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New Technique uses to Evaluate Cerebrospinal Fluid Lactic Acid as an Aid Differential Diagnosis of Bacterial and Viral Meningitis

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Abstract:

The level of lactic acid in cerebrospinal fluid has been suggested as useful diagnostic. Parameter to differentiate between bacterial and viral meningitis, especially in patients partially treated before admission to hospital. A concentration of> (35 mgm/dl) determined by an enzymatic methods has been considered in several studies to provide definite evidence of meningitis of bacterial origin,whereas lower level indicates no bacterial involvement, over past (20) months we had analyzed by the enzymatic methods, the lactate level in (302) cerebrospinal fluids submitted from adults patients with various conditions involving in central nervous system. Fifty fluids had lactate levels of> (35 mg/dl) of which (162) were cases of infective meningitis of varying etiology.

In this adults study the lactate level in the cerebrospinal fluid did provide equivocal evidence of bacterial infection and provide assistance to any greater degree than the standard parameters of leucocytes counts, protein and glucose contents in the differential diagnosis of bacterial meningitis from that of any other etiology.

Introduction:

The concentration of lactic acid in cerebrospinal fluid (CSF) in patients with suspected infective meningitis as auseful parameter to differentiate bacterial from viral or noninfectious etiology.It was hoped that this test might be especially useful in patients with bacterial meningitis partially treated before hospitalization. Alactate level of 35 mg/dl or greater has been considered as definitive evidence of bacterial involvement. The purpose of this study is to report our findings with emphasis on lactic acid levels in cases of infective meningitis in adukts and to discuss the usefulness of the test in our experience.

Material and Methods:

Study population: All patients were adults ranging in age from 16 to 86 years. A total l98 (65.5%) were males; 104 (34.5%) were females. These 302 patients from

whom 302 specimens of CSF were received in Teaching Laboratory in Medical City Hospital Baghdad, all had a greater or lesser degree of central nervous system involvement as part of their illness. The underlying pathology, which varied in seriousness; included intervertebral disc disease, multiple sclerosis, primary or metastatic neoplasms, intracranial hemorrhage meningitis and metabolic disorder.

The majority of the patients admitted to hospital with primary meningitis had received no antibiotics before admission. In several cases, it was it was not possible to obtain a clear history because of the confused mental status of the patients; but no patient received more than one to two prehospital doses of chemotherapy and it was felt that this did not influence of lactic acid levels.

Examination of CSF: The 302 specimens of CSF represented all such samples submitted to our laboratory over an (20) months periods. The following tests were carried out on each specimen.

Cell counts: The cell count was performed on all mixed unspan sample of CSF unstained in a Fuchs-Rosenthal counting chamber. Corrections were made for total leucocytes present with regard to the number of erythrocytes in the specimen. When greater than none leucocytes per mm3 were found, a, differential count was made on a Gram-stained preparation of the sediment after centrifugation of the fluid. A search for organism was carried out on the same preparation

Microscopic examination: Gram-stained smears for bacteria and India ink preparation of Cryptococcus were routinely performed, Auramine O stains for Mycobacterium tuberculosis[1] were made whom indicated on the basis of cell count, differential count, glucose and protein concentrations and clinical history.

Culture: Cultures were made for bacteria, fungi, viruses and *M. tuberculosis*. If these was insufficient fluid, this routine was modified to the most appropriate cultures on the basis of cell count, glucose and protein concentration and clinically history, but always the specimens was cultured for bacteria.

Protein Concentration:

Total protein concentration was determined by a 3% trichloroacetic acid precipitation method [2]. Reading were made with a Colman Spectrophotometer; appropriate standard and control were included in all determination. Results were expressed in milligram per deciliter (mg/dl).

Glucose Concentration: An ortho-toludine method was used to determine glucose concentration.Approperiate standards were used in each test. Results were expressed in mg/dl.

