Procalcitonin levels in fresh serum and fresh synovial fluid for the differential diagnosis of knee septic arthritis from rheumatoid arthritis, osteoarthritis and gouty arthritis

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Abstract. Whether the levels of procalcitonin (PCT) in the serum and synovial fluid are effective indicators for distinguishing septic arthritis (SA) from non-infectious arthritis remains controversial. The present study aimed to evaluate whether PCT levels in fresh serum or fresh joint fluid may be used in the differential diagnosis of SA from rheumatoid arthritis (RA), osteoarthritis (OA) and gouty arthritis (GA). From January 2012 to June 2013, 23 patients with knee SA, 21 patients with RA, 40 patients with OA and 11 patients with GA were enrolled in the current study. The levels of PCT were measured within 24 h after specimen collection at room temperature. An enzyme-linked fluorescence assay (ELFA) was used to detect the levels of PCT in the serum and synovial fluid. The correlations between the levels of PCT in the serum and synovial fluid and the arthritic patient groups were determined by the Nemenyi test. Areas under the receiver operating characteristic (ROC) curve were calculated to evaluate the accuracy of the correlations. The levels of PCT in the serum and joint fluid of the patients in the SA group were higher compared with those of the other groups (P<0.01) and there were no significant differences among the RA, OA and GA groups in these levels. A PCT level of <0.5 µg/l in the serum and synovial fluid had high specificity in the differential diagnosis of SA from RA, OA and GA. Synovial fluid PCT revealed significantly greater sensitivity than serum PCT. The accuracy of the differential diagnosis of SA by the serum levels of PCT was significantly lower than that by the synovial fluid levels of PCT. The levels of PCT in the serum and synovial fluid may be used as alternative laboratory indicators to distinguish between SA and the non-infectious types of arthritis; however, the PCT levels in fresh synovial fluid are more sensitive and accurate indicators than PCT levels in fresh serum.

Introduction

The incidence rate of septic arthritis (SA) has been increasing over the last few years. Early diagnosis as well as a prompt and effective treatment are vital in order to avoid severe outcomes (1). However, the clinical manifestation of SA is similar to that of non-septic arthritis, including rheumatoid arthritis (RA), osteoarthritis (OA) and gouty arthritis (GA), which causes difficulty in the differentiation of SA from RA, OA and GA in clinics. Currently, the detection of bacteria in synovial fluid culture remains the primary index for the diagnosis of SA. However, this has a number of disadvantages including aseptic surgery, a long turn-around time and the potential generation of a false positive or negative result (2,3). Prior to the bacterial culture results becoming available, several other clinical tests, including X-ray imaging (4), routine blood tests (5), erythrocyte sedimentation rate (ESR) measurements (6), synovial fluid white blood cell (WBC) count (7) and levels of CRP (C reactive protein) (8,9) may be used for SA diagnosis. However, none of these tests are sensitive enough to produce an accurate diagnosis and they frequently lead to misdiagnosis and/or the delay of treatment. For example, CRP is another positive predicator in the diagnosis of SA (10-14); however, the diagnostic accuracy of CRP is affected by steroids (15). A quick and sensitive test is thus required.

Procalcitonin (PCT), a precursor of the calcitonin peptide produced due to bacterial endotoxins, tumor necrosis factor (TNF)-α and interleukin (IL)-6 (16,17), is a novel predictor for the diagnosis of bacterial infection (18,19). As a secondary inflammatory factor, PCT is not directly involved in initiating the septic process but may enlarge and aggravate the pathological process of sepsis (20) and is unresponsive or only mildly reactive to aseptic inflammation and viral infection (21). PCT has been used in the diagnosis of systemic infections or infectious shock (22-27). Unlike CRP, the diagnostic accuracy of PCT is not affected by steroids (28). A previous meta-analysis demonstrated that PCT was more accurate than CRP in diagnosing systemic bacterial infection, regardless of pathogen type (29). Despite the widespread use of PCT in the diagnosis of numerous systemic infectious diseases, including sepsis
and pneumonia (30-33), the use of PCT in the diagnosis of SA, RA, OA and GA remains limited. Serum levels of PCT perform better than synovial fluid levels of PCT in the diagnosis of SA (34). However, PCT levels among non-infectious types of arthritis (OA, RA and GA) have not, to the best of our knowledge, been compared, although the level of PCT in SA has been compared with that of non-inflammatory arthritis in the current study. The synovial fluid levels of PCT have been reported to be positive indicators of SA (35). A previous study has demonstrated that the synovial fluid level of PCT is significantly higher in patients with SA than in patients with OA, and that CRP levels differ significantly among patients with SA, RA and OA (36). The serum level of PCT is a specific marker of SA but with a low sensitivity; serum PCT in association with CRP has not been useful for the diagnosis of SA (37).

