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Original article

Reliability of white blood cell scan in the follow-up of osteomyelitis

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Abstract

Introduction: The question of whether antibiotic treatment does or does not affect reliability of white blood cell scan (WBCS) to detect disease activity in clinical practice is still unanswered. Our aim was to study the relationship between scintigraphic findings of WBCS and antibiotic therapy in a group of patients affected with osteomyelitis (OM).
Methods: We retrospectively reviewed 57 scans, performed in 18 patients affected by OM and who were on antibiotic treatment. The number of therapy weeks was calculated for each antibiotic. A comparison of results obtained during and after discontinuation of the antibiotic treatment was made. Overall sensitivity, specificity and accuracy of WBCS were calculated and compared with those obtained in patients undergoing therapy.
Results: Forty-seven scans were performed during treatment and 10 scans after discontinuation of treatment. The scintigraphic results obtained during and after discontinuation of treatment were as follows: TN 14 and 8, TP 31 and 2, FN 2 and 0, FP 0 and 0, respectively. Sensitivity, specificity and accuracy of WBCS, calculated in all patients, were 94.3%, 100% and 96.5% respectively. In patients receiving antibiotic therapy, the same parameters were 93.9%, 100% and 95.7% respectively. In patients treated with antibiotics that can decrease leukocyte function, there were 10 TN, 14 TP, 2 FN and 0 FP, while in patients treated with antibiotics that have not effect on leukocyte function there were 4 TN, 17 TP, 0 FN and 0 FP.
Conclusion: The reliability of WBCS in the detection of disease activity during antibiotic treatment does not change significantly. It can be assumed that the influence of antibiotic therapy on labelled leukocyte behaviour is negligible.

Keywords: Osteomyelitis; Follow-up; Antibiotic therapy; Labelled leukocytes scintigraphy

1. Introduction

It is well known that ^{99m}Tc-HMPAO-labelled leukocyte scan (WBCS) is a useful tool in the diagnosis of osteomyelitis (OM) [1–20]. However, the more relevant problem of follow-up of the disease has not been resolved, and the need for a diagnostic method capable of monitoring the response to medical or surgical treatment may play a significant role in clinical practice. Unfortunately, only limited data is available on the reliability of WBCS in the follow-up of OM [2,4,16,18]. This is probably due to the difficulty to find an absolute gold standard for assessing the clinical outcome, the difficulty of matching scintigraphic findings with microbiological results and the inevitable need for a very long follow-up period. In addition, there is also the question whether antibiotic treatment has any affect on the reliability of WBCS to assess disease activity. The present study is a retrospective analysis of the relationship between scintigraphic findings, treatment and clinical outcome of OM

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aimed at assessing the usefulness of WBCS in the follow-up of the disease.

2. Materials and methods

Fifty-seven scans, performed in 18 consecutive (14 male, 4 female) patients affected by OM and receiving medical and/or surgical treatment, were taken into account. The mean age of the patients was 45.4 years (range 17 to 79 years). Potential predisposing factors to OM included diabetes, age >70 years, drug abuse, multiple myeloma and Berger's nephropathy (6 patients = 33.3%).

The diagnoses of haematogenous OM (3 patients) or OM in association with an orthopaedic device (15 cases) was obtained on the basis of clinical, instrumental and, when available, microbiological findings. Bone segments involved were tibia (7), femur (6), patella (1), mandible (1), tarsus (1), acetabulum (1), metacarpus (1). The number of scans performed on the 18 patients was as follows: 3 scans in 11 patients, 2 scans in 4 patients, 7 scans in 1 patient, 5 scans in 1 patient and 4 scan in 1 patient.

The leukocytes were labelled with ^{99m}Tc-HMPAO using standard methods [20]. A sample of labelled leukocytes was submitted to trypan-blue test to assess the viability of the labelled cells. The mean injected activity was 340 MBq (range: 260–390) and the mean administered dose was 4.76 mSv (range 3.64–5.46). Scintigraphic studies were performed using a large-field-of-view gamma camera (GE Millennium) equipped with a low energy all-purpose collimator. Static acquisitions of involved bone segments were performed at 20 min, 4 h and 20 h after injection in two different views depending on the studied bone segment. The scintigraphic images were reviewed by two nuclear medicine specialists making a comparison between the acquisitions at various times by the following evaluation criteria:

(1) When the scans showed significant change in leukocyte distribution between 20 min and/or 4-h images compared to the 20-h images, they were considered positive.
(2) The presence of areas of progressive leukocyte concentration in proportion to time, was also considered as sign of presence of disease.
(3) Scintigraphic examination not matching the above mentioned criteria were considered as negative. Only the scans judged as positive or negative by both specialists were finally accepted as being so.