Lactic acid Concentration: An enzymatic method was employed using nicotinamide adenine dinucleotide and lactic dehydrogenase (Sigma chemical Company). Reading was taken with Colman Spectrpphotometer at 340 nm. Standard curve of lactic acid concentrations were used to determine the unknown lactic acid concentration in the speciemen; results were expressed in mg/dl.

Result:

The mean lactic acid level of all samples regardless of etiology was 21 mg/dl with a standard deviation of+/- 12.1. Levels ranged from 11 to 140 mg/dl. Fifty fluids from 43 patients were found to have lactic acid level of > 35 mg/dl; of these 32 cases of infective meningitis of varying etiology of which eight were nonbacterial, presumed viral in origin (Table-1).The remaining 24 patients with elevated lactic acid levels had a variety of intracranial or metabolic disorders (Table-2). In the remaining 270 patients with CSF lactic acid levels >35 mg/dl, there were 17 cases of infective meningitis of which two were of proven bacterial etiology and two were proven cryptococcal meningitis (Table-3). Three patients with meningococcal meningitis had repeat lumber punctures after a 14 days course of therapy; results are shown in (Table-4). The complete CSF profile of all 33 cases is displayed in (Table-5).

Etiology	**No.of Cases**
Neisseria meningitis	12
Streptococcus pneumoniae	2
Listeria monocytogene	1
Haemophilus influenzae	2
Staphylococcus aureus	2
Brain abscess and meningitis (anaerobic)	2
Candida albicans	1
Streptococcus epidermidis, infected ventriculo-peritoneal shunt	1
Enterococcus, posttraumatic	1
Viral or presumed viral	8

Table-1: Cases of infective meningitis with CSF lactate levels > 35 mg/dl

Etiology	No.of Cases
Postcraniotomy	5
Subarchnoid hemorrhage	3
Head trauma	3
Cerebral metastases	3
Pneumonia, confusion hypoxia	2
Subdural hematoma	1
Postoperative hydrocephalus	1
Lymphomatous meningitis	1
SBE? Septic emboli	1
Postcardiac arrest	1
Coma,metabolic acidosis	1
Undiagnosed	2

Table-2: Cases of noninfectious intracranial pathology with CSF lactate ≥ 35 mg/dl

Etiology	No. of cases
Haemophilus influenzae	2
Cryptococcus neoformas	2
Enterovirus	1
Other viral or presumed viral etiology	12

Table-3: Cases of infective meningitis with CSF lactic acid level> 35 mg/dl

Case		Cell Count	Mg/dl		
			Glucose	Protein	Lactic acid
1	Day 1 (pre)	877	15	88	120
	Day 14 (post)	40	35	71	35
2	Day 1 (pre)	2.700	25	194	78
	Day 14 (post)	30	50	75	21
3	Day 1 (pre)	1500	20	222	86
	Day 18 (post)	2	46	32	45

Table-4; Lactic acid levels pre-and posttreatment in meningococcal meningitis

Case	Cell counts	Glucose	Protein	Lactic acid	Gram - stain	Culture	Diagnosis
1	16,200	0	290	140	+	+	Neisseria meningitis
2	827	15	88	120	+	+	Neisseria meningitis
3	42	180	133	40.5	-	+	Neisseria Meningitis
4	14,000	N.D.	N.D.	100	+	+	Neisseria meningitis
5	2,700	25	194	78	+	+	Neisseria meningitis
6	1,500	20	222	86	+	+	Neisseria meningitis
7	13,800	62	130	42	+	+	Strep. pneumoniae
8	300	20	290	64.5	+	+	L. monocytogensis
9	5,200	55	162	56	-	+	H. influenzae
10	1600	50	106	48	-	+	Staphylococcus aureus
11	98	40	140	60	+	+	Staphylococcus aureus
12	3,200	25	210	130	-	+	Mixed anaerobic
13	2,700	40	252	57	+	+	Mixed anaerobic
14	209	80	48	42	-	-	Candida albicans
15	53	120	40	59	-	-	Viral meningitis
16	1,700	70	88	96	-	-	Viral Meningitis
17	13	65	142	24	-	-	Viral Meningitis
18	1,120	57	86	13.5	-	+	Staph. epidermidis
19	800	20	142	96	+	+	Enterococcus
20	192	45	86	24	-	+	Cryp. neoformis
21	160	40	75	13.5	-	+	H. influenzae
22	2	85	18	24.5	+	+	Cryp. neoformis
23	197	70	37	24	-	-	Viral meningitis
24	126	55	50	29	-	-	Viral meningitis
25	60	60	35	21	-	-	Viral meningitis
26	196	40	60	29	-	-	Viral meningitis
27	3	55	22	20	-	-	Viral meningitis
28	4	65	48	15.5	-	-	Viral meningitis
29	1	65	37	13.5	-	-	Viral meningitis

