

# HEMATOLOGICAL CHANGES IN TUBERCULOUS SPONDYLITIS PATIENTS AT THE HOSPITAL UNIVERSITI SAINS MALAYSIA

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**Abstract.** In this study, we compared the platelet count with erythrocyte sedimentation rates (ESR) in patients with tuberculous spondylitis to evaluate the correlation. This was a retrospective 3-year study covering January 2004 to December 2006 at the Hospital Universiti Sains Malaysia. Platelet counts, hemoglobin levels, ESR, peripheral blood counts and peripheral blood smears on 17 patients with tuberculous spondylitis were obtained. The ages of the patients ranged from 20 to 70 years old. The male to female ratio was 3.2:1. The majority of the patients were anemic (88.2%) and 52.9% of the patients had thrombocytosis. All the patients had normal lymphocyte counts and a high in ESR at diagnosis. There was a linear correlation between the platelet count and ESR ( $r = 0.60$ ,  $p < 0.01$ ). The platelet count was also significantly correlated with the hemoglobin level ( $r = -0.6$ ,  $p < 0.02$ ). The degree of thrombocytosis was related to the degree of inflammation measured by the ESR. Thrombocytosis also correlated with the hemoglobin level. We suggest that evaluating hematological values in suspected cases of tuberculosis should be considered. The presence of hematological changes should raise the suspicion of tuberculosis in spondylitis patients.

## INTRODUCTION

Tuberculosis (TB) is a major public health problem in Malaysia. Although involvement of bones accounts for 1 to 5% of all TB cases, multifocal involvement of the skeleton is extremely rare (Ozol *et al*, 2006). Spinal TB is the commonest form of skeletal TB (Turgut, 2001; Kumar, 2005). TB of the spine (Pott's disease) is both the most common and most dangerous form of TB infection. Spinal TB occurs as a result of hematogenous dissemination from a primary focus in the lungs or lymph nodes. Delay in establishing the diag-

nosis and management may lead to spinal cord compression and spinal deformity (Turgut, 2001). Early recognition is therefore necessary to minimize residual spinal deformity and/or permanent neurological sequelae (Sinan *et al*, 2004). Spinal TB, in its atypical forms, is a rare clinical entity and a low index of suspicion on the part of the surgeon may result in misdiagnosis as a neoplasm (Tanriverdi *et al*, 2003). The diagnosis of spinal TB is difficult and commonly occurs at an advanced stage (Cormican *et al*, 2006).

The differential diagnosis of tuberculosis should be entertained in patients with some abnormal hematological findings (Singh *et al*, 2001). Hematological parameters are useful indicators of severity in TB infection (Bozoky, 1997). Hematological changes associated with TB infection have been incompletely investigated (Singh *et al*, 2001). To the best of our

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knowledge, there is no comprehensive study assessing the hematological abnormalities in spinal TB patients in Malaysia.

## MATERIALS AND METHODS

This retrospective study evaluated hematological findings in 17 adult patients with TB spondylitis treated at the Hospital Universiti Sains Malaysia from January 2004 to December 2006. Infection was diagnosed in patients having characteristic histologic and/or microbiologic evidence of TB spondylitis, diagnostic radiographic features or following adequate response to antituberculous therapy. All patients had a peripheral blood count and erythrocyte sedimentation rate (ESR) test on diagnosis. A hemoglobin level, lymphocyte count, platelet count and ESR were also obtained. Pearson correlation was used for statistical analysis.

## RESULTS

Seventeen patients were diagnosed with TB spondylitis from January 2004 to December 2006. The ages of the patients ranged from 20 to 70 years old, with a mean age of 48.5 years old. The male to female ratio was 3.2:1. The majority of patients were anemic (88.2%) with hemoglobin levels ranging from 8.6 g/dl to 14.3 g/dl with a mean hemoglobin of 11.4 g/dl. Normocytic normochromic anemia was the most common abnormality observed. The total white cell count ranged from  $4.4 \times 10^9/l$  to  $16.0 \times 10^9/l$  with the mean total white count of  $8.3 \times 10^9/l$ . The lymphocyte counts ranged between  $1.0\text{-}3.9 \times 10^9/l$ . Thrombocytosis was noted in 52.9% of patients, which were ranged from  $190 \times 10^9/l$  to  $665 \times 10^9/l$ . All patients had an elevated ESR ranging from 21 mm/h to 123 mm/h.

