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## CASE REPORT

# Diagnostic utility of enzyme-linked immunospot assay for interferon- $\gamma$ in a patient with tuberculous arthritis and pyomyositis<sup>☆</sup>

Che-Kim Tan<sup>a</sup>, Chih-Cheng Lai<sup>b</sup>, Sheng-Hsiang Lin<sup>c</sup>, Yu-Tsung Huang<sup>d,e</sup>,  
Chun-Hsing Liao<sup>f</sup>, Po-Ren Hsueh<sup>d,e,\*</sup>

<sup>a</sup> Department of Intensive Care Medicine, Chi-Mei Medical Center, Tainan, Taiwan

<sup>b</sup> Department of Internal Medicine, Cardinal Tien Hospital, Taipei County, Taiwan

<sup>c</sup> Department of Internal Medicine, Taipei County Hospital, Taipei County, Taiwan

<sup>d</sup> Department of Internal Medicine, National Taiwan University Hospital,  
National Taiwan University College of Medicine, Taipei, Taiwan

<sup>e</sup> Department of Laboratory Medicine, National Taiwan University Hospital,  
National Taiwan University College of Medicine, Taipei, Taiwan

<sup>f</sup> Department of Internal Medicine, Far Eastern Memorial Hospital, Taipei, Taiwan

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### KEYWORDS

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The indolent and nonspecific presentations of tuberculous arthritis and pyomyositis render their diagnosis a great challenge for clinicians. We describe a 78-year-old man with swelling and pain of right knee for 6 months. The patient was empirically treated for tuberculosis because positive enzyme-linked immunospot assay for interferon- $\gamma$  of blood was reported at 2 days after aspiration of synovial fluid, which was negative for acid-fast stain but subsequently grew *Mycobacterium tuberculosis* 6 weeks later. He recovered uneventfully with 1-year antituberculous combination therapy.

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\* Corresponding author. Departments of Laboratory Medicine and Internal Medicine, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei 100, Taiwan.

E-mail address: [hsporen@ntu.edu.tw](mailto:hsporen@ntu.edu.tw) (P.-R. Hsueh).

## Introduction

Musculoskeletal tuberculosis (TB) accounts for 1–3% of all forms of TB and approximately 10% of cases with extrapulmonary TB.<sup>1,2</sup> The definite diagnosis requires the identification of *Mycobacterium tuberculosis* from the synovial fluid or biopsied tissue; however, only 60–80% of cases had the positive cultures of *M tuberculosis*.<sup>3</sup> An enzyme-linked immunospot (ELISPOT) assay was developed to detect interferon- $\gamma$  produced by activated T cell after exposure to two specific antigens of *M tuberculosis*, that is, early secretory antigenic target 6 and culture filtrate protein 10, which are present in *M tuberculosis* but absent in *Mycobacterium bovis* bacilli Calmette–Guerin and most environmental nontuberculous mycobacteria.<sup>4</sup> Previous studies showed that ELISPOT assay would be useful for the

diagnosis of extrapulmonary TB in both immunocompetent and immunocompromised patients.<sup>4–10</sup> We, hereby, demonstrate the usefulness of ELISPOT assay in one patient with tuberculous arthritis and pyomyositis.

## Case report

A 78-year-old HIV-negative man was referred to our hospital because of swelling and pain of the right knee for 6 months. On admission, fever up to 39°C was noted. Physical examinations were unremarkable except for a swollen right knee with local heat and tenderness. The range of motion of the right knee was moderately limited in all directions. Laboratory examinations revealed a white blood cell count of 4,510/mm<sup>3</sup> and C-reactive protein of 4.75 mg/dL (normal range, <0.8 mg/dL). Magnetic resonance imaging of the



**Figure 1.** Short-tau inversion recovery (STIR) magnetic resonance images (A and C) and contrast-enhanced T1WI with fat saturation (B and D) of the right knee showing effusion in suprapatellar fossa with diffuse synovial thickening and enhancement (white arrow); some foci of abnormal signal intensity and enhancement in the subchondral bone marrow (arrow head); and large pyomyositis with heterogeneous content in the popliteus muscle (black arrow).

