Delayed Methotrexate Excretion Due to Sequestration in a Thymic Cyst

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INTRODUCTION

High-Dose Methotrexate (HD-MTX) (Figure 1) is a folic acid antagonist that began as a treatment for acute lymphoblastic leukemia (ALL) and is now commonly used in the treatment of rheumatic diseases and many types of cancers (3). While this drug is extremely effective at inducing remission, it has many side effects due to its toxic potential. For this reason, it is important that HD-MTX levels are continuously monitored while administering this medication. The normal timeframe for HD-MTX clearance is 2-3 days. In most patients, the levels should decline as the kidneys filter the medicine from the blood; however, in rare cases, impaired excretion can lead to prolonged duration within a patient causing serious toxic side effects.

HD-MTX has been reported multiple times to accumulate in "physiological third spaces", for example pleural effusions or ascites (2). It is standard practice for adult and pediatric oncologists to closely monitor renal function and clearance levels in patients with physiological third space fluid accumulation (6). In even scarcer instances, HD-MTX has been reported to be sequestered within adults in cysts in the ovaries and the liver which led to severe local and systemic toxicity (2,4).

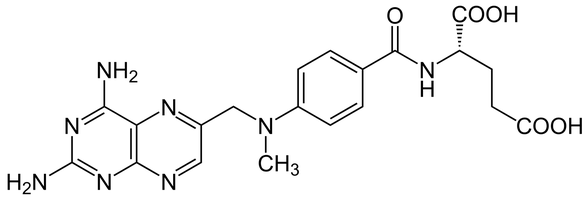

Figure 1. Methotrexate chemical formula.

CASE PRESENTATION

A 16-year-old female patient with a history of Li-Fraumeni syndrome with presentations of cancer types began treatment at Cook Children's Medical Center (CCMC) with HD-MTX for osteosarcoma in early 2019. Her renal values were within normal limits. During this instance of chemotherapy, she endured delayed clearance of MTX. It took her approximately 7.00 days for her to clear the drug from her system (Figure 2). Over the next two months, her clearances for HD-MTX were 5.95 days and 7.08 days.

Six weeks later, the patient presented to the clinic for chest pain that was unrelated to her chemotherapy treatment. Upon evaluation, a CT angiogram scan revealed an elongated cystic structure in the superior mediastinum (Figure 3). This cyst had been noted in 2014 but at that time it was decided to be a benign thymic cyst.

Because of the intense pain and pressure sensations causing discomfort to the patient, it was surgically resected. The pathology report of the cyst showed that there was inflammation, including cholesterol clefts found, but it was not neoplastic.

At the patient's next two scheduled HD-MTX treatments for osteosarcoma 10- and 11-weeks post-diagnosis without delay in 2.66 and 2.93 days, respectively.

However, two weeks later, the patient presented to the Emergency Department at CCMC for migrating numbness of the upper and lower extremities, blurred vision, and slurred speech. These symptoms were consistent with MTX toxicity. The patient was treated symptomatically and released home.

Six months after her initial treatment, the patient was treated with HD-MTX and had prolonged sequestration of the drug once again. Upon further testing, it was found that she now had impaired renal clearance. The patient was administered carboxypeptidase G2 and responded well.

CASE PRESENTATION (cont.)

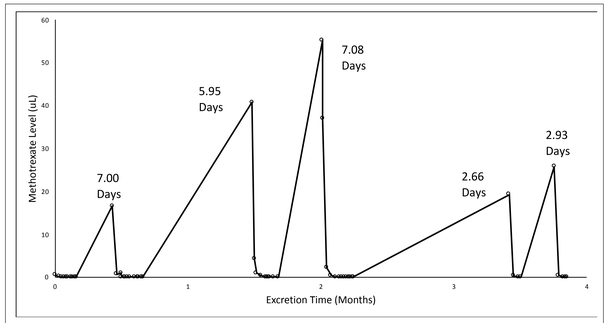

Figure 2. Methotrexate Clearance Times After Initial Treatment Dose Before and After Cyst Resection.

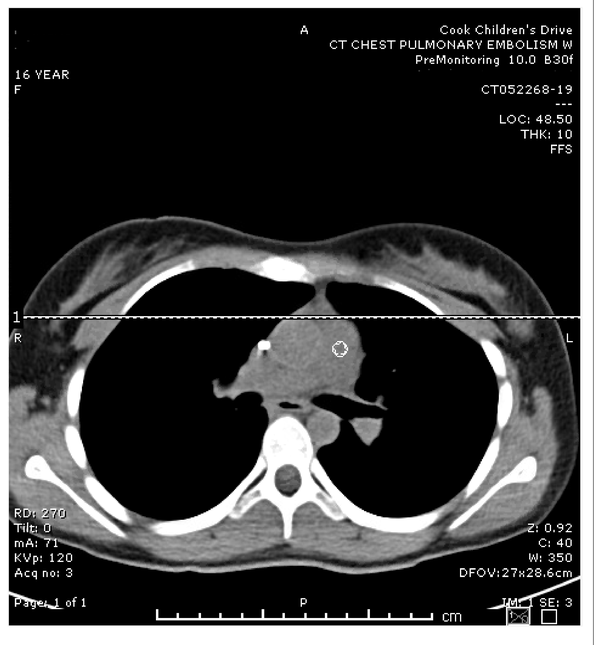

Figure 3. CT Scan of chest (3/19) showing large thymic cyst.

CONCLUSION

The importance of this case study brings to light an incidence of MTX sequestration within a pre-existing cyst and the need for radiographic evaluation during prolonged methotrexate toxicity in chemotherapy patients.

One of the most important highlights in this case is the fact that the prolonged exposure to MTX potentially led to impaired renal function which increases the likelihood for MTX toxicity in the future.

There are many negative implications associated with MTX toxicity such as impaired patient quality of life, prolonged chemotherapy treatments, and increased cost to patients due to additional hospitalizations (8,9).

To prevent this instance from occurring in the future, it would be prudent to image all patients with potential physiological third spaces and a documented history of cysts or cystic diseases, specifically for pediatric patients whose renal function can be significantly impaired (7).

If there is any evidence of prolonged methotrexate in a pediatric patient, using leucovorin and carboxypeptidase G2 to ensure proper clearance and rescue of renal function is essential (1,10).

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To the patient of this, and all, case studies, your contributions to the advancement of medicine have led to the greatest discoveries.