Intensive Care Med (2002) 28:208–210
DOI 10.1007/s00134-001-1176-3

BRIEF REPORT

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Serum procalcitonin monitoring for differential diagnosis of ventriculitis in adult intensive care patients

Received: 17 January 2001
Accepted: 9 November 2001
Published online: 12 January 2002

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Abstract The objective of our study was to assess the value of serum procalcitonin (PCT) monitoring in the differential diagnosis of ventriculitis in adult intensive care (ICU) patients. We analyzed 15 consecutive patients with ventriculitis in which a ventricular catheter had been inserted and contrasted these data with the observations in 10 patients with community-acquired bacterial meningitis. Cerebrospinal fluid (CSF) and blood samples were collected daily to assess serum PCT, C-reactive protein (CRP) and CSF leukocyte count. PCT levels were normal or slightly elevated in patients with ventriculitis with either positive or negative CSF bacterial culture but elevated in patients with bacterial meningitis. A PCT cut-off value of 1.0 ng/ml or more showed a specificity of 77% and a sensitivity of 68% for ventriculitis with positive CSF bacterial culture. Serum PCT levels reflected more accurately the time phases of disease during therapy. We conclude that the monitoring of serum PCT alone is not helpful for the differential diagnosis of ventriculitis, in contrast to that of bacterial meningitis. The value of PCT as an additional marker with which to assess the efficacy of therapy in ventriculitis is suggested, but requires further assessment.

Keywords Procalcitonin · Ventriculitis · Meningitis · C-reactive protein · Ventricular drainage

Introduction

Ventriculitis in neurosurgical intensive care (ICU) unit patients is usually associated with favorable outcome and rarely with potentially lethal complications such as meningitis. Ventricular catheters used for both monitoring intracranial pressure (ICP) and draining the cerebrospinal fluid (CSF) when ICP is elevated are associated with a 10–17% incidence of ventriculitis [1]. Early diagnosis and treatment of ventriculitis are crucial for a good outcome, but little has been reported in the literature about its management. Microbiological and chemical analyses of both CSF and blood do not allow an early therapeutic decision based on the identification of a pathogen in culture [2]. Serum procalcitonin (PCT) has been reported as an excellent marker for generalized non-viral infection and sepsis [3, 4, 5] and is not elevated in response to non-infectious stimuli [6]. PCT is also a reliable parameter for differentiation between viral and bacterial meningitis [7, 8, 9], but it has not been systematically investigated in ventriculitis after ventricular catheter placement. We therefore measured PCT levels in

adults with ventriculitis, aiming to investigate the hypothesis that PCT levels would remain within the normal range in these patients but not in those with bacterial meningitis.

Patients and measurements

Fifteen consecutive patients with ventriculitis after ventricular catheter and ten patients with bacterial meningitis were prospectively studied. Table 1 shows the demographic data, the clinical severity of the disease and the microbiological findings. Diagnosis of ventriculitis was based on compatible clinical findings and either (1) a positive CSF culture or (2) negative culture but identification of bacteria on CSF Gram stain or (3) negative CSF culture accompanied by a CSF pleocytosis of less than 500 neutrophils/mm^3 with a predominance of 50% or more of polymorphonuclear cells. The diagnosis of bacterial meningitis was based on the criteria published by Durand et al. [10]. We excluded patients who had received antibiotic therapy before admission and patients with evidence of extracranial infection during monitoring. This study was conducted with the consent of the institutional ethics committee and informed consent for blood samples and data analysis was obtained from each patient or the patient's caretaker.

Clinical data including core body temperature, blood leukocyte (differential) count, platelet count, serum PCT and CRP (upper reference range: 10 mg/l) as well as CSF analyses (leukocytes, erythrocytes, protein, glucose) were collected daily for at least 10 days. In all patients hemodynamic, pulmonary, renal, hematological and coagulation parameters were constantly monitored, in mechanically ventilated patients also the arterial blood gases, the pH, the plasma lactate concentration and the base deficit.

The ventricular catheters were inserted under standard sterile conditions in the operating room. Manipulation for CSF collection was performed using sterile techniques. PCT levels were measured with an immunoluminometric assay (LUMItest-PCT, B.R.A.H.M.S. Diagnostica, Berlin, Germany) using a luminometer (Auto-CliniLumat LB 952, Wilbad, Germany). The detection limit of PCT was 0.1 ng/ml. The assay was specific for PCT using two different antibodies targeting two moieties (calcitonin and katacalcin) of the PCT molecule.

