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CASE REPORT

Leucovorin-induced hypersensitivity reaction in acute lymphoblastic leukemia - A case report

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ABSTRACT

Leucovorin (LCV) acts as an essential coenzyme for nucleic acid synthesis and also it is an active metabolite of folic acid. LCV can be used to selectively "rescue" cells from the adverse effects of methotrexate (MTX). Here, we report a case of LCV-induced hypersensitivity reaction when used in combination with high dose MTX (HDMTX). We describe a 2-years-old female baby diagnosed with B-cell acute lymphoblastic leukemia on chemotherapy with pediatric berlin-frankfurt-munster protocol; she is on HDMTX and injection LCV. After initiation of LCV (folinic acid) at 42 h she was noted to have hypersensitivity reaction. Despite reaction to LCV is uncommon, one should be aware of the reactions that can be caused by LCV.

KEY WORDS: Leucovorin; High-dose Methotrexate; Acute Lymphatic Leukemia

INTRODUCTION

Leucovorin (LCV) acts as an essential coenzyme for nucleic acid synthesis and also it is an active metabolite of folic acid. LCV is used to selectively "rescue" the cells from the adverse effects caused by methotrexate (MTX)blocks the activation of folic acid and inhibits nucleic acid synthesis.[1] LCV is folic acid in its reduced form (active), where nucleic acid synthesis is continued in the presence of MTX. LCV competes with MTX for the same transport processes into the cell. LCV should be administered 24 h after dose of MTX so that it does not intrude with the therapeutic effects of MTX.[2] High-dose MTX (HDMTX) shows continued effectiveness in the treatment of childhood acute lymphatic leukemia (ALL) osteosarcoma and brain tumors. Higher doses are often more effective than lower doses. The use of ''too large'' rescue doses of folinic acid (LCV, itrovorum factor) after HDMTX has been blamed for rescuing malignant cells and negating the MTX chemotherapy effect.[3] LCV rescue has been a cornerstone of HDMTX treatment. LCV is particularly effective in the prevention of myelosuppression, gastrointestinal toxicity, and neurotoxicity during treatment with HDMTX.[4]

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CASE REPORT

A 2-years-old female child was diagnosed to have ALL. On chemotherapy with pediatric berlin-frankfurt-munster protocol. Completed induction phase 1 and 2. She was admitted for consolidation with HDMTX 2 g/m^2.

First cycle with HDMTX injection LCV was started. After initiation of LCV (folinic acid) at 42 h, she was noted to have itching over forehead, but no rashes or features suggestive of anaphylaxis noted. Hence considering probable insect bite

reaction, further doses were administered. But over next 2 doses, she developed erythematous rashes over faces neck, back of trunk, both upper limbs with ptosis secondary lid edema. Ophthalmology consultation was given to rule out conjunctival involvement. On their evaluation showed both eyes allergic edema which is drug induced, they advised tear drops 1-1-1-1 in both eyes. Dermatology was consulted, they advised medications which was followed. Over 4 days with 4 hydrocortisone and injection pheneramine maleate, the lesion subsided. In view of LCV hypersensitivity, it was decided to defer further doses of HDMTX and follow the Capeazzi MTX protocol.

DISCUSSION

The literatures have reported very few cases of LCV hypersensitivity reactions. In our case, symptoms include erythematous rashes over faces neck, back of trunk, both upper limbs with ptosis secondary lid edema. LCV is reduced form of folic acid; the mechanism behind LCV is that it provides the cofactors which were blocked by MTX. LCV displaces MTX from the intracellular binding sites and actively competes with MTX for transport sites; thereby restores the active folate stores required for DNA/RNA synthesis. Successful rescue by LCV depends on rapid elimination of methotrexate by the kidneys, which requires aggressive pretreatment as well as posttreatment hydration and urinary alkalinization.[5] Hypersensitivity reaction to LCV has been previously reported in patients receiving treatment for colorectal cancer.[6,7] In this case report, LCV is used with HDMTX for the treatment of ALL after initiation of LCV patient develop anaphylactic reactions. The main highlight of our case report is that LCV hypersensitivity can be observed even in children and should be aware about this possible serious reaction when considering the drug.

CONCLUSION

In patients who have developed hypersensitivity reactions to LCV were extensively treated with this agent, although it is not commonly seen. Our case was also challenging as this patient was receiving combination of HDMTX and injection LCV among which injection LCV is more prone to cause hypersensitivity reactions. There is scarcity regarding the data[8] on the hypersensitivity reaction to LCV. Physicians need to be aware of such case.

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