Thus, the applicability of using the levels of PCT in the serum or synovial fluid as effective indicators for distinguishing SA from non-infectious forms of arthritis remains controversial. A study involving patients with SA, RA, OA and GA would be instrumental in resolving the controversy. The discrepancy in the effectiveness of applying serum or synovial fluid PCT in diagnosis may result from the condition of the serum or synovial fluid or inflammatory arthritis in particular. However, PCT levels among non-infectious types of arthritis (OA, RA and GA) have not, to the best of our knowledge, been compared, although the level of PCT in SA has been compared with that of non-inflammatory arthritis in the current study. The synovial fluid levels of PCT have been reported to be positive indicators of SA (35). A previous study has demonstrated that the synovial fluid level of PCT is significantly higher in patients with SA than in patients with OA, and that CRP levels differ significantly among patients with SA, RA and OA (36). The serum level of PCT is a specific marker of SA but with a low sensitivity; serum PCT in association with CRP has not been useful for the diagnosis of SA (37).

Thus, the applicability of using the levels of PCT in the serum or synovial fluid as effective indicators for distinguishing SA from non-infectious forms of arthritis remains controversial. A study involving patients with SA, RA, OA and GA would be instrumental in resolving the controversy. The discrepancy in the effectiveness of applying serum or synovial fluid PCT in diagnosis may result from the condition of the serum or synovial fluid samples. The specimens in certain previous studies (34-37) were frozen for longer than 24 h prior to the experiments being conducted while the half-life of PCT in the synovial fluid has been reported to be ~20-24 h (38). The present study aimed to evaluate whether serum or joint fluid levels of PCT may be used in the differential diagnosis of SA from RA, OA and GA using fresh serum and synovial fluid samples.

Materials and methods

Patients. A non-blind method was used for selection of participants in the present study and subjects volunteered to become study subjects. All subjects were selected from the outpatient service of Xiangya Hospital of Central South University (Changsha, China) from January 2012 to June 2013. The patients were selected according to the following criteria: i) Patients with various types of arthritis other than SA, RA, OA or GA were excluded from the present study. Diagnosis was carried out according to the criteria set by the American College of Rheumatology (ACR) and confirmed by bacterial culture of the patients' synovial fluid. ii) The patients had not received any antibiotic or joint puncture treatments prior to enrollment in the current study. iii) Patients were excluded if the joint(s) being treated had been subjected to artificial joint surgery. iv) All patients included in the present study had been evaluated using the joint fluid bacterial culture test. Patients with SA were excluded if the result of their bacterial culture test was negative; RA, OA and GA patients were excluded if the result of their bacterial culture test was positive. v) Each patient provided informed written consent and approval from the Institutional Review Board (IRB) of the Xiangya Hospital was obtained prior to data extraction and analysis.

Collection of specimens. A total of 5 ml blood was drawn from a vein at the elbow of each patient followed by centrifugation at 2,756 x g for 10 min. A synovial fluid sample ≥200 μl in volume was aseptically aspirated from the patellofemoral articular surface. Patients from which <200 μl synovial fluid was collected were excluded from the study. If the two knees of a patient exhibited symptoms of SA, RA, OA or GA, synovial fluid was only drawn from the knee with the more severe symptoms. All samples were stored at room temperature (10-25°C) prior to analysis.

Determination of the levels of PCT in the serum and synovial fluid. Levels of PCT were tested within 24 h after serum and fluid collection at room temperature (10-25°C) by enzyme linked fluorescent analysis (ELFA) using a PCT quantitative determination kit and fluorescence reading machine (Vidas® B.R.A.H.M.S PCT™; bioMérieux, Marcy l'Etoile, France) according to the manufacturers' instructions.