For statistical evaluation, we employed the non-parametric Mann-Whitney U test. Accuracy and cut-off levels for PCT and CRP were analyzed by the receiver operating characteristic curve (ROC), plotting sensitivity against specificity. Statistical significance was assumed at a p value of less than 0.05.

Results

According to CSF findings, 11 patients had ventriculitis with negative CSF bacterial culture (group I) and 4 patients ventriculitis with positive bacterial culture (group II). Ten patients suffered from community-acquired bacterial meningitis (group III).

Procalcitonin levels were normal or slightly elevated in patients with ventriculitis. The median PCT values were: 0.61 ng/ml (range: 0.1–1.9 ng/ml) in group I and 0.49 ng/ml (range: 0.1–1.8 ng/ml) in group II. At day 1 of study entry, the PCT levels in patients with ventriculitis were at detection limit in all cases (median PCT in group I: 0.2 ng/ml, range: 0.15–0.5 ng/ml; in group II: 0.3 ng/ml, range: 0.1–0.6 ng/ml). No significant correlation (Fig. 1) was found between serum PCT and CSF leukocyte count in patients with ventriculitis (p_I=0.51, p_{II}=0.43). Increased PCT levels persisted for a longer time in patients with ventriculitis and positive CSF bacterial culture compared to in those with negative CSF culture (p=0.035).

Table 1 Clinical severity and incidence of complications in the patient groups studied during PCT monitoring. Systemic inflammatory response syndrome (*SIRS*) was defined as involving at least two of the following criteria: core body temperature more than 38°C, tachycardia (heart rate >100 beats/min), tachypnea (>20 breaths/min), blood leukocyte count more than 12000 cells/mm^3. Shock was defined as systolic pressure of below 80 mmHg over 15 min. Pulmonary insufficiency was defined by a PaO_2 below 60 mmHg. Renal insufficiency was diagnosed by serum creatinine more than 200 µmol/l. Multiple organ failure (*MOF*) was defined as two or more organs/systems failure and requiring mechanical ventilation, dialysis or catecholamines administration

Parameter	Ventriculitis and negative CSF bacterial culture (n=11)	Ventriculitis and positive CSF bacterial culture (n=4)	Community-acquired meningitis (n=10)
Gender (M/F)	6/5	2/2	7/3
Mean age (years; range)	44.3 (17–67)	56.2 (47–64)	49.4 (21–74)
Glasgow Coma Score (median, range)	8 (4–15)	11 (6–15)	11 (7–15)
Mechanical ventilation initially (%)	8 (72.7)	1 (25)	3 (30)
Pulmonary insufficiency (%)	8 (72.7)	1 (25)	4 (40)
Renal insufficiency (%)	1 (9.1)	0	1 (10)
Shock (%)	2 (18.2)	0	0
Catecholamines requirement (%)	2 (18.2)	0	0
SIRS (%)	10 (90.9)	3 (75)	8 (80)
MOF (%)	1 (9.1)	0	0
Death (%)	1 (9.1)	0	0
CSF-culture/PCR findings (number of cases)	Negative	*Staphylococcus* species (2) *Propionibacterium acnes* (1) *Acinetobacter baumannii* (1)	*Staphylococcus* species (1) *Streptococcus* species (4) *Neisseria meningitidis* (4) *Escherichia coli* (1)

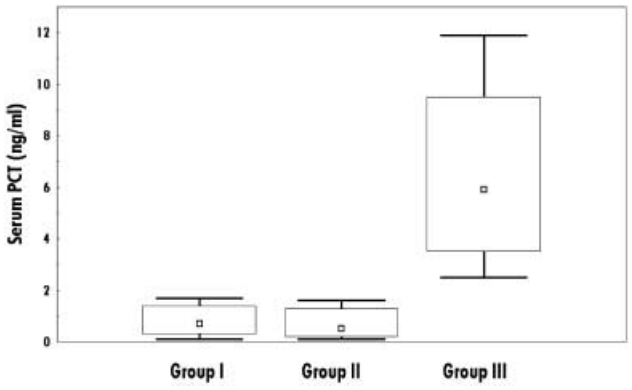

Fig. 1 Box-whisker-plot of initial serum procalcitonin (PCT) in patients with ventriculitis and negative CSF bacterial culture (group I, *n*=11), ventriculitis and positive CSF bacterial culture (group II, *n*=4) and community acquired bacterial meningitis (group III, *n*=10). Data are median (*squares*), 10th–90th percentiles (*boxes*) and range (*whiskers*)