Case	Cell counts	Glucose	Protein	Lactic acid	Gram - stain	Culture	Diagnosis
30	60	45	55	27	-	-	Viral meningitis
31	1	60	23	11	-	-	Viral meningitis
32	3	75	32	27	-	-	Viral meningitis
33	1	65	28	16	-	-	Viral meningitis

Table-5: Complete CSF profile of 33 cases of infective meningitis

Discussion:

During the course of this study our purpose was to ascertain whether the lactic acid level in CSF should be introduced as part of our routine for processing spinal fluids. We did not report the lactic acid levels to the attending staff unless it was specifically requested, there were major false positive and false negative among the cases of infective meningitis. The false negative were the most worrisome in that one case of haemophilus influenza meningitis and two cases of cryptococcal meningitis had lactate levels below 35 mg/dl case 20,21,and 22) , and with Haemophilus influenza meningitis was culture positive, but the other parameters including lactic acid level were little help. Clinically this patient was severly ill and despite the immediate CSF findings was treated as having bacterial meningitis with both penicillin and chloramphenicol pending culture results. Case 22 was a renal transplant patient who presented with fever, nuchal rigidity and confusion. Despite the benign CSF parameter, the india ink preparation was positive as was culture. Case 20 was apparently classical viral meningitis from CSF analysis, however the culture was positive for Cryptococcus neoformis as was asample of aspirate from an upper lobe lesion in the right lung. This patient had no underlying disease and was perfectly healthy before presenting with symptoms.

The three cases of presumptive viral meningitis (case 15,16 and 17 Table 5), with lactic acid levels of > 35 mg/dl all had cell counts, protein and glucose levels and a clinical picture suggestive of viral etiology. Culture for bacteria, viruses and M.tuberculosis were well all negative. Case 17 was restudied at 24 and 48 hours to ensure that no bacteria were present and the patient was not treated with antibiotics at any time; by 48 hours the lactate level had returned to > 35 mg/dl and the patient made on uncomplicated recovery without specific therapy. She had no other disorder that might have accounted for the elevation of lactic acid.

On further cases deserved mention (case 3) in this case it appeared that the elevated lactate could have helped to make the diagnosis of bacterial as opposed to nonbacterial meningitis, however clinically this patient was severlyobtunded with

fever and nuchal rigidity; despite the low cell count,the fluid was turbid and this plus the clinical presentation was highly suggestive of bacterial infection and was treated as such pending culture results which positive within 24 hours. Some of the cases of viral meningitis (case 27 to 33, table-5) were not seen by the infectious diseases consultation team; the diagnosis is taken from the discharge diagnosis in the medical records. The low cell count i.e <5 makes the diagnosis of viral meningitis questionable, however all these patients had lactic acid (and all other measure parameter) within the normal ranges.

References:

1- Mulemans,O. (1960). Determination of total protein in spinal fluid with sulphosalicylic acid and trichloroacetic acid Clinical Chemistry Acta. 5: 757-761

2 - U.S. Department of Health Education Welfare(l975). Procedure for isolation and identification of Mycobacteria. U.S. Department of Health Education and Walfare, Washington D.C.