

Use of ^{99m}Tc -anti-TNF- α scintigraphy in a patient with non-radiographic axial spondyloarthritis

Dângelo José de Andrade Alexandre · Sergio Augusto Lopes de Souza ·
Clarissa Canella Moraes do Carmo · Bruno Schau · Lea Mirian Barbosa da Fonseca ·
Luis Roimicher · Bianca Gutflen

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Abstract The aim of this study was to describe the use of ^{99m}Tc -anti-TNF- α scintigraphy for detecting inflammation of the sacroiliac joints in a patient with non-radiographic axial spondyloarthritis. A 47-year-old female patient, non-smoker and non-drinker, complained of a low back pain inflammation, which began 4 years before her condition have exacerbated to morning stiffness and anterior uveitis in the last 6 months. Initially diagnosed as mechanical low back pain, she irregularly took non-steroidal anti-inflammatory drugs and corticosteroids, without significant long-lasting results. Radiographic findings were negative. There was increased uptake of ^{99m}Tc -anti-TNF- α in an area corresponding to the topography of ileum and sacroiliac right joint upon ^{99m}Tc -anti-TNF- α scintigraphy. Magnetic resonance imaging (MRI), the most used image diagnosis tool, showed minimum impregnation of gadolinium in the right sacroiliac joint and at the iliac face of the inferior

third of the right sacroiliac joint. We suggest that ^{99m}Tc -anti-TNF- α can facilitate early diagnosis of patients with non-radiographic axial spondyloarthritis. More studies are now ongoing.

Keywords Spondyloarthritis · Spondylitis · Radionuclide imaging · Biological marker · Sacroiliitis

Introduction

In recent years, drugs that inhibit tumor necrosis factor alpha (anti-TNF- α) have been reported to significantly alter the activity of the spondyloarthritis group of diseases. They do so by reducing pain, improving functional capability, increasing the mobility of the spine, and suppressing enthesitis and peripheral joints inflammations [1]. However, diagnosis of such diseases is often delayed and usually only occurs several years after the onset of the inflammatory

All authors equally contributed to this study.

D. J. de Andrade Alexandre
Instituto Nacional de Traumatologia e Ortopedia (Into),
Ministério da Saúde, Rio de Janeiro (RJ), Brazil

S. A. L. de Souza · L. M. B. da Fonseca · B. Gutflen
Laboratório de Marcação de Células e Moléculas (LMCM),
Departamento de Radiologia, Faculdade de Medicina,
Universidade Federal do Rio de Janeiro (UFRJ),
Rio de Janeiro (RJ), Brazil

C. C. Moraes do Carmo
Clínica de Diagnóstico por Imagem (CDPI), Rio de Janeiro (RJ),
Brazil

B. Schau
Serviço de Reumatologia, Hospital Federal dos Servidores do
Estado (HSE), Rio de Janeiro (RJ), Brazil

L. Roimicher
Departamento de Clínica Médica, Faculdade de Medicina,
Universidade Federal do Rio de Janeiro (UFRJ),
Rio de Janeiro (RJ), Brazil

B. Gutflen (✉)
Departamento de Radiologia, Sub-solo, Universidade Federal do
Rio de Janeiro, Hospital Universitário Clementino Fraga Filho,
Rua Professor Rodolpho Rocco 255, Ilha do Fundão,
Rio de Janeiro (RJ) CEP: 21941-913, Brazil
e-mail: bianca.gutflen@gmail.com

symptoms (up to 8.5 years for HLA B27 positive and 11.4 years for HLA B27 negative patients) [2]. Even the more common imaging tests used to diagnose and follow up rheumatic diseases, such as radiography and magnetic resonance imaging (MRI), present several limitations [3]. Compared with other imaging methods, the use of MRI is restricted by some patient-related circumstances like claustrophobia (especially in high-field whole body scanners), pacemakers, pregnancy in the first trimester and existing alloplastic implants causing metallic artifacts. Other important limitations are the need of a trained and experienced reader, the long examination time, the possible allergic reaction to contrast agents, the increased cost, lower availability worldwide and the fact that MRI is restricted to only make contrast enhanced imaging of one area that can fit in the scanner's field of view [4]. New tests to facilitate early diagnosis and follow-up of patients suffering from non-radiographic axial spondyloarthritis, which is considered the early stage of ankylosing spondylitis, are thus required. One approach with a new potential therapeutic has been the use of biomarkers reflective of a specific biological process. Identification of new compounds is becoming increasingly important because the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level, which are biomarkers commonly used to monitor inflammatory response, have poor sensitivity and specificity [5]. In the present study, we describe the use of scintigraphy using a fully human monoclonal anti-TNF- α antibody (Adalimumab) labeled with ^{99m}Tc for detecting inflammation of the sacroiliac joints in a patient with non-radiographic axial spondyloarthritis.