There was a significant correlation (Fig. 1) between PCT and CSF leukocyte count (p=0.0005) in patients with bacterial purulent meningitis (group III). At day 1 of study entry, patients with bacterial meningitis showed the highest PCT levels (median: 5.2 ng/ml) ranging from 2.9 ng/ml to 11.9 ng/ml. The receiver operating characteristic (ROC) analysis showed that, at a cut-off of 1.0 ng/ml or more, the specificity and sensitivity of PCT for patients with ventriculitis and positive CSF bacterial culture were 77% and 68%, with ventriculitis and negative CSF bacterial culture 73% and 67% and with bacterial meningitis 100% and 83%, respectively.

C-reactive protein levels were elevated in all patients with either ventriculitis (group I: median: 32.3 mg/l, range: 0.1–229 mg/l; group II: median: 19.6 mg/l, range: 0.5–188 mg/l) or meningitis (group III: median: 119.1 mg/l, range: 0.8–517 mg/l). Serum CRP first increased under antibiotic therapy in patients with bacterial meningitis and remained elevated for 4–12 days. In patients with ventriculitis, CRP levels were increased at day 1 (group I median: 49.7 mg/l, group II median: 23.1 mg/l) and remained elevated for 7 and 5 days, respectively.

A correlation between neither CRP levels and CSF leukocyte count (p_I=0.51, p_{II}=0.59, p_{III}=0.65) nor blood leukocyte count and CSF leukocyte count (p_I=0.63, p_{II}=0.59, p_{III}=0.62) were observed in any of the groups.

Discussion

We report for the first time that, in patients with ventriculitis and ventricular catheter, the PCT levels usually remain within the normal range even in the presence of a positive bacterial culture. Possible explanations are as follows: firstly, ventricular catheter-related ventriculitis is a circumscribed infection without systemic involvement; secondly, the CSF of these patients was closely monitored for CSF leukocyte count and microbiological findings, hence any infection was detected early. Under these circumstances, the progression of a catheter infection to meningitis (which would elicit a systemic PCT release) was excluded. Monitoring of serum PCT alone (as well as CRP) was not helpful for the detection of catheter-related ventriculitis that did not progress to meningitis. PCT levels reflected the time phases of ventriculitis during therapy more accurately than CRP. Whether PCT monitoring is suitable to determine the efficacy of therapy requires further investigation.

References

1. Korinek AM and the French study group of Neurosurgical infections, the SEHP and the C-CLIN Paris-Nord (1997) Risk factors for neurosurgical site infections after craniotomy: a prospective multicenter study of 2944 patients. Neurosurg 41:1073–1079
2. Holloway KL, Barnes T, Chol S, Bullock R, et al. (1996) Ventriculostomy infections: the effect of monitoring duration and catheter exchange in 584 patients. J Neurosurg 85:419–424
3. Assicot M, Gendrel D, Carsin H, Raymond J, Guilbaud J, Bohuon C (1993) High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 341:515–518
4. Meisner M, Tschaikowsky K, Beier W, Schüttler J (1996) Procalcitonin (PCT): a novel parameter for diagnosis and monitoring of bacterial inflammation and sepsis. Anaesth Intensivmed 10:529–539
5. Reinhart K, Karzai W, Meisner M (2000) Procalcitonin as a marker of the systemic inflammatory response to infection. Intensive Care Med 26:1193–2000
6. Meisner M, Tschaikowsky K, Hutzler A, Schick C, Schüttler J (1998) Postoperative plasma concentrations of procalcitonin after different types of surgery. Intensive Care Med 24:680–684
7. Gendrel D, Raymond J, Assicot M, et al. (1997) Measurement of procalcitonin levels in children with bacterial or viral meningitis. Clin Infect Dis 24:1240–1242
8. Schwarz S, Bertram M, Schwab S, Andrassy K, Hacke W (2000) Serum procalcitonin levels in bacterial and abacterial meningitis. Crit Care Med 28:1828–1832
9. Viallon A, Zeni F, Lambert C, et al. (1999) High sensitivity and specificity of serum procalcitonin levels in adults with bacterial meningitis. Clin Infect Dis 28:1313–1316
10. Durand M, Calderwood S, Weber D, et al. (1993) Acute bacterial meningitis in adults. N Engl J Med 328:21–28