There was a linear correlation between the platelet count and ESR ( $r = 0.60$ ,  $p < 0.01$ ). The platelet count was also significantly cor-

related with the hemoglobin level ( $r = -0.6$ ,  $p < 0.02$ ). There was no significant correlation between the platelet count and the total white cell count.

## DISCUSSION

This retrospective study of hematological changes in tuberculous spondylitis patients was the first carried out in Malaysia. The mean age of spinal TB infections in our patients was similar to a study by Tasova *et al* (2006) who reported a mean age of 44.7 with a range of 18 to 80 years old.

In this study we found the majority of patients had normocytic normochromic anemia with thrombocytosis. These findings are similar to a study by Morris *et al* (1989) who found hematological abnormalities among their patients with pulmonary TB included normochromic normocytic anemia, thrombocytosis and elevated ESR. There was a close correlation between acid-fast bacilli in sputum and abnormal values, particularly those with low body weight, low hemoglobin, high platelet count, abnormal white cell count and erythrocyte sedimentation rate (Morris, 1989). Olaniyi and Aken'ova (2003) also observed significant hematologic abnormalities in TB patients which included high ESR, anemia, leukocytosis, neutrophilia, lymphopenia, thrombocytosis and thrombocytopenia.

Most of the patients in our study with TB spondylitis had thrombocytosis. Reactive thrombocytosis (RT) is found in a number of clinical situations including infectious diseases, such as pulmonary TB (Unsal *et al*, 2005). The regulation of thrombopoiesis is under the control of an array of hematopoietic growth factors (Hsu *et al*, 1999). The concentration of cytokines in the bone marrow correlates well with those in the peripheral blood. The endogenous levels of thrombopoietin (TPO), interleukin 6 (IL 6) and soluble interleukin 6 (sIL6) receptor were significantly higher in

reactive thrombocytosis (Hsu *et al*, 1999). Significant elevation of TPO during the acute phase of infection precedes the development of thrombocytosis, suggesting an important role for TPO in RT (Ishiguro *et al*, 2002).

Elevated values of TPO were found in a majority of patients with acute infections and were observed more frequently during the acute phase with fever than after the fever disappeared (Ishiguro *et al*, 2002). TPO was found to be significantly elevated in the first week of infections. In contrast to TPO, the platelet count were peaked in the second and third weeks (Ishiguro *et al*, 2002).

The exact mechanism of elevated TPO levels in RT is still unknown, however it has been observed to be correlated with IL 6 and production can be enhanced by inflammatory processes (Hsu *et al*, 1999).

Serum IL6 concentrations are significantly correlated with thrombocyte counts and albumin concentrations. IL6 may play a contributory part in reactive thrombocytosis and the acute phase response in pulmonary TB (Unsal *et al*, 2005).

Interleukin 8 (IL 8) was also found to be elevated in RT. IL 8 is a potent chemoattractant and activating factor for neutrophils and has proinflammatory effects. Elevated levels of IL 8 in patients with RT are probably caused by an increased population of megakaryocytes (Hsu *et al*, 1999).

Baynes *et al* (1987) reported the degree of thrombocytosis correlated significantly with the degree of inflammation measured by the ESR and serum C-reactive protein concentration. We also observed that there was a significant correlation between thrombocytosis and elevated ESR.

The ESR, a sensitive measure of the inflammatory response, is elevated in 90% of patients who have a serious orthopedic infection (Schulac *et al*, 1982). Out patient determination of the ESR is useless for early de-

tection of malignancy but valuable in detecting inflammatory arthritides and major sepsis (Schulac *et al*, 1982).

An ESR value exceeding 100 mm/hr has a 90% predictive value for serious underlying disease, such as infection, collagen vascular disease or metastatic tumor (Brigden, 1998). ESR and CRP are both significantly increased in patients with infection, inflammation or both (Katz *et al*, 1989). However, CRP is a superior diagnostic test to ESR (Mok *et al*, 2008).

Body weight loss, white blood cell count, hemoglobin level and ESR are useful indices of severity in TB. The return of these indices to a normal level is a good indication of disease control in that they correlate with sputum conversion to acid-fast bacilli negative (Olaniyi and Aken'Ova, 2003). Hematological and biochemical abnormalities in pulmonary tuberculosis are common and may be valuable aids in diagnosis. Some hematological markers also reflect response to treatment (Morris *et al*, 1989).

