who are at risk for a complicated course, and who therefore may benefit from early preventive measures appears to be limited [3–5]. When febrile patients are screened for bacteremia at admission to the hospital to identify those for whom a complicated course is possible, sound clinical judgment, based on age, underlying disease, recent history, and, especially, the likely source of infection, rather than measurement of laboratory markers like PCT levels, should guide clinical decisions regarding further microbiological diagnostic tests and empirical antibiotic therapy.

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References


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High Serum Procalcitonin Levels Do Not Predict Bacteremia in Adult Patients with Acute Fever

Sir—We have been interested in the recent article by Chirouze et al. [1] that demonstrated the usefulness of procalcitonin (PCT) measurement for ruling out a diagnosis of infection in acutely febrile patients admitted to the hospital. Chirouze et al. [1] found that a PCT level of <0.4 ng/mL was associated with a high negative predictive value (98.8%) for ruling out bacteremia, and we agree with this finding. However, the authors’ conclusion that “PCT findings...can accurately predict bacteremia” ([1], p. 160) in those patients is questionable. Indeed, the authors reported a positive predictive value of only 25% for PCT levels above a threshold of 0.4 ng/mL. Furthermore, even with a PCT cutoff level of 6.2 ng/mL (see table 3 in Chirouze et al. [1]), the positive predictive value of PCT remained very poor (31%).

Several studies have already provided evidence that increased PCT levels may occur independently of any bacterial stimulus [2–6]. In support of this fact, we describe in this letter a patient who had elevated PCT levels during an attack of acute gouty arthritis. A 62-year-old man was admitted to the hospital for assessment of severe anaemia (hemoglobin concentration at the time of admission, 24 g/L). No underlying disease was known to be present; however, the patient had a history of tophi and polyarticular arthritis, and both of these conditions had been effectively treated with nonsteroidal anti-inflammatory drugs. During the patient’s stay, the polyarticular arthritis, which mainly involved the knees and ankles, worsened. At this time, the patient’s body temperature was ~38°C, the WBC count was 25,760 cells/µL (85% neutrophils), the serum C-reactive protein level was 241 mg/L (reference level, <4 mg/L), and the fibrinogen level was >7 g/L (reference level, 2–4.5 g/L); these results indicated a severe inflammatory response. Examination of a synovial fluid sample obtained from an inflamed knee revealed 5600 WBCs/µL (85% neutrophils), the majority of which were neutrophils. Culture of the synovial fluid was sterile. Many needle-shaped urate crystals were found, which suggested acute gouty arthritis. Consequently, treatment with colchicine (1 mg per day) and methylprednisolone (20 mg per day) was initiated. Morphine therapy was also required for several days to alleviate severe pain. On the basis of the painful polyarticular attack, the evidence of tophi, and the dramatic response to colchicine therapy that led to a favorable outcome without antibiotherapy, a diagnosis of acute gouty arthritis was established.

Because the initial clinical signs of acute pain and mild fever were also suggestive of septic arthritis, serum PCT concentra-
tions were also measured. To our surprise, we found elevated PCT levels that were consistent with PCT levels associated with bacterial infection. The PCT level on 25 September, the day that acute gouty arthritis was diagnosed, was 4.1 ng/mL. The PCT level was then found to be 9.3 ng/mL on 27 September (the patient’s TNF level on the same date was 60 pg/mL), 8.3 ng/mL on 30 September, 1 ng/mL on 3 October, and 0.5 ng/mL on 8 October (reference level, <1 ng/mL).

To the best of our knowledge, this is the first reported case of such a large increase in PCT levels in the context of an attack of acute gouty arthritis, a disease that is known to consist exclusively of an inflammatory process caused by the interaction of urate crystals with polymorphonuclear leukocytes in synovial fluid [7]. Furthermore, the systemic inflammatory response was also retrospectively confirmed by a serum TNF-α level of 60 pg/mL (reference level, <15 pg/mL). This report extends the work of previous studies that reported high PCT levels in clinical contexts where a diagnosis of bacterial infection had clearly been ruled out. For example, high PCT levels have been found in nonbacteremic patients after injection of pan-T cell antibodies [2] or TNF [3], or after cardiopulmonary bypass [4], during acute respiratory distress [5], and during the first days of life [6].

If the PCT concentration is to be considered a good marker for the diagnosis of bacterial infection, as was reported by Chirouze et al. [1], it must be kept in mind that PCT cutoff values used for clinical decision making must be context specific. As demonstrated by the present report, an ongoing and severe systemic inflammatory response that is not associated with bacterial infection may induce elevation of PCT levels.

References


Reply

Sir—In our article [1], we advocated that, for patients admitted to the hospital for suspected community-acquired infection, antibiotic administration could be deferred in the absence of signs of severe infection when the patient’s serum procalcitonin (PCT) level at admission is <0.4 ng/mL. Indeed, this threshold value was associated with a negative predictive value (NPV) as high as 98.8% for the diagnosis of bacteremic infection (95% CI, 0.95–1).

We totally agree with Villanueva and Cervin [2] that either the absence of bacteremia or the absence of any clinical evidence of severe infection are insufficient criteria for delaying antibiotic administration. In our practice, antibiotic therapy is initiated whenever there is clinical evidence of bacterial infection requiring such therapy (e.g., pneumonia or urinary tract infection [UTI], as Villanueva and Cervin [2] have emphasized. However, in a situation in which the initial diagnosis is uncertain, we deem it preferable to restrict indications for antibiotic therapy to those patients who need it most. In this respect, our study showed that PCT can precociously identify patients whose blood cultures would subsequently remain negative for bacterial growth. This strategy could help physicians refrain from overprescribing antibi-otics to patients with fever; such over-prescribing is a much too frequent habit, at least among French physicians, who prescribe more than twice as many antibiotics as do their German colleagues [3].

We would like to answer specific concerns raised by Villanueva and Cervin [2] regarding the number of cases of community-acquired pneumonia reported in our study and the complications that warranted hospitalization in this group. Of the 28 patients with respiratory tract infection, 6 had acute pneumonia, and 4 of these 6 patients were bacteremic (3 patients were infected with Streptococcus pneumoniae and 1 patient was infected with Klebsiella oxytoca). All 23 cases of UTI in nonbacteremic patients were uncomplicated pyelonephritis. Admission to the hospital of patients with a respiratory tract infection and patients with a UTI had been confirmed by the emergency department physicians.

Nylen et al. [4] question the validity of the NPV we found in our study, because the commercially available assay (Brahms Diagnostica) that we used reportedly is unreliable for measuring PCT levels of <0.3 ng/mL [5]. Although the so-called functional sensitivity [6] of this assay has been calculated to be 0.33 ng/mL, the assay’s lower limit of detection is actually 0.08 ng/mL. In our study, 50% of the pa-