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RESEARCH ARTICLE

MYOCARDIAL INFARCTION UNDER METHOTREXATE IN A PATIENT WITH LOW RISK GESTATIONAL TROPHO BLASTIC NEOPLASIA: A CASE REPORT

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Abstract

Background: Methotrexate, an antifolateantimetabolite, finds extensive application in the field of oncology as well as for managingvariousautoimmunediseases. It isconsidered as backbone treatment for bothlow and high risk, trophoblasticgestationalneoplasia, as mono therapy or in combination withothercytotoxic agents.Whileitisconsideredcardioprotective, datas regardingmethotrexate-inducedcardiomyopathy are rare. we report the case of a woman, initiallydiagnosedwithlow-risk trophoblasticgestationalneoplasia, whosuffered a myocardial infraction after the second course of methotrexate.

Case Presentation:A 47-year-old woman, with no othercomorbidities, wasinitiallydiagnosedwith a low-risktrophoblasticgestationalneoplasia, characterized by a Bhcg value of 12,022. Shewasundergoingmethotrexatemonotherapy for the condition. Following the second course of chemotherapy, the patient experiencedchest pain, and an electrocardiogramrevealed an elevation of the ST segment. As a result, thrombolytictreatmentwasadministered at H9 of pain onset.Due to the uncertaintysurrounding the relationbetween Methotrexate and the myocardialinfarction and consideringpotential interactions betweennonsteroidal anti-inflammatorydrugs (NSAIDs) and methotrexate, a decisionwas made to switch to Actinomycin D.The evolutionwas favorable, the patient isstillunder surveillance aftertwoyears of follow up.

Conclusion: This case report highlights a possible methotrexateinducedmyocardial infraction. Inthis setting our attitude was to switch for anotherdrug, whichwasverywelltolerated, withgood oncologicincome for our patient.

Introduction:-

Methotrexate (MTX) is an antifolateantimetabolitecommonlyprescribed in oncology, as well as rheumatology conditions like rheumatoidpolyarthritis and otherchronicinflammatorydiseases . By inhibiting dihydrofolate reductase and acting as a false substrate, MTX interfereswith DNA synthesis, specificallyinhibiting purine and pyrimidine synthesis(1).

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It isconsidered backbone treatment for GestationalTrophoblasticNeoplasia, either as monotherapy (lowrisk GTN),(2) or in combination withothercytotoxicdurgs (high risk GTN)(3).

However, MTX isalsoassociatedwithvarioustoxicities, includingnausea, vomiting, diarrhea, myelosuppression, pancytopenia, liverdysfunction, acute renalfailure, pulmonarysymptoms, mucositis, stomatitis, gastrointestinal system ulceration/erosion, and cutaneousulcerations. In general, MTX isbelieved to have cardioprotective effects(4), and occurrences of MTX-inducedcardiomyopathy are extremely rare, typicallyinvolving high doses or dosingerrors(5).

This case report highlights a possible methotrexateinducedmyocardial infraction, in a patient diagnosedwithlowrisk GTN.

Case Description:
47 years old women, with no other relevant comorbidities, wasinitiallydiagnosedwith a lowrisk GTN, with an initial BhCG value of 12022. Initial work up showed a uterine mass invading the cervix, withlungmetastasis.

Due to the classification of the tumor as low-risk GTN, the patient wasstarted on methotrexatemonotherapy as a treatment. However, after the second round of chemotherapy, sheexperiencedchest pain. An electrocardiogram (ECG) wasconducted, showing an elevation in the ST segment. Consequently, a thrombolytictreatmentwasadministered. Following this, a coronaryangiographywasperformed, revealing no significantcoronarydisease.

A report to pharmacovigilance was made, and a literaturesearchdid not establish a linkbetweenmethotrexate and myocardialinfarction. However, this association could not becompletelyruled out as the patient did not have high cardiovascularrisk.

Therefore, and due to the potential interaction betweenmethotrexate and hercardiactreatment, the decisionwas made to switch to a new drug, Actinomycin D.

The patientevolutionwas favorable, withnegativation ofBhCGlevelsafter 5 courses of treatment. The diseaseremainswellcontrolledafter 3 yearssince the cessation of treatment.

Discussion:-

Therapeutic use of MTX (methotrexate) hinders the body'sability to use folicacid by inhibiting dihydrofolate reductase, leading to the inhibition of DNA synthesis, repair, and cellular replication, ultimatelyresulting in celldeath. The organsmostcommonlyaffected by MTX toxicityinclude the bonemarrow (causingleukoneutropenia and thrombocytopenia), lungs (pneumonitis), kidneys (precipitation of MTX metabolites), brain (encephalopathy), and liver (hepatitis to fulminant liverfailure).

Whenitcomes to cardiaceffect, severalclinical trials have demonstratedthat MTX (methotrexate) islinked to enhancedendothelialfunction, a slower progression of atherosclerosis, reducedrisk of major cardiovascular adverse events, and improvedcardiovascularsurvival(4,6). The favorable cardiovascular reffects of MTX, although not fullycomprehended, are attributed to itsantiproliferative, immunosuppressive, anti-inflammatory, and antiatherogenicproperties.

In contrast to thesefindings, twoprevious case reports have suggested a potentiallinkbetweenmethotrexate and cardiomyopathy. The first case describesleftheartfailure in a patient takingmethotrexate, afteraccidentallymistakingherprescribed dose of 5 mg/week for 5 mg/day(5). In the second case, a patient undermethotrexatetreatmentexperiencedheartfailure but laterrecoveredafterreceivingLeucovorin injection(7).

On the other hand, our patient wasprescribed a treatmentthatincludedPPIs (Proton PumpInhibitors) and NSAIDs (Nonsteroidal Anti-InflammatoryDrugs), both of whichmayinteractwithmethotrexate and potentiallyincreaseitstoxicity(8)(9).

Conclusion:-

Considering the potential association of methotrexatewith the occurrence of myocardialinfarction, as well as its possible interactions withotherdrugs, Actinomycin D emerged as a suitable and well-tolerated alternative treatment. The patient respondedpositively to thistreatment, achievingcompletedisease control, and remainsunder control threeyearsaftercompleting the treatment.

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