A new parameter in the differential diagnosis of bacterial and viral meningitis

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Meningitis, since described first in the year 1805, has been one of the major lethal infectious diseases especially for the neonates and elderly in developing countries.[1] It is not always possible to distinguish between bacterial and viral meningitis according to CSF findings, which leads to unnecessary antibiotic usage.[2] During the last few years, procalcitonin (PCT) has been a new parameter in the diagnosis of systemic infections, observation of the progression of diseases and response to treatment.[3] Procalcitonin is a peptide consisting of 116 amino acids and the prohormone of calcitonin, the hormone composed of 32 amino acids and synthesized by the C cells of the thyroid gland. The basal PCT level measured with LUMI test PCT assay in a healthy person is <0.5 ng/ml. The PCT can be used as a parameter of bacterial infection induced systemic inflammation (sepsis, septic shock). Bacterial toxins have the major role in PCT production. Conditions like sepsis, septic shock, and multiple organ failure, in which the bacterial toxins are involved in the etiology are characterized with high PCT concentrations like 10-100 ng/ml.[4] The production and increase in the plasma level of PCT correlates with the type and dissemination of the inflammation. Also, it reflects the severity of the disease and the progression of the inflammatory activity in patients with sepsis. The PCT, not only a diagnostic marker, is also useful in assessment of prognosis and evaluation of the treatment effectivity.[4] This study was performed to search for the PCT levels in the early period of bacterial and viral meningitis in pediatric patients and its utility in early diagnosis.

This prospective study was conducted in patients hospitalized with the diagnosis of meningitis between January and June 2001 in the Department of Pediatric Infectious Diseases, SB Bakirkoy Maternity and Childhood Diseases Training Hospital, Istanbul, Turkey. Informed consent from the parents of all patients was provided and the hospital ethics committee approved the study protocol. Thirty patients with the diagnosis of bacterial (n:16) and viral (n:14) meningitis according to CSF findings and culture results without any history of systemic antibiotic or corticosteroid use in the previous one week, were included in this study. The mean age was 3.2 ± 4.36 years, range 3 months to 12 years, 50% boys for bacterial meningitis and mean age was, 5.2 ± 3 years, range 6 months to 13 years, 78% boys for viral meningitis. The diagnosis of bacterial meningitis was made according to the documentation of infection in CSF culture, CSF pleocytosis (>10 cells/mm^3) and predominance of polymorphonuclear neutrophilic leukocyte (PNL) in direct examination of CSF, presence of bacteria in direct examination of CSF, CSF glucose: blood glucose ratio <0.6, increase in CSF protein, and positivity of bacterial antigens in CSF. The patients with predominance of lymphocytes in CSF pleocytosis, slight increase in protein, and with normal glucose levels in CSF, no bacteria in direct examination of CSF and negativity of bacterial antigens were considered to have viral meningitis. From all patients in the 2 groups, blood samples were drawn and a lumbar puncture was performed prior to treatment. Leucocyte count, absolute neutrophil count (ANC) of blood, blood culture, erythrocyte sedimentation rate (ESR), procalcitonin, and cell count, direct examination, latex agglutination, culture, glucose, and protein levels of CSF were studied (**Table 1**). In all patients with the diagnosis of bacterial meningitis ampicillin + cefotaxime treatment was started, whereas viral meningitis cases were followed with symptomatic treatment. Plasma PCT level was determined in 24 hours with an immunoluminometric assay (LUMItest PCT, B.R.A.H.M.S. Diagnostica GmbH, Henningsdorf/Berlin, Germany). C-reactive protein (CRP) was studied in a qualitative manner. The comparison of 2 groups was made with the nonparametric Mann Whitney U test.

Table 1 - Comparison of cerebrospinal fluid (CSF) findings, blood leucocyte, erythrocyte sedimentation rate (ESR), and procalcitonin (PCT) in cases of bacterial and viral meningitis.

Variable	Bacterial meningitis (n=16)	Viral meningitis (n=14)	Z-test	*P*-value
Cell count (/mm^3)	1693±1352.76	255.71±128.47	-4.667	p=0.001
Protein (mg/dl)	154.88±50.36	37.79±23.43	-4.663	p=0.001
CSF glucose/blood glucose (%)	0.4794±8.98 E-02	7171±5.8 E-0.2	-4.663	p=0.001
Leucocyte (/mm^3)	17856.25±5667.45	9550±4773.77	-3.266	p=0.01
ESR (mm/h)	96.06±25.46	33.14±23.28	-4.332	p=0.001
PCT (ng/ml)	21.9±12.45	0.35±4.95 E-0.2	-4.639	p=0.001

In 16 patients with bacterial meningitis (50% boys) the diagnosis was established with lumbar puncture. In 14 patients (85.7%) leucocytosis and neutrophilia were detected on first admission and CRP and ESR levels were increased in all patients (100%). On CSF examination, the protein level was >0.1 g/lt in 14 cases (87.5%) and CSF glucose/blood glucose ratio <0.6 in 13 cases (81%). In 14 patients with viral meningitis (78% boys) leucocytosis was detected in 3 (21.4%), neutrophilia in 4 (28.6%), increased ESR in 5 (35.7%), and CRP in 5 (35.7%) patients. The CSF pleocytosis with predominance of lymphocytes was present in all but 2 patients with viral meningitis. None of the patients with viral meningitis had bacteria in CSF direct examinations and all had sterile CSF and blood cultures. Ten (71.5%) of the cases had history of parotitis at the time of admission or within one week time. The CSF protein was slightly increased in 3 (21.4%) cases and glucose was normal in all patients. The comparison of the 2 groups showed significant differences for blood leucocyte counts (p=0.01), sedimentation rate and plasma PCT levels (p=0.001). When the CSF findings of the 2 groups were compared, a significant difference was detected in cell count, protein level and the ratio of CSF/blood glucose (p=0.001). With the cut off value of 0.5 ng/ml, plasma PCT level was in the normal range in all patients with viral meningitis and high in 15 (93.7%) patients with bacterial meningitis (mean ± SD: 21.9 ± 12.45) except one patient with normal level. With these results, in 30 patients diagnosed as meningitis, using a cut off value of 0.5 ng/ml for PCT showed a sensitivity of 93.7%, specificity of 100%, positive predictive value of 100% and negative predictive value of 93.3%.

In the last few years, serum PCT level has been reported to be useful in the establishment of severe bacterial infections and in the follow up of treatment. To date, there have been only a few reports in the literature on serum PCT as a marker in the differential diagnosis of meningitis in childhood.[5] In these studies, serum PCT was shown to be sensitive and specific with a range of 69-100%.[5] In the study reported by Schwarz et al,[5] sensitivity of PCT was lower (69%). The current study showed that PCT was as specific as the CSF leucocyte count, CSF:blood glucose ratio, and protein level (100%), but more specific than CSF:PNL ratio (85.7%). The PCT was observed to be more sensitive (93%) than CSF leucocyte count (75%), CSF protein level (85.7%), CSF:blood glucose ratio (93%), but less specific than CSF PNL ratio (100%).

The small number of cases can be a limitation of this study. Most of the viral meningitis cases were composed of mumps meningitis and this can limit the results to be generalized to all viral meningitis cases. The number of studies concentrating on PCT is still not enough, and further studies are needed. In conclusion, serum PCT level is a new parameter that can be used in the diagnosis of bacterial meningitis with those classical parameters.

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