluble than its parent compound. This allows it to remain at the site of injection for longer periods of time, establishing a prolonged duration of action [2]. This facilitates a pooling effect that can result in the slow release of steroid, potentially increasing systemic levels of steroid [1,2]. High systemic levels of corticosteroids are known to cause idiopathic intracranial hypertension [3]. We suggest monitoring of signs and symptoms of raised intracranial pressure in children receiving prolonged intralesional steroids therapy.

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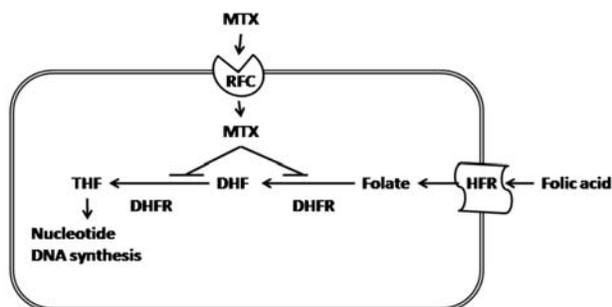
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Are Concerns about Folic Acid Supplementation in Children with Acute Lymphoblastic Leukemia Justified?

The issue of folic acid supplementation to children with acute lymphoblastic leukemia (ALL) remains unresolved pending adequate clinical data. Folic acid supplementation is believed to reduce chemotherapy related complications and improve tolerance allowing adequate drug dosages, particularly for methotrexate, but the fear of rescuing leukemic clones prevents routine supplementa-

tion [1]. However, folic acid is unlikely to interfere with anti-neoplastic action of methotrexate as: (i) there is apparently no competition between folic acid and methotrexate as the former preferentially utilizes the human folate receptor for entry into the cell whereas the latter and its antagonist folinic acid (reduced folic acid) use reduced folate carrier for their uptake (**Fig. 1**); (ii) Folic acid needs to be reduced by dihydrofolatereductase (DHFR) (an enzyme blocked by methotrexate but can be circumvented by folinic acid) in order to take part in DNA synthesis; (iii) Folic acid gets active upon regeneration of the DHFR enzyme only after methotrexate is eliminated from the system; (iv) methotrexate and folinic acid are administered at thousand-fold higher dosages as



RFC, Reduced Folate Carrier; HFR, Human Folate Receptor; MTX, methotrexate; DHFR, Dihydrofolate reductase; DHF, Dihydrofolate; THF, Tetrahydrofolate.

FIG.1 Interaction between methotrexate and folic acid.

compared to the recommended daily allowance of folic acid; and (v) the proposed competition of folic acid with methotrexate for renal excretion may in fact increase the exposure of leukemic cells to methotrexate in presence of adequate folic acid [1].

Nutritional deficiency of folate and its further depletion with chemotherapy is common in children with ALL, especially in countries with high prevalence of malnutrition and lack of folate fortification [2]. Despite a documented higher infection-related deaths during induction, and interruption of maintenance chemotherapy in folate deficient children, the theoretical concern of

increased relapse has prevented us from supplementing with folic acid. Developed countries with mandatory folate fortification have not encountered increased relapses in the post-fortification era; this is further supported by data from adults where routine folate use during chemotherapy helps in improving the chemotherapy tolerance without compromising efficacy [3].

We propose that careful consideration should be given towards folic acid supplementation in deficient children undergoing chemotherapy for ALL, especially in countries without mandatory folate fortification.

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Low Dose of Carglumic Acid for Treatment of Hyperammonemia due to N-Acetylglutamate Synthase Deficiency

N-acetylglutamate synthase (NAGS) deficiency is an autosomal recessive disorder of the urea cycle. N-carbamylglutamate (NCG) is a structural analogue of human N-acetylglutamate and is licensed for the treatment of hyperammonemia due to NAGS deficiency [1,2].

A 5-day-old boy – first child of a consanguineous Turkish couple – had an elevated ammonia level of 328 mmol/L. Treatment with intravenous glucose, oral sodium benzoate (200 mg/kg/day) and arginine (200 mg/kg/day) was started and enteral feeding was stopped. Despite this, his ammonia level remained elevated.

Carglumic acid was started with a dose of 100 mg/kg/day, and the ammonia level was normalized. His clinical and laboratory findings were consistent with NAGS deficiency. Mutation analysis revealed classical mutation of the NAGS gene (Exon6: c.1450T>C (p. Trp484Arg)). The patient was discharged with carglumic acid (100 mg/kg/day) and a protein-restricted, high-calorie diet.

The patient was not brought to our outpatient clinic for the following 6 months. At 8 months of age, he was not using protein-restricted diet, and carglumic acid dose was reduced to 12.5 mg/kg/day as the child was now heavier. Carglumic acid dose was raised to 25 mg/kg/day. The patient did not attend to our clinic for another 7 months, and he was taking carglumic acid at the dose of 10 mg/kg/day when he was 15 months of age. Carglumic acid dose was again raised to 20 mg/kg/day, and a protein-restricted diet was continued. At 27 months, reported to emergency unit with an elevated ammonia level of 228 mmol/L along with an upper respiratory tract infection. The carglumic acid dose was raised to 50 mg/kg/day, and ammonia level