All patients were submitted to initial treatment with the following antibiotic: patients no. 1 and no. 7 with teicoplanin for 10 and 6 weeks respectively; patients no. 2 and no. 6 with ciprofloxacin plus cefuroxime plus rifampicin for 12 and 4 weeks respectively; patients no. 5 and no. 9 with amoxicillin-clavulanic acid for 20 and 28 weeks respectively; patient no. 4 with ciprofloxacin plus cefuroxime for 24 weeks; patient no. 3 with vancomycin plus gentamicin plus teicoplanin plus fosfomycin for 39 weeks; patient no. 8 with teicoplanin plus rifampicin for 8 weeks; patient no. 10 with teicoplanin plus cefuroxime plus ciprofloxacin for 16 weeks; patient no. 11 with teicoplanin plus ciprofloxacin plus rifampicin for 8 weeks; patient no. 12 with ciprofloxacin plus amoxicillin-clavulanic acid for 36 weeks; patient no. 13 with ciprofloxacin plus teicoplanin for 13 weeks; patient no. 14 with teicoplanin plus co-trimoxazole plus rifampicin plus ciprofloxacin for 50, 24 and 24 weeks respectively; patient no. 15 with ampicillin plus amoxicillin-clavulanic acid for 70 weeks; patient no. 16 with ceftriaxone for 4 weeks; patient no. 17 with cefuroxime plus ciprofloxacin for 24 weeks; patient no. 18 with teicoplanin plus fosfomicin for 28 weeks.

Twelve patients (no. 1, no. 3, no. 4, no. 6, no. 7, no. 8, no. 10, no. 11, no. 13, no. 14, no. 15, no. 16) received a subsequent oral treatment with the following antibiotics: patients no. 14 and no. 16 with minocycline plus rifampicin for 120 and 12 weeks respectively; patient no. 1 with co-trimoxazole and minocycline for 18 and 10 weeks respectively; patient no. 3 with minocycline for 12 weeks; patient no. 4 with co-trimoxazole plus rifampicin for 8 weeks; patient no. 6 with ciprofloxacin plus rifampicin for 20 weeks; patient no. 7 with minocycline and rifampicin for 27 weeks; patient no. 8 with co-trimoxazole plus minocycline plus rifampicin for 12, 40 and 40 weeks respectively; patient no. 10 with cefuroxime plus ciprofloxacin plus rifampicin for 84, 120 and 36 weeks respectively; patient no. 11 with ciprofloxacin plus rifampicin for 24 weeks; patient no. 13 with minocycline plus rifampicin plus levofloxacin for 72 weeks; patient no. 15 with ciprofloxacin for 96 weeks.

The total number of therapy weeks was calculated for each antibiotic. On the basis of data available from the literature [13], concerning the interference "in vitro" of antibacterial agents with leukocyte functions, antibiotics were subdivided into two groups taking into account only the chemotaxis and cytokines release functions: (1) antibiotics potentially increasing or with no effect on chemotaxis and cytokines release functions; and (2) antibiotics decreasing chemotaxis and cytokines release functions. The number of therapy weeks for each group of antibiotic was calculated.

The clinical outcome was evaluated on the basis of a clinical follow-up ranging from 18 to 80 months (mean = 56).

In assessing reliability of scintigraphic results, the first scan (positive in all patients) was considered as true positive. The last scan, when negative, in cured patients was judged as true-negative while in relapsed (not cured) patients, it was considered false-negative. On the contrary, a positive last scan was considered as false-positive in cured patients and true-positive in relapsed patients. The reliability evaluation of other scintigraphic studies was performed according to the following criteria: (1) In cured patients a positive scan was considered true-positive if the last scan was negative and false-positive if the last scan was positive. In the same patients a negative scan was judged true-negative independently of the result of last scan; and (2) In patients who were not cured, a positive and a negative scan was considered true-positive and true-negative respectively, independently of the result of the last scan.

A comparison of results obtained during the treatment and after discontinuation of the treatment itself was done. Overall sensitivity, specificity and accuracy of WBCS in detecting OM