Statistical analysis. All statistical analyses were performed using SPSS software, version 19.0 (SPSS, Inc., Chicago, IL, USA), unless otherwise specified. P<0.01 was considered to indicate a statistically significant difference. Correlations of the serum and synovial fluid levels of PCT between groups were determined by the Nemenyi test. Areas under the

| Characteristic                  | SA     | RA     | OA     | GA     |
|--------------------------------|--------|--------|--------|--------|
| Number of cases                | 23     | 21     | 40     | 11     |
| Male/female (n)                | 15/8   | 6/15   | 19/21  | 10/1   |
| Average age (years)            | 46.6±3.6| 35.0±2.2| 66.2±2.6| 60.8±5.6|
| Types and numbers of pathogenic bacteria |        |        |        |        |
| Staphylococcus aureus          | 12     | 0      | 0      | 0      |
| Hemolytic Streptococcus        | 5      | 0      | 0      | 0      |
| Tubercle bacillus              | 2      | 0      | 0      | 0      |
| Escherichia coli               | 2      | 0      | 0      | 0      |
| Streptococcus pneumoniae       | 2      | 0      | 0      | 0      |

The mean ± standard deviation is shown for the average ages. SA, septic arthritis; RA, rheumatoid arthritis; OA, osteoarthritis; GA, gouty arthritis.
receiver operating characteristic (ROC) curve were calculated to evaluate the accuracy of the correlations.

**Results**

*Patient characteristics.* A total of 95 patients were enrolled in the current study. Of these, 23, 21, 40 and 11 patients had SA, RA, OA and GA, respectively. The corresponding male/female ratios were 15/8, 6/15, 19/21 and 10/1, respectively, and the corresponding average ages were 46.6±3.6, 35.0±2.2, 66.2±2.6 and 60.8±5.6 years, respectively (Table I). The types and number of pathogenic bacteria of SA are also listed in the table.

*Levels of PCT in the serum and synovial fluid.* The levels of PCT in the serum and synovial fluid in the SA group were significantly higher compared with those in the other three groups (P<0.01). No significant differences in the levels of PCT in the serum or synovial fluid were observed among the RA, OA and GA groups (P>0.01; Fig. 1).

*Correlation between the levels of PCT in the serum and synovial fluid.* The majority of the serum levels of PCT in the SA group were <0.5 µg/l (65.2%). Serum levels of PCT in ~34.8% of patients with SA were in the range 0.5-10.0 µg/l. The levels of PCT in the synovial fluid in the majority of patients in the RA, OA and GA groups were <0.5 µg/l (95.2%, 95.0% and 90.9%). The levels of PCT in the synovial fluid of 39.1% and 30.4% of patients in the SA group were 0.5-2.0 µg/l and 2.0-10.0 µg/l, respectively (Table II).

To differentiate SA from the forms of non-infectious arthritis, serum and synovial fluid levels of PCT <0.5 µg/l had great specificity, positive predictive value (PPV) and a negative predictive value (NPV). Synovial fluid levels of PCT <0.5 µg/l had significantly higher sensitivity compared with serum levels of PCT. Serum and synovial fluid levels of PCT at 2 or 10 µg/l revealed great specificity but low sensitivity (Table III).

*Accuracy of serum and synovial fluid PCT in discriminating SA from RA, OA and GA.* The areas under the ROC curve of the serum and synovial fluid levels of PCT were calculated and the accuracy of serum and synovial fluid PCT in discriminating SA from RA, OA and GA was determined. The area under the ROC curve of the serum levels of PCT was 0.761 and the area under ROC curve of the synovial fluid levels of PCT was 0.951 (Fig. 2 and Table IV). The accuracy of serum PCT was significantly lower compared with that of

| PCT (µg/l) | SA (n=23) | RA (n=21) | OA (n=40) | GA (n=11) | χ² | P-value |
|-----------|-----------|-----------|-----------|-----------|----|---------|
| Serum     |           |           |           |           |    |         |
| <0.5      | 15  65.21 | 21  100.0 | 39  97.50 | 11  100.0 | 23.002 | 0.001   |
| 0.5-2.0   | 6   26.09 | 0     0.00 | 1    2.50 | 0    0.00 |        |         |
| 2.0-10.0  | 2   8.70  | 0     0.00 | 0    0.00 | 0    0.00 |        |         |
| >10.0     | 0    0.00 | 0     0.00 | 0    0.00 | 0    0.00 |        |         |
| Total     | 23   100.0 | 21  100.0 | 40  100.0 | 11  100.0 |      |         |
| Synovial fluid |       |           |           |           |    |         |
| <0.5      | 3    13.04 | 20   95.24 | 38  95.00 | 10  90.90 | 62.669 | <0.001 |
| 0.5-2.0   | 9    39.14 | 0     0.00 | 1    2.50 | 1    9.10 |       |         |
| 2.0-10.0  | 7    30.43 | 1     4.76 | 1    2.50 | 0    0.00 |       |         |
| >10.0     | 4    17.39 | 0     0.00 | 0    0.00 | 0    0.00 |       |         |
| Total     | 23   100.0 | 21  100.0 | 40  100.0 | 11  100.0 |     |         |

PCT, procalcitonin; SA, septic arthritis; RA, rheumatoid arthritis; OA, osteoarthritis; GA, gouty arthritis.

