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Ara-C SYDROME FOLLOWING LOW DOSE CYTARABINE INFUSION IN A CHILD TREATED FOR ACUTE MYELOID LEUKEMIA (AML)

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ABSTRACT

Cytarabine (Ara-C) syndrome is a rare condition characterized by acute febrile reaction, myalgia, bone pain and occasionally chest pain, maculopapular rash, conjuctivitis and malaise. This complication is mostly described with standard or high dose cytarabine infusion, and rarely following low dose cytarabine infusion. We report a case of 2 year old boy who developed cytarabin syndrome following low dose ara-C infusion as part of treatment for AML despite prior pre-medication with dexamethasone

KEYWORDS: Ara-C syndrome, Low dose cytarabine, Dexamethasone, acute myeloid leukemia.

INTRODUCTION

Cytarabine (Ara-C) syndrome is a rare clinical syndrome characterized by fever, myalgia, bone pain and occasionally chest pain, maculopapular rash, conjuctivitis and malaise.[1] It often occurs following high dose cytarabin infusion, and rarely with low dose infusion.[2] The exact mechanism is unclear; however pro-inflammatory cytokines (interleukin-6 (IL-6), IL-1, tumour necrosis factor α and interferon- α) are believed to play a role.[3] Cytarabine syndrome usually occurs 6-12 hours following drug administration and may occur following first exposure to the drug and has been associated with the concentration of the drug and infusion rate.[4] The reaction can be prevented by slower infusion rate and premedication with corticosteroids and antihistamines.[4] Our patient developed cytarabine syndrome approximately 26 hours of initiation of low dose cytarabine infusion during induction treatment for acute myeloid leukemia despite being on premedication with dexamethasone.

CASE REPORT

We present a 2 year old boy diagnosed with Acute Myeloid Leukemia on induction chemotherapy with cyatrabine 100/m^2/day IV infusion for 7 days and daunorubicine 40mg/m^2day for the first 3 days of treatment. The antiemetic regimen included ondansetron 2mg/dose IV 8 hourly and dexamethasone 2mg/dose IV 8 hourly all for seven days. On the third day of cytarabine infusion, patient developed fever, rigor, fast breathing and irritability about 40 minutes into the commencement of cytarabine infusion. Examination reveals febrile axillary temperature of 38.7^{o}C, shivering, and not pale, anicteric. Respiratory system reveals, tachypnea respiratory rate 50bpm, equal chest expansion and transmitted breath sound. Increase heart rate of 140bpm with normal 1st and 2nd heart sounds. No skin rash noted. Examinations of ears, nose, throat and abdomen were normal. Patient had stable vital signs prior to cytarabine infusion. Blood was drawn for complete blood count, malaria parasite test, blood culture, and urine analysis. Also chest radiograph was done. Infusion cytarabine was withheld. Intravenous hydrocortisone 50mg; acetaminophen was administered with resolution within 90 minutes of onset of symptoms. Complete blood count was essentially normal and malaria parasite and blood culture were negative. Chest radiograph was also normal. Cytarabine infusion was continued the following day, with dexamethasone dose adjusted to 4mg IV 8hourly. Patient completed chemotherapy successfully with no further recurrence of symptoms.

DISCUSSIONS

Cytarabine syndrome is rare complication usually following high dose Ara-C infusion. Our patient developed fever, respiratory distress and irritability approximately 26 hours of initiation of cytarabine infusion, which is consistent with previous reports where majority of children, develop fever within 36 hours of commencement of therapy.[3,7] Most reports in the literature described cytarabine syndrome to be associated with standard and high doses Ara-C infusions (1-3g/m^2).[3] In contrast, our patient developed this rare syndrome following low dose (100mg/m^2) cytarabine infusion and despite receiving adequate dose of dexamethasone. Similar reports of ara-C syndrome following low dose cytarabine infusion have been described by Powell,[4] and Jirasek et al.[5] The exact pathophysiological mechanism of cytarabine syndrome has not been fully understood however; it has been

shown that cytarabine administration is associated with consistent elevations of several pro-inflammatory cytokines in a temporal pattern strongly resembling that of cytokine release during systemic inflammatory response syndrome.[2,3,5] Though there is no standard therapy for cytabine syndrome, corticosteroid has been shown to play a role in its treatment and prevention.[4,5,6] Steroid have been known to have a multitude of immunosuppressive effects, therefore administration of corticosteroids during treatment with cytarabine may dampen the production and release of inflammatory cytokines that are likely responsible for the symptoms of cytarabine syndrome.[5] Our patient developed this syndrome despite being on adequate dose of dexamethasone (6mg IV daily). Previous reports of premedication failure have been associated with low dose dexamethasone administration, and rarely following optimal dexamethasone dose.[7,8] In an adult case reported by Jirasek et al,[5] an initial dexamethasone dose of 8mg PO daily used as premedication failed to prevent symptoms of cytarabine syndrome. A higher dose given subsequently prevented the recurrence of symptoms. The researchers postulated that, a high tumor burden might play a potential role in patient's failure to respond to optimal corticosteroids premedication regimens. Although the initial dexamethasone dose used (2mg IV three times daily) for our patient that failed to prevent symptoms of cytarabine syndrome was higher than dosage used as successful in previous adults reports.[4,5] It is possible that, there may be variability between different patients and children might require a higher corticosteroids dose for successful premedication.

CONCLUSION

Ara-C syndrome is possible complication of treatment with cytarabine even with low dose infusion despite corticosteroid premedication. Children may require high dose of corticosteroids to prevent the occurrence of this complication.

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