right knee showed moderate amount of effusion and marked synovial proliferation and enhancement in the right suprapatellar bursa and knee joint with some debris and multifocal subchondral marrow edema/hyperemia (Fig. 1). Aspiration of joint effusion yielded 3 mL of serosanguinous fluid. No crystal was found on microscopic examination. Synovial fluid analysis revealed a white blood cell count of 800/mm<sup>3</sup>. The Gram stain and acid-fast stain of the aspirated synovial fluid were negative, and the routine aerobic and anaerobic bacterial cultures were also negative. Chronic monoarthritis and myositis were suspected. The autoantibody screening assays, including rheumatoid factor and antinuclear antibody, were negative. ELISPOT assay was performed on peripheral blood showing 102 early secretory antigenic target 6 and 84 culture filtrate protein 10 interferon- $\gamma$  spot-forming cells per 250,000 peripheral blood mononuclear cells. More than five spot-forming cells per 250,000 peripheral blood mononuclear cells is regarded as a positive result by the manufacturer. The ELISPOT assay of the patient's blood specimen revealed a positive result 2 days later. Six weeks later, the synovial fluid grew *M tuberculosis*, and the diagnosis of TB arthritis and pyomyositis was confirmed. The patient received anti-TB treatment for 1 year and remained uneventful.

## Discussion

The clinical manifestations of extrapulmonary TB were protean and included meningitis, genitourinary infection, pericarditis, lymphadenitis, pleurisy, peritonitis, musculoskeletal infection, and cutaneous TB. The prevalence of extrapulmonary TB ranges from 15% to 25%, according to the estimation of the World Health Organization surveillance study.<sup>11</sup> Furthermore, about 3% of patients with TB have musculoskeletal involvement, which mostly causes spondylitis, osteomyelitis, or arthritis.<sup>12</sup> In addition, tuberculous myositis has rarely been described in the medical literature, and its manifestations may mimic malignant or other inflammatory diseases, leading to misdiagnosis.<sup>13</sup> Although the mechanism of how *M tuberculosis* reaches the musculoskeletal system is not fully understood, hematogenous dissemination and direct inoculation have been suggested. However, like our case, there is no evidence of concurrent active or arrested tuberculous foci in any location other than the musculoskeletal system.

Tuberculous arthritis and pyomyositis usually present in a slow indolent manner with nonspecific clinical presentations; therefore, the diagnosis of tuberculous arthritis is often difficult and even delayed. The definite diagnosis usually requires histological and microbiological confirmations. The microbiological gold standard is too insensitive and time consuming to be used along for making the diagnosis. Either the solid media-based techniques, such as Lowenstein–Jensen and Middlebrook 7H10/11, or liquid media-based methods, such as BACTEC (BD Diagnostics, Sparks, MD, USA) and MGIT (BD Diagnostics) take weeks to complete the test.<sup>14,15</sup> In contrast, several studies report that the ELISPOT assay is a rapid and adjunct test for diagnosing extrapulmonary TB,<sup>5</sup> including TB pleurisy,<sup>6</sup>

lymphadenitis,<sup>7</sup> intestinal TB,<sup>8</sup> meningitis,<sup>9</sup> and pericarditis.<sup>10</sup> Moreover, Liao et al.<sup>16</sup> showed that the sensitivity of ELISPOT assay for the diagnosis of extrapulmonary TB could range from 100% for tuberculous meningitis, tuberculous pericarditis, and intestinal TB; 95% for lymphadenitis; to 42.9% for tuberculous peritonitis. This case further illustrates the potential advantages and usefulness of measuring mycobacterium-specific immune response by the ELISPOT assay for the rapid diagnosis of tuberculous arthritis and pyomyositis; particularly, the microbiological culture results are still not available.

In conclusion, we demonstrate the diagnostic utility of ELISPOT assay in a patient with TB arthritis and pyomyositis; however, further large-scale studies are needed to clarify its diagnostic value in this rare disease category.

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