Figure 1. Serum and synovial fluid levels of procalcitonin (PCT) among patients with septic arthritis (SA), rheumatoid arthritis (RA), osteoarthritis (OA) and gouty arthritis (GA). Correlations of the serum and synovial fluid levels of PCT between each pair of patients with arthritis were determined by the Nemenyi method.

Table II. Serum and synovial fluid levels of PCT in the knees of patients with SA, RA, OA and GA.
synovial fluid PCT in discriminating SA from RA, OA and GA (P<0.01).

**Discussion**

To investigate whether serum and/or joint fluid PCT can be used in distinguishing SA from RA, OA and GA, the levels of PCT in fresh serum and synovial fluid samples of patients diagnosed with SA, RA, OA or GA were measured. The present study demonstrated that the levels of PCT in the serum and synovial fluid samples from patients in the SA group were significantly higher compared with those in the RA, OA, or GA groups. Levels of PCT in the serum and synovial fluid <0.5 µg/l had high specificity in the differential diagnosis of SA from RA, OA and GA. The accuracy of the differential diagnosis of SA from RA, OA and GA using serum PCT was significantly lower compared with that by synovial fluid PCT.

To the best of our knowledge, the present study is the first to simultaneously examine all three non-infectious forms of arthritis (RA, OA and GA) using serum and synovial fluid not stored under frozen conditions for >24 h. The levels of PCT in the two types of sample were compared among the four groups using the Nemenyi method. The results revealed that the levels of PCT in the serum and synovial fluid of patients with SA were significantly higher compared with those in the other three groups. No significant difference was observed in the levels of PCT among the RA, OA and GA groups. A PCT level in the two specimens of <0.5 µg/l had significantly higher sensitivity than those of PCT in the serum at the same level. The results of the present study are in accordance with certain previous studies in which synovial levels of PCT were revealed to be positive indicators of SA (35) and were able to differentiate SA from OA (36). Serum PCT has previously been reported as a specific marker of SA but with low sensitivity and was considered not to be useful for the diagnosis of SA, even in association with CRP (37). Nevertheless,
sperm PCT has been reported to have an improved performance compared with synovial fluid PCT in the diagnosis of SA (35) and serum levels of PCT ≥0.3 µg/l have been revealed to have a specificity of 98% in the differential diagnosis of SA infection from prosthetic joint infection and a sensitivity of <35% (38-40).

Using ROC curve analysis, the present study demonstrated that the accuracy of the differential diagnosis of SA from the three types of non-infectious arthritis using synovial fluid levels of PCT was significantly higher compared with using the levels of PCT in the serum. This may be attributed to the fact that joint SA, RA, OA and GA do not cause systemic inflammation; therefore, serum levels of PCT are unable to differentiate SA from RA, OA and/or GA. Certain studies have demonstrated that low levels of PCT may result from limited inflammation or early infection (41,42). Other studies have revealed that the lack of a systemic inflammatory response causes the sensitivity of serum PCT in the differential diagnosis of infectious prosthesis to be extremely low (38-40).

In conclusion, the sensitivity and accuracy of synovial joint fluid PCT at certain levels was significantly higher than that of the serum levels of PCT. Therefore, the level of synovial fluid PCT may be used as an alternative indicator in the differential diagnosis of SA from RA, OA and GA, which may be valuable in guiding the use of antibiotics to SA. However, further studies with a larger patient sample size are required to validate this result. Further work is required to determine the optimal serum and synovial fluid levels of PCT for the differential diagnosis of SA from non-infectious arthritis.

References

1. Favero M, Schiavon F, Riatto L, Carraro V and Punzi L: Septic arthritis: a 12 years retrospective study in a rheumatological university clinic. Reumatismo 60: 260-267, 2008 (In Italian).

