The positron emission tomography in diagnosis of abdominal sepsis

A tomografia por emissão de pósitrons no diagnóstico da sepse abdominal

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ABSTRACT

Purpose: In the perioperative phase, sepsis is associated with high morbidity and mortality and is the most important problem for the surgeon. Critically ill patients profit from an early identification and implementation of an interdisciplinary diagnostic and therapy. The purpose of this review on septic peritonitis is to give an update on the diagnosis by the use of image examination, mainly Fluor18-FDG pet scan**. Methods:** The literature for this review was collected with PubMed and SciElo search using the combination of “FDG,” “peritonitis” “sepsis,” and the specific terms for sepsis. **Results**: Rapid diagnosis for sepsis is essential for patient´s survival. A bundle of studies was performed on early recognition and on new diagnostic tools for abdominal sepsis. Although surgical intervention is considered as an essential therapeutic step in abdominal sepsis therapy, the time-point of diagnostic and source control is still controversially discussed in the literature. **Conclusion:** Despite many efforts, mortality of abdominal septic patients remains unacceptably high, the early diagnosis of sepsis is challenging for health care providers, and high performance methods of radiographic imaging like positron emission tomography scan can be helpful in some cases. Their diagnostic impact has to be evaluated in future studies.

Key words: Peritonitis. Sepsis. Diagnosis. Fluor18-FDG. PET scan.

RESUMO

Objetivo: Na fase perioperatória, a sepse está associada com alta morbidade e mortalidade, sendo um dos problemas mais importantes para o cirurgião. Doentes criticamente enfermos são beneficiados com diagnóstico e terapia

interdisciplinar precoces. O objetivo desta revisão em peritonite séptica é fazer uma atualização sobre o diagnóstico através da utilização de exames de imagem, especificamente Fluor18-FDG PET scan. **Métodos:** Para esta revisão os artigos foram coletados em pesquisa pelo PubMed e SciELO, utilizando a combinação de "FDG", "peritonite" "sepse", e os termos específicos para sepse. **Resultados:** Foi detectado na análise da literatura que o diagnóstico rápido de sepse é essencial para a sobrevivência do paciente. Alguns estudos abordaram a importância do reconhecimento precoce utilizando novas ferramentas de diagnóstico para sepse abdominal. Embora a intervenção cirúrgica seja considerada como um passo essencial na terapia da sepse abdominal, o melhor meio de diagnóstico por imagem é ainda controverso na literatura, despontando o PET como uma ferramenta nova e promissora. **Conclusão:** Apesar de muitos esforços, a mortalidade de pacientes com sepse abdominal permanece inaceitavelmente elevada. O diagnóstico precoce da sepse é um desafio para os prestadores de cuidados de saúde, e os métodos de alto desempenho de imagens radiográficas, como tomografia por emissão de pósitrons pode ser útil em alguns casos. Seu impacto no diagnóstico tem de ser avaliado em estudos futuros.

Descritores: Peritonite. Sepse. Diagnóstico. Fluor18-FDG. PET**.**

INTRODUCTION

This review provides an overview of the use of FDG-PET in sepsis, infectious and inflammatory diseases, not only in the setting of diagnosis but also in the evaluation of treatment efficacy. For some cases of sepsis, infections and inflammations, scientific evidence indicates that FDG-PET/CT is useful for diagnosis and for therapy evaluation. For other diseases, such as peritonitis, autoimmune pancreatitis, osteomyelitis, prosthetic joint infection, and fungal infections, a strong evidence is lacking. In any case where FDG can be used for therapy follow up, a pre-therapy scan is of relevance to compare it with the post therapy scan. It is a repeating problem in nuclear medicine that no large patient studies are available in the literature to give final answers. The aim of this review is to discuss the importance of FDG-PET in diagnosis of peritonitis and identification of isolated focus in peritoneal cavity.

METHODS

The literature for this review was collected with PubMed and SciElo database search using the combination of “FDG,” “peritonitis”, “sepsis,” and specific term for sepsis. The search included case reports with clinical importance, review articles, and reports of false-positive or false-negative PET results in inflammation, advantages and limitations of PET in acute and chronic infections, and the role of PET in differentiating pathological processes in patients with peritonitis and superimposed foci.

LITERATURE REVIEW

Although the terms peritonitis and abdominal sepsis are generally used to describe an intra-abdominal infection, which develops after the rupture of a hollow viscus, the true peritonitis definition includes both etiologies, infectious and not infeccious[1]. Peritonitis results in so-called systemic inflammatory response syndrome that occurs in sepsis, such as an inflammatory response due to intra-abdominal infection. So, peritonitis should be synonymous with intra-abdominal sepsis, which ranges from simple abscess or generalized peritonitis. There has been a remarkable improvement in treatment outcome peritonitis, reducing mortality rates of 30 to 50% to 20% level, anyway considered too high[2,3]. Malangoni summarized the risk factors most often associated with peritonitis treatment failure[4]. These include malnutrition, highly compromised general condition, antibiotic-resistant bacteria, fever, leukocytosis, multiple organ failure, advanced age and delay in diagnosis and treatment.

The signs and symptoms of peritonitis can be supported by laboratory data, including leukocytosis, C-reactive protein increased, calcitonin and radiological findings, such as air under the diaphragm or localized fluid collections and visual examinations of images[5-8].