In conclusion, awareness of the demographics, clinical, and laboratory features of spinal TB patients may facilitate earlier diagnosis (Cormican *et al*, 2006). The unexplained presence of any of these hematological or biochemical abnormalities should raise suspicion of the disease (Morris *et al*, 1989). In view of the varied hematological abnormalities observed in patients with tuberculosis in this part of the world, we suggest the differential diagnosis of tuberculosis should be entertained in patients with varied hematological disorders.

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## REFERENCES

- Baynes RD, Bothwell TH, Flax H, *et al.* Reactive thrombocytosis in pulmonary tuberculosis. *J Clin Pathol* 1987; 40: 676-9.
- Bozóky G, Ruby E, Góhér I, Tóth J, Mohos A. Hematologic abnormalities in pulmonary tuberculosis. *Orv Hetil* 1997; 138: 1053-6.
- Brigden M. The erythrocyte sedimentation rate. Still a helpful test when used judiciously. *Postgrad Med* 1998; 103: 257-62.
- Cormican L, Hammal R, Messenger J, Milburn HJ. Current difficulties in the diagnosis and management of spinal tuberculosis. *Postgrad Med J* 2006; 82: 46-51.
- Hsu HC, Tsai WH, Jiang ML, *et al.* Circulating levels of thrombopoietic and inflammatory cytokines in patients with clonal and reactive thrombocytosis. *J Lab Clin Med* 1999; 134: 392-7.
- Ishiguro A, Suzuki Y, Mito MYS, *et al.* Elevation of serum thrombopoietin precedes thrombocytosis in acute infection. *Br J Haematol* 2002; 116: 612-8.
- Katz PR, Gutman SI, Richman G, Karuza J, Bartholomew WR, Baum J. Erythrocyte sedimentation rate and C-reactive protein compared in the elderly. *Clin Chem* 1989; 3: 466-8.
- Kumar R. Spinal tuberculosis: with reference to the children of northern India. *Childs Nerv Syst* 2005; 21: 19-26.
- Mok JM, Pekmezci M, Samantha MP, *et al.* Use of C-reactive protein after spinal surgery. Comparison with erythrocyte sedimentation rate as predictor of early postoperative infectious complications. *Spine* 2008; 33: 415-21.
- Morris CD. The radiography, haematology and biochemistry of pulmonary tuberculosis in the aged. *Q J Med* 1989; 71: 529-36.
- Morris CD, Bird AR, Nell H. The haematological and biochemical changes in severe pulmonary tuberculosis. *Q J Med*, 1989; 73: 1151-9.
- Olaniyi JA, Aken'Ova YA. Haematological profile of patients with pulmonary tuberculosis in Ibadan, Nigeria. *Afr J Med Med Sci*, 2003; 32: 239-42.
- Ozol D, Koptener A, Uyar ME. Active pulmonary tuberculosis with vertebra and rib involvement: case report. *South Med J* 2006; 99: 171-3.
- Schulac DJ, Lippert FG, Convery FR. The erythrocyte sedimentation rate in orthopaedic patients. *Clin Orthop Relat Res* 1982; 167: 197-202.
- Sinan T, Al-Khawari H, Ismail M, Bennakhi A, Sheikh M. Spinal tuberculosis: CT and MRI feature. *Ann Saudi Med* 2004; 24: 437-41.
- Singh KJ, Ahluwalia G, Sharma SK, Saxena R, Chaudhary VP, Anant M. Significance of haematological manifestations in patients with tuberculosis. *J Assoc Physicians India* 2001; 49: 788, 790-4.
- Tasova Y, Sarpel T, Ayse Sesa I, *et al.* A clinical review of 40 cases with tuberculous spondylitis in adults. *Neurosurg Q* 2006; 14: 169-75.
- Tanriverdi T, Kizilkilic O, Hanci M, Kaynar MY, Unalan H, Oz B. Atypical intradural spinal tuberculosis: report of three cases. *Spinal Cord* 2003; 41: 403-9.
- Turgut M. Spinal tuberculosis (Pott's disease): its clinical presentation, surgical management, and outcome. A survey study on 694 patients. *Neurosurg Rev* 2001; 24: 8-13.
- Unsal E, Aksaray S, Koksai D, Sipit T. Potential role of interleukin 6 in reactive thrombocytosis and acute phase response in pulmonary tuberculosis. *Postgrad Med J* 2005; 81: 604-7.