Case report

A 47-year-old female patient, non-smoker and non-drinker, complained of a low back inflammation, which began 4 years before her condition have exacerbated to morning stiffness and anterior uveitis in the last 6 months. Initially diagnosed as mechanical low back pain, she irregularly took non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, without significant long-lasting results. The findings of a functional evaluation by our research team were as follows: Bath Ankylosing Spondylitis Functional Index (BASFI): 7.7; visual analog scale (VAS) for pain: 7/10 for night pain in the spine and 6/10 for pain without a defined schedule scheme, both 1 week before scintigraphy; mobility of the spine assessed by chest expansion: 4.2 cm; modified Schober's test: 20 cm; occiput-wall distance: 5 cm; disease activity and its symptoms evaluated by erythrocyte sedimentation rate (ESR): 39 mm/h assessed by the Westergren method; C-reactive protein (CRP) level:

2.9 mg/dL; white blood cell count: 4,580 million/mm³; Bath Ankylosing Spondylitis Disease Activity Index (BASDAI): 8.3; and Ankylosing Spondylitis Disease Activity Score (ASDAS): 2.2; radiographic changes assessed by Bath Ankylosing Spondylitis Radiology Index (BASRI): 7; and radiographic examination of the sacroiliac joints: healthy joints or sacroiliitis grade zero, according to the New York criteria proposed in 1984; MRI of sacroiliac joints demonstrating contrast enhancement of the iliac surface of inferior third of right sacroiliac joint on T1-weighted images with fat saturation. Based on a previous experience in which we successfully labeled anti-CD3 [6], monoclonal human antibody anti-TNF- α (Abbott Laboratories, IL, USA) was labeled with Tc-99m using a direct method [7] yielding >95 % labeling efficiency and stability until 24 h. Scintigraphs were obtained 30 min after intravenous administration of the radiopharmaceutical. Whole-body, planar and SPECT ^{99m}Tc -anti-TNF- α images were obtained using a dual gamma camera (Millennium MG, Xeleris workstation, GE Medical Systems, Milwaukee, WI, USA) with a 15 % window centered at 140 keV with high resolution, parallel-whole collimators, showed an increased uptake of ^{99m}Tc -anti-TNF- α in an area corresponding to the topography of sacroiliac right joint. No HLA B27 was detected by polymerase chain reaction (PCR). Findings from the imaging tests are shown in Fig. 1.

This study was approved by the National Committee for Research Ethics (CONEP: 14576; NCT02134613). The patient signed the written informed consent to this case report.

Discussion

Based on this assessment, non-radiographic axial spondyloarthritis was diagnosed according to the Assessment of Spondyloarthritis International Society criteria [8]: low back pain of more than 3 months' duration, age of onset <45 years and sacroiliitis identified on MRI. Moreover, the patient had an elevated CRP level, inflammatory low back pain, and anterior uveitis. ^{99m}Tc -anti-TNF- α increased uptake by the sacroiliac joints suggested an active inflammation process, confirmed by laboratory findings. Based on our previous experience obtained with ^{99m}Tc -anti-TNF- α in the evaluation of patients with rheumatoid arthritis [7] we observed that images obtained within 30 min to 1 h after the administration of the radiopharmaceutical are better than those obtained after 3 h. Thus, in this study, we have chosen this period for imaging acquisition. The limited sensitivity of MRI for non-radiographic axial spondyloarthritis and ankylosing spondylitis (estimated at around 38–51 %) makes it challenging to evaluate young patients with suspected early