2. Ma L, Cranney A and Holroyd-Leduc JM: Acute monoarthritis: what is the cause of my patient's painful swollen joint? CMAJ 178: 1849-1851, 2008.

3. Margareten ME, Kohljes J, Moore D and Bent S: Does this adult patient have septic arthritis? JAMA 294: 1748-1887, 2008.

4. Mathews CJ, Kingsley G, Field M, et al: Management of septic arthritis: a systematic review. Postgrad Med J 84: 265-270, 2008.

5. Schiavon F, Favero M, Carraro V and Riatto L: Septic arthritis: what is the role for the rheumatologist? Reumatismo 60: 1-5, 2008 (In Italian).

6. Buess T and Ludwig C: Diagnostic value of C-reactive protein in comparison with erythrocyte sedimentation as routine admission diagnostic test. Schweiz Med Wochebnchr 125: 120-124, 1995 (In German).

7. McGillicuddy DC, Shah KH, Friedberg RP, Nathanson LA and Edlow JA: How sensitive is the synovial fluid white blood cell count in diagnosing septic arthritis? Am J Emerg Med 25: 749-752, 2007.

8. Saeed K, Ahmad N, Pallett A, Guiver M and Marsh P: Specific staphylococcal polymerase chain reaction can be a complementary tool for identifying causative organisms and guiding antibiotic management in orthopaedic infections. Curr Ortho Prat 21: 628-631, 2010.

9. Yang S, Ramachandran P, Hardick A, et al: Rapid PCR-based diagnosis of septic arthritis by early Gram-type classification and pathogen identification. J Clin Microbiol 46: 1386-1390, 2008.

10. Caird MS, Flynn JM, Leung YL, Millman JE, D’Italia JG and Dormans JP: Factors distinguishing septic arthritis from transient synovitis of the hip in children. A prospective study. J Bone Joint Surg Am 88: 1251-1257, 2006.

11. Khachatourians AG, Patatzik MJ, Roidis N and Holtom PD: Laboratory monitoring in pediatric acute osteomyelitis and septic arthritis. Clin Orthop Relat Res: 186-194, 2003.

12. Lorrot M, Fitoussi F, Faye A, et al: Laboratory studies in pediatric bone and joint infections. Arch Pediatr 14 (Suppl 2): S86-S90, 2007 (In French).

13. Gupta MN, Sturrock RD and Field M: A prospective 2-year study of 75 patients with adult-onset septic arthritis. Rheumatology (Oxford) 40: 24-30, 2001.

14. Levine MJ, McGuire KJ, McGowan KL and Flynn JM: Assessment of the test characteristics of C-reactive protein for septic arthritis in children. J Pediatr Orthop 23: 373-377, 2003.

15. Monneret G, Labaune JM, Isaac C, Bienvenu F, Putet G and Bienvenu J: Procalcitonin and C-reactive protein levels in neonatal infections. Acta Paediatr 96: 209-212, 1997.

16. Alfran H, Annaqir C, Ralat MR and Millman JE: Procalcitonin measurement at 24 hours of age may be helpful in the prompt diagnosis of early-onset neonatal sepsis. Int J Infect Dis 15: e854-e858, 2011.

17. Reith HB, Mittelkötter U, Debus ES, Küssner C and Thiede A: Procalcitonin in early detection of postoperative complications. Dig Surg 15: 260-265, 1998.

18. Caliskan B, Guven A, Ozler M, et al: Ozone therapy prevents renal inflammation and fibrosis in a rat model of acute pyelonephritis. Scand J Clin Lab Invest 71: 473-480, 2011.

19. Wacker C, Prkno A, Brunkhorst FM and Schlattmann P: Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis. Lancet Infect Dis 13: 426-435, 2013.

20. Bohouc N: Inflammatory cascade response to toxin release: therapeutic perspectives. Ann Pharmacol 59: 191-197, 2001 (In French).

21. Balog A, Ocsovsky I and Mándy Y: Flow cytometric analysis of procalcitonin expression in human monocytes and granulocytes. Immunol Lett 84: 199-203, 2002.

22. Das RR: Should procalcitonin be used as a routine biomarker of bacterial infection? Infection 40: 713-714, 2012.

23. Giamarellos-Bourboulis EJ, Mega A, Grecka P, et al: Procalcitonin: a marker for early and late differentiation of septic and non-septic inflammatory response syndrome and sepsis in the critically ill patient? Intensive Care Med 28: 1351-1356, 2002.

