

CASE STUDY

Open Access

Clinical utility of anti-lipoarabinomannan antibodies testing for the diagnosis of tuberculous arthritis

Giuseppe Passiu¹, Gian Luca Erre¹, Pietro Pirina² and Leonardo Antonio Sechi^{3*}

Abstract

Diagnosis of extrapulmonary tuberculosis (TB) is often challenging. In this work we discuss the utility of an assay for Lipoarabinomannan (LAM) antibody detection in synovial fluid. LAM is one of the three major groups of lipopolysaccharides within the *Mycobacterium tuberculosis* (MTB) cell wall. An ELISA based test was used to investigate the presence of antibodies against LAM in an immunocompetent patient with knee arthritis. The symptoms resolved after isoniazid treatment. LAM positivity has been used as a diagnostic tool for TB in different settings, including veterinary field. The test could be of some value to diagnose tuberculous arthritis in selected patients when gold standard test returned negative although further investigations are welcome.

Keywords: Arthritis; Mycobacteria; ELISA; Lipoarabinomannan

Tuberculosis (TB) remains one of the leading infectious cause of mortality world-wide. Musculoskeletal manifestations account for 10% of extrapulmonary tuberculosis and include tuberculous arthritis.

A 48-year-old otherwise healthy man presented with a 3-month long history of oligoarthritis (left hip and knees) preceded by three weeks of mild night sweats. Personal history was not informative, with the exception of a recent travel in a TB endemic area. General physical examination was unremarkable.

Intensive rheumatological work-up, including serology, complete joint imaging, chest X-rays and comprehensive synovial-fluid analysis was inconclusive. A diagnosis of undifferentiated arthritis was considered and two courses of intra articular steroid injection along with non steroidal antiinflammatory drugs were undertaken with only short relief.

Therefore, in the view of the recent history of TB contact and of IFN-gamma release assay positivity (19 U, cut off at 0.35 U) extensive search for *M. tuberculosis* on multiple biological specimens was performed: microscopy, polymerase chain reaction (PCR) and cultures of sputum, urine, synovial fluid and synovial tissue returned

all negative. On the contrary, an intense positivity for anti-lipoarabinomannan (LAM) antibodies IgG (Erre et al. 2014) in synovial fluid, but not in peripheral blood was demonstrated.

A presumptive diagnosis of tuberculous arthritis was then considered and an expectancy therapy with a 6-month short course of isoniazide was started. Arthritis gradually improved in 6 months and after 10 months the end of treatment the patient is fully recovered.

TB diagnosis largely rely on clinical suspicion, smear staining, liquid culture for *M. tuberculosis* and nucleic acid amplification tests. The International Standards for TB Care strongly discourages the use of serological tests in routine practice for the diagnosis of pulmonary and extrapulmonary TB (Hopewell et al. 2006).

However, extrapulmonary TB may represent a diagnostic dilemma due to the relative insensitivity of smear, PCR and cultures of body fluid or tissues (Valdes et al. 1998). In TB arthritis synovial fluid smear staining is positive in only 20–40% of cases (Mahowald 2000) and 21% of the synovial fluid cultures have been reported to be negative (Malaviya & Kotwal 2003).

The accuracy of a commercial kit testing antibodies to LAM, a lipoglycan of the mycobacterial cell wall, has been recently tested showing a good discrimination power between TB and non-TB subjects (Malaviya &

* Correspondence: sechila@uniss.it

³Dipartimento di Scienze Biomediche, Università di Sassari, Sassari, Italy
Full list of author information is available at the end of the article

Kotwal 2003). The use of anti-LAM antibodies testing has been reported to be of utility in diagnosing pulmonary and extrapulmonary TB (Dhana et al. 2014; Yokoyama et al. 2005; Lawn et al. 2014; Bua et al. 2009).

In our case, the diagnosis of tuberculous arthritis could be established on the basis of patient history (including recent exposure to *M. tuberculosis* contacts), absence of an alternative clear diagnosis, positivity for anti-LAM antibodies on synovial fluid and complete recovery after anti-tuberculous chemotherapy.

Negativity of anti-LAM antibodies in peripheral blood, further strengthened the hypothesis of a true *M. tuberculosis* localization in the joint triggering anti-LAM antibodies production restricted to the synovial microenvironment.

The analysis of our case suggests that, anti-LAM testing could be of some value to diagnose tuberculous arthritis in selected patients when gold standard test returned negative. However, further investigations are required in the matter, before anti-LAM antibodies testing could be recommended as a routine TB diagnostic test.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

GP, GE, PP and LAS conceived the study. GE and LAS drafted the manuscript. PP and LAS carried out the tests. All authors read and approved the final manuscript.

Acknowledgments

This investigation was supported by grants from: the Sardinian Region LR.7 2010 Progetti di ricerca di base CRP-25160, and the Fondazione Banco di Sardegna year 2014-0184.

Author details

¹Dipartimento di Medicina Clinica e Sperimentale, Università di Sassari, Sassari, Italy. ²Unità di Pneumologia, Università di Sassari, Sassari, Italy. ³Dipartimento di Scienze Biomediche, Università di Sassari, Sassari, Italy.

Received: 26 January 2015 Accepted: 27 January 2015

Published online: 05 February 2015

References

- Bua A, Rosu V, Mollicotti P, Das Gupta SK, Ahmed N, Zanetti S, Sechi LA (2009) Phages specific for mycobacterial lipoarabinomannan help serodiagnosis of tuberculosis. *New Microbiol* 32:293–296
- Dhana AV, Howell P, Spencer D (2014) When smear and molecular diagnostics fail: identification of tuberculosis in advanced HIV infection using the newly developed urine lipoarabinomannan lateral-flow assay. *BMJ Case Rep* 10:2014
- Erre GL, Cossu D, Masala S, Mameli G, Cadoni ML, Serdino S, Longu MG, Passiu G, Sechi LA (2014) Mycobacterium tuberculosis lipoarabinomannan antibodies are associated to rheumatoid arthritis in Sardinian patients. *Clin Rheumatol* 33:1725–1729
- Hopewell PC, Pai M, Maher D, Uplekar M, Raviglione MC (2006) International standards for tuberculosis care. *Lancet Infect Dis* 6:710–725
- Lawn SD, Kerkhoff AD, Burton R, Meintjes G (2014) Underestimation of the incremental diagnostic yield of HIV-associated tuberculosis in studies of the Determine TB-LAM Ag urine assay. *AIDS* 28:1846–1848
- Mahowald ML (2000) Arthritis Due To Mycobacteria, Fungi and Parasites. In: Koopman WJ (ed) *Arthritis and Allied Conditions*, 14th edn, on-line version, chapter 128. Lippincott Williams & Wilkins, Philadelphia

- Malaviya AN, Kotwal PP (2003) Arthritis associated with tuberculosis. *Best Pract Res Clin Rheumatol* 17:319–343
- Valdes L, Alvarez D, San Jose E, Penela P, Valle JM, Garcia-Pazos JM, Suárez J, Pose A (1998) Tuberculous pleurisy. a study of 254 patients. *Arch Intern Med* 158:2017–2021
- Yokoyama T, Rikimaru T, Kinoshita T, Kamimura T, Oshita Y, Aizawa H (2005) Clinical utility of lipoarabinomannan antibody in pleural fluid for the diagnosis of tuberculous pleurisy. *J Infect Chemother* 11:81–83

Submit your manuscript to a SpringerOpen[®] journal and benefit from:

- Convenient online submission
- Rigorous peer review
- Immediate publication on acceptance
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

Submit your next manuscript at ► springeropen.com