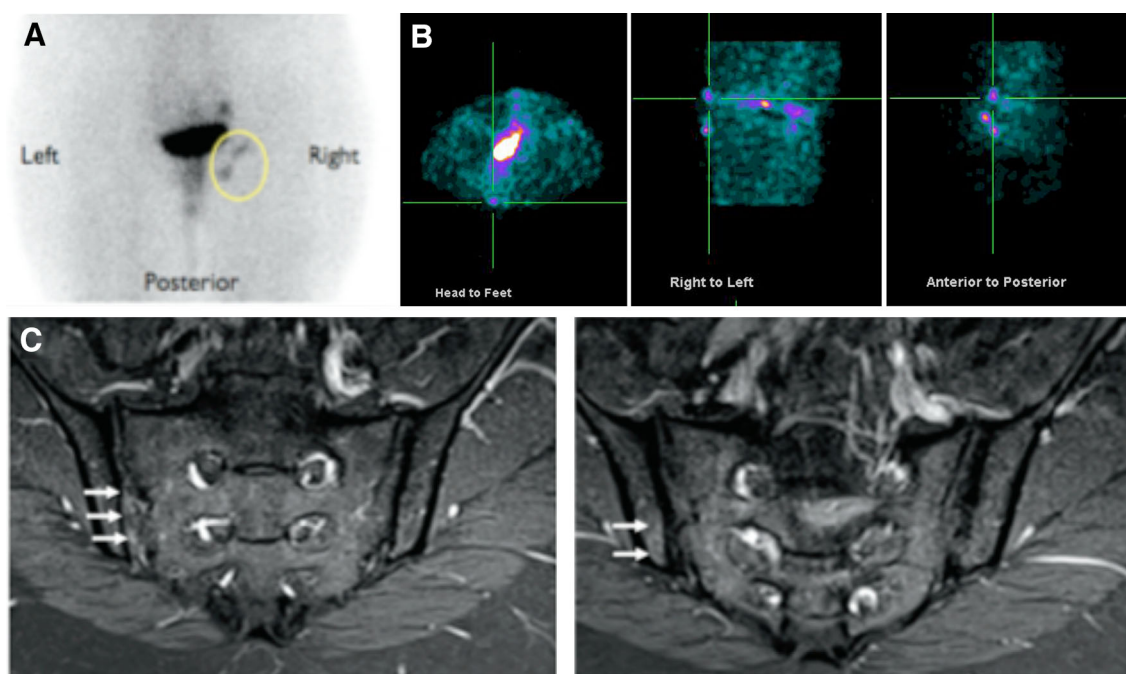


Fig. 1 ^{99m}Tc -anti-TNF- α scintigraphy. **a** Image of planar scintigraphy uptake of ^{99m}Tc -anti-TNF- α into the right sacroiliac joint (yellow circle). **b** SPECT images showing ^{99m}Tc -anti-TNF- α uptake in transversal, sagittal and coronal views (green triangulation). **c** MRI of

the sacroiliac joint showing minimum impregnation of gadolinium in the right interline sacroiliac joint and at the iliac face of the inferior third of the right sacroiliac joint (white arrows)

disorders who have normal pelvic radiographs and negative magnetic resonance findings relating to the sacroiliac joints [4]. Okumara et al. [8] have evaluated whether there is a correlation between the differences in joint uptake of 2-[18F]-fluoro-2-deoxy-D-glucose and the improvement of clinical findings in RA patients undergoing anti-TNF therapies with good results. Quantitative analysis of the sacroiliac joints by bone scintigraphy with ^{99m}Tc -MDP is limited by unsatisfactory visualization of the bone, which hampers subsequent discrimination of the sacrum and the sacroiliac joints from other regions of interest. Different groups have been using ^{99m}Tc -infliximab to assess the degree of TNF- α expression in different rheumatological diseases [9, 10].

Our group of research has been successfully performing ^{99m}Tc -anti-CD3 and ^{99m}Tc -anti-TNF- α scintigraphy in patients with rheumatic diseases for several years [6, 7], as an alternative for detecting inflammatory activity in joints by scintigraphy. In this report, we describe what we believe to be the first successful case of the use of anti-TNF- α for detecting inflammatory activity in the sacroiliac joints in a patient with non-radiographic axial spondyloarthritis.

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Conflict of interest The authors have no conflict of interest to declare.

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