24. Chalupa P, Beran O, Herwalt H, Kaspírková N and Holub M: Evaluation of potential biomarkers for the discrimination of bacterial and viral infections. Infection 39: 411-417, 2011.

25. Lipinska-Gediga M, Mierzchala M and Derek G: Pro-atrial natriuretic peptide (pro-ANP) level in patients with severe sepsis and septic shock: prognostic and diagnostic significance. Infection 40: 303-309, 2012.

26. Stankovic Stojanovic K, Steichen O, Lionnet F, et al: Is procalcitonin a marker of invasive bacterial infection in acute sickle-cell vaso-occlusive crisis? Infection 39: 41-45, 2011.

27. Saeed K, Dryden M, Bourne S, Paget C and Proud A: Reduction in antibiotic use through procalcitonin testing in patients in the medical admission unit or intensive care unit with suspicion of bacterial infection. J Hosp Infect 78: 289-292, 2011.

28. Christ-Crain M and Müller B: Procalcitonin in bacterial infections - hype, hope, more or less? Swiss Med Wkly 135: 451-460, 2005.

29. Simon L, Gauvin F, Amre DK, Saint-Louis P and Lacroix J: Procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. Clin Infect Dis 39: 206-213, 2004.

30. Assicot M, Gentili D, Carsini H, Raymond J, Guilbaud J and Bohouc C: High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 341: 515-518, 1993.

31. Martinez JM, Wagner KE, Snider RH, et al: Late immunoneutralization of procalcitonin arrests the progression of lethal porcine sepsis. Surg Infect (Larchmt) 2: 193-202, 2001.

32. Sener G, Ozgur E, Rad AY, Uzan L, Say R and Denizli A: Rapid real-time detection of procalcitonin using a microarray imprinted surface plasmon resonance biosensor. Analyst 138: 6422-6428, 2013.

33. van Vugt SF, Broekhuizen BD, Lammens C, et al; GRACE consortium: Use of serum C reactive protein and procalcitonin concentrations in addition to symptoms and signs to predict pneumonia in patients presenting to primary care with acute cough: diagnostic study. BMJ 342: e1450, 2010.

34. Talebi-Taher M, Shirani F, Nikjamaan N and Shekarabi M: Septic versus inflammatory arthritis: discriminating the ability of serum inflammatory markers. Rheumatol Int 33: 319-324, 2013.

35. Saeed K, Dryden M, Satar A and White G: Measuring synovial fluid procalcitonin levels in distinguishing cases of septic arthritis, including prosthetic joints, from other causes of arthritis and aseptic loosening. Infection 41: 845-849, 2013.

36. Streit G, Alber D, Toubin MM, Toussriot E and Wendling D: Procalcitonin, C-reactive protein, and complement-3a assays in synovial fluid for diagnosis of septic arthritis: preliminary results. Joint Bone Spine 75: 238-239, 2008.
37. Martinot M, Sordet C, Soubrier M, et al: Diagnostic value of serum and synovial procalcitonin in acute arthritis: a prospective study of 42 patients. Clin Exp Rheumatol 23: 303-310, 2005.
38. Bottner F, Wegner A, Winkelmann W, Becker K, Erren M and Götze C: Interleukin-6, procalcitonin and TNF-alpha: markers of peri-prosthetic infection following total joint replacement. J Bone Joint Surg Br 89: 94-99, 2007.
39. Randau T, Wiminer M, Kuberra D, et al: Detection of peri-prosthetic joint infections: blood infection markers in patients undergoing revision arthroplasty. Eur Cells Mater 21: 36, 2011.
40. Worthington T, Dunlop D, Casey A, Lambert R, Luscombe J and Elliott T: Serum procalcitonin, interleukin-6, soluble intercellular adhesion molecule-1 and IgG to short-chain extracellular lipoteichoic acid as predictors of infection in total joint prosthesis revision. Br J Biomed Sci 67: 71-76, 2010.
41. Butbul-Aviel Y, Koren A, Halevy R and Sakran W: Procalcitonin as a diagnostic aid in osteomyelitis and septic arthritis. Pediatr Emerg Care 21: 828-832, 2005.
42. Hügle T, Schuetz P, Mueller B, et al: Serum procalcitonin for discrimination between septic and non-septic arthritis. Clin Exp Rheumatol 26: 453-456, 2008.