The plain abdominal radiography is able to detect a reasonable number of radiological signs that may suggest septic foci and ultrasound allows the opportunity to perform in certain cases the diagnosis and drainage of abdominal

purulent collections guided by ultrasound. It has shown high rates of sensitivity for the diagnosis for patients with secondary and post-operative peritonitis[9]. Other methods of radiographic images, such as computed tomography (CT) and positron emission tomography (PET) have proven useful in many cases. The diagnostic impact of PET needs to be evaluated in future studies, because little is known about its use in the diagnosis of peritonitis.

The positron emission tomography (PET) provides an important imaging, which can provide information about the anatomy, physiology and pathology. It is increasingly used to image cancer, infection and/or inflammatory diseases; for example, it has shown promising results in patients with unknown fever[10] source and gained much popularity for the identification of inflammatory foci in soft tissues, bone and vascular structures[11,12]. In the PET technique is used the radioisotope fluorine-18 fluorodeoxyglucose (18F-FDG). Its capability to localize disease allows precise differentiation between infection on rigid structures like bone and soft tissues[12]. Thus, 18F-FDG-PET can be gold standard in infectious disorders, focal and generalized inflammation, especially those in which the PET has had a significant impact.

Malignant cells have enhanced glycolysis because of the high content of glucose transport proteins or increased activity of hexoquinase[13,14]. The same principle applies to infection and inflammation. The following mechanisms play an important role: (1) the inflammatory reaction cascade in response to a stimulus, which results in increased glicolisis[15]; (2) increasing the number of glucose transporters in cells; and (3) greater affinity of glucose transporters for FDG[16-18]. Glucose transporters type 1 to type 7 mediate glucose and FDG transport to the cells. Inside the cell, the carriers are located in the plasma membrane and intracellular vesicles. After stimulation, occurs translocation of transporters to the cell membrane. Lymphocytes demonstrate this transport effect within 30 minutes after estimulation[19], which explains the utility of 18F-FDG PET in early diagnosis of inflammation and infection, and the attractiveness of this imaging exam modality for diagnosis of infectious foci.

18-FDG PET has certain advantages over other types of morphological image: (1) it detects the metabolic activity at the cellular level and is independent of non-specific signals such as edema or increased perfusion; (2) provides full-

body images in one session; and (3) it is not contraindicated in cases of metallic implants. Also, it uses low radiation dose and offers high spatial resolution and contrast[20]. The anatomical design of the precise location of the areas involved in the infection is a major challenge to which the 18F-FDG PET-CT, as a new technique in evolution, is a great promise. The ease of doing full body image, correct anatomical location, metabolic information and high spatial resolution, are some of the advantages offered by 18F-FDG PET compared to other techniques of nuclear medicine and conventional radiology. The 18F-FDG PET indication in the diagnosis of infectious processes are well established sarcoidosis, tuberculosis, osteomyelitis, endocarditis, vasculitis, vascular prosthesis infections and fever of obscure source[20]. The role of the method under discussion is in fungal infections, asbestosis, pericarditis and central nervous system infections. The purpose and PET potential advantage is able to detect the infection before tissue necrosis and set abscess formation. Specifically in cases of peritonitis and septic foci in the peritoneal cavity, there are few studies and little is known about this[21-24].

The positron emission tomography (PET) is an image examination of high-cost, but it has been extremely useful for accurate diagnosis of cancer and the monitoring of their tratament[25,26]. PET is an imaging technique using positron emitting radionuclide tracers, predominantly 18F-fluorodeoxyglucose (18FDG), which allows a non-invasive assessment of metabolic and physiological activities in healthy and diseased states at a molecular and celular level[27]. This tracer can switch to glycolytic activity that is high in cancer, inflammation and infection[28].

In addition to the PET in cardiology applications, another application is the role of PET in the diagnosis of cardiovascular infections. Although 18FDG-PET was useful in the evaluation of infection, the value of this approach for the diagnosis of myocardial infection seems limited. PET/CT has been used in the diagnosis of various inflammatory and infectious diseases involving cardiovascular[29,30], musculoskeletal system, etc[31]. However, with regard to its use for the diagnosis of infectious foci in cases of peritonitis, published reports are scarce.

However, the use of nuclear medicine to characterize and diagnose infectious and inflammatory diseases is rapidly increasing. Several SPECT and

PET radiopharmaceuticals have been developed and applied in this field, radiolabelled white blood cells being the centerpiece[32]. However, [18F]-FDG-PET combined with low dose or diagnostic computed tomography (CT) is gaining interest in the diagnosis of many infectious and inflammatory diseases and is already the gold standard for some indications. The accumulation of FDGin inflammatory and infectious diseases is based on the high uptake in activated granulocytes. This accumulation is based on the fact that these cells use glucose as an energy source only after activation during the metabolic burst. Transport of FDG across the cellular membrane is mediated by the glucose transporter proteins, which are also to a higher amount present on the cell membrane of inflammatory and infectious cells[33]. Despite this lack of studies about this issue, we think that FDG-PET/CT is not only valuable for therapy monitoring in some infectious and inflammatory diseases but could even play a pivotal role in their management, leading to better drug dosage, proof of the usefulness of the treatment, and early modification of the therapeutic strategy.

In conclusion, despite many efforts, mortality of abdominal septic patients remains unacceptably high. The early diagnosis of sepsis is challenging for health care providers, and high performance methods of radiographic imaging like positron emission tomography scan can be helpful in some cases. Their diagnostic impact has to be evaluated in future studies.

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