DETERMINATION OF GENETIC POLYMORPHISMS IN THE DIHYDROPYRIMIDINE DEHYDROGENASE GENE IN A PATIENT WITH GASTRIC ADENOCARCINOMA TREATED WITH FLUOROPYRIMIDINES: A CASE REPORT

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BACKGROUND AND IMPORTANCE

Fluoropyrimidines are a foundational component of chemotherapy for solid tumour malignancies. The best-known cause of intolerance to fluoropyrimidines is dihydropyrimidine dehydrogenase enzyme (DPD) deficiency, which can result from deleterious polymorphisms in the gene encoding DPD (DPYD). Partial or total deficiency of this enzyme is related to severe toxicity and in some cases it can cause the death of the patient.

AIM AND OBJECTIVES

To determine polymorphisms in the DPYD gene in a patient with gastric adenocarcinoma treated with fluoropyrimidines in order to avoid overexposure and toxicity associated to these drugs.

MATERIAL AND METHODS

1. A 66-year-old man was diagnosed with stage III gastric tubular adenocarcinoma
2. Treatment plan → four cycles of neoadjuvant chemotherapy with the FLOT protocol: docetaxel 50 mg/m² + calcium folinate 200 mg/m² + oxaliplatin 85 mg/m² + 5-FU 2600 mg/m² as a 24-hour intravenous infusion, every 14 days; followed by surgical intervention
3. Before starting the chemotherapy regimen, determination of DPD deficiency was requested

RESULTS

The results showed mutation c. 1236 G/A (HapB3) for the DPYD gene, which indicated overexposure to fluoropyrimidines and increased toxicity like diarrhea, mucositis, neutropenia and neurotoxicity. Due to the polymorphism detected in DPYD gene, a 5-fluorouracil dose adjustment was required.

The patient received four cycles of chemotherapy from April to June 2021 according to the dose recommendations of the oncology pharmacist. Treatment was started with a 50% dose reduction of 5-fluorouracil. After first infusion, it was well tolerated with few reported adverse side effects such as low-grade fever, xerostomia and neutropenia. Neutropenia was successfully treated with granulocyte colony stimulating factors and the patient was able to continue the treatment, increasing the 5-fluorouracil dose by 25% in the last two cycles. Despite excellent tolerance to chemotherapy, the patient died after gastrectomy due to post-surgical complications.

CONCLUSION AND RELEVANCE

Genetic analysis for the determination of polymorphisms in the DPYD gene allows us to predict the potentially serious toxicity of fluoropyrimidines, encouraging the individualised use of these drugs. In our case, the patient was at risk of developing severe toxicity so a dose adjustment of 5-fluorouracil was required.