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The Implementation of a PIPAC (Pressurized Intraperitoneal Aerosol Chemotherapy) Program in Portugal

A Implementação de um Programa de PIPAC (Quimioterapia em Aerossol Intraperitoneal Pressurizada) em Portugal

Keywords: Aerosols/administration & dosage; Antineoplastic Agents/administration & dosage; Hyperthermic Intraperitoneal Chemothe-rapy; Peritoneal Neoplasms/drug therapy
Palavras-chave: Aerossóis/administração e dosagem; Antineoplásicas/administração e dosagem; Neoplasias Peritoneais/tratamento farmacológico; Quimioterapia Intraperitoneal Hipertérmica

Dear Editor,

Last June, Centro Hospitalar Universitário de São João started a pressurized intraperitoneal aerosol chemotherapy (PIPAC) program, having treated three patients until now.

Despite all the therapeutic advances in oncology, with remarkable survival improvements in different cancers, peritoneal metastasis (PM) continues to be a challenging field with no efficient therapeutic options, other than for a few patients with limited disease that can be candidates for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC). However, the majority will have extensive disease that prevents this strategy.[1]

A theory that tries to explain the poor prognosis and the lack of a valid therapeutic option for PM is called the 'plasma-peritoneal barrier'.[2] This phenomenon is similar to the blood–brain barrier, in which the diffusion of systemic drugs is limited. In 2011, Marc Reymond described an experimental treatment with an optimized technology for the peritoneal delivery of aerosolized chemotherapy.[3] It allows to overcome the limitation of systemic chemotherapy in terms of the drug distribution and poor penetration into peritoneal nodules, but also to improve the delivery of peritoneal chemotherapy compared to HIPEC. A PIPAC treatment consists usually of three sessions across a six-eight-week period. However, in patients with good response, the number of sessions can be extended.[1]

Due to the selection bias and lack of randomized trials, it is impossible to properly appraise the survival benefits of this approach. However, the results have been encouraging, with an objective tumor response according to the histological Peritoneal Regression Grading Score of around 70%[4] and, in some patients, with a reduction in PM that allows subsequent cytoreduction surgery and HIPEC.[1] The research around PIPAC has been focusing on optimizing the procedure as well as treatment regimen/doses to allow the development of clinical trials.

Even though the two surgeons involved in this program took part in the Scandinavian PIPAC Workshop in 2018 and 2019, the pandemic situation prevented this from happening until now. We are very pleased to have this treatment option now available for selected patients with PM from different cancers. In Denmark, all PIPAC procedures are centralized in one center, and we agree that a similar strategy should also be employed in Portugal, to allow the accrual of crucial knowledge and expertise about this treatment. We are collaborating with other PIPAC centers around the world[5] and have a dedicated multidisciplinary team to evaluate candidate patients referred to our center for this new treatment approach.

AUTHOR CONTRIBUTIONS

TBM: Conception of the original idea; writing of the manuscript.

MA, SM, MG, EB: Revision of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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Síndrome do Linfócito Passageiro Após Transplante Hepático: Uma Entidade Causadora de Anemia Hemolítica

Passenger Lymphocyte Syndrome After Liver Transplantation: A Cause of Hemolytic Anemia

Palavras-chave: Anemia Hemolítica/etiologia; Sistema de Grupo Sanguíneo ABO; Transplante de Fígado/efeitos adversos
Keywords: ABO Blood-Group System; Anemia, Hemolytic/etiology; Liver Transplantation/adverse effects

A anemia é comum em qualquer pós-operatório. Em particular no pós-transplante, há que lembrar diagnósticos diferenciais. As causas mais comuns são, até à segunda semana, a hemorragia, sépsis e complicações locais (trombose da artéria hepática ou das veias cava inferior/hepática/porta e vias biliares); entre a segunda e a sexta semana, a anemia aplástica, infeções por citomegalovírus (CMV) ou parvovírus e doença do enxerto contra o hospedeiro (DECH); após as seis semanas, as causas mais comuns são défices vitamínicos, doença linfoproliferativa pós-transplante e multifatorialidade.[1,2] Os fármacos recomendados são agentes tempo-independente, sendo de salientar imunossupressores como o tacrolimus, que está associado à anemia hemolítica microangiopática.[1,2] À semelhança do que acontece em doentes não transplantados, esta última pode ser também secundária a infeções ou imunomediada.[1,2] A etiologia hemolítica ocorre entre o terceiro e o 24.º dia sendo habitualmente auto-limitada, mas podendo evoluir de forma fatal.[1,2]

O caso clínico de síndrome do linfócito passageiro (SLP) após transplante hepático que espelhamos na Fig. 1 motivou a reflexão sobre esta entidade.

Dada a lista de espera para transplante hepático *versus* o número de órgãos disponíveis, o transplante hepático é por vezes realizado com incompatibilidade ABO *minor*, nomeadamente no caso de dador vivo, falência hepática aguda, doentes do tipo AB ou retransplantes urgentes.[3-5] Nestes casos, a SLP é um tipo de DECH relativamente comum e tende a ser subdiagnosticada, pois não é observada frequentemente por clínicos não dedicados à transplantação. Os doentes nesta situação acabam por recorrer, naturalmente, a qualquer unidade de cuidados de saúde, sendo importante que todos os médicos tenham conhecimento desta síndrome. A SLP ocorre por incompatibilidade ABO *minor*, em que os linfócitos B do dador produzem anticorpos contra os antigénios dos eritrócitos do hospedeiro, levando à sua *lise*.[3,5] A SLP é mais frequente nos transplantes de coração e pulmão (70%), fígado (40%) e rim (17%) respetivamente, dada a maior quantidade de tecido linfoide transplantado.[3-5]

O tratamento é de suporte com transfusão de sangue