

MEDICAL GRAND ROUNDS

Parkland Memorial Hospital

November 16, 1962

Evaluation of Spinal Fluid in "Aseptic" Meningitis

CASE #1: [REDACTED]

This 48-year-old [REDACTED] male laborer was in good health except for mild chronic cough, and developed headache and dizziness one day prior to admission. On the evening of admission he was observed to abruptly stop speech, stare blankly for a moment, then develop a brief grand mal seizure. He was brought to the EOR, where another seizure was observed. Admission physical examination revealed postictal stupor which gave way to mental clarity after 20 to 30 minutes. Temperature 100°, BP 115/80, P 75 and R 18. Neck was supple, ENT exam negative and fundi normal. Neurological exam was completely normal, as were heart, lungs and abdomen. Admission WBC was 20,000 with 90% polys. CSF exam revealed OP 16 cm., 28 mononuclear cells, protein of 50 and glucose of 92. Bacterial smear and culture of the fluid were negative. Blood and CSF Wasserman reactions were negative.

Differential diagnosis on admission included brain tumor, brain abscess, subdural hematoma and aseptic meningitis, and a course of expectant observation was elected. The next 48 hours were marked by varying sensorium and intermittent brief seizures. On the 3rd hospital day he became comatose and had marked nuchal rigidity without localizing neurological signs. Repeat CSF exam revealed pressure of 28 cm., 1700 WBC (90% PMN), protein 546 mg. and glucose 9 mg.% with blood sugar of 100. Smear of CSF revealed gram-positive diplococci and culture was ultimately positive.

Large doses of penicillin and steroids were instituted and by the 3rd day of therapy, the patient was lucid and afebrile. CSF exam on the 7th day revealed 300 WBC (60% monos), protein 92, sugar 50; smear and culture were negative. X-rays of skull, mastoids and sinuses failed to reveal lesion predisposing to infection. He was well when discharged on the 15th day.

CASE #2: [REDACTED] [REDACTED]

This 39-year-old [REDACTED] was well until 2 weeks prior to admission when she developed vague malaise. A week later she noted dull occipital and temporal headaches which initially responded to ASA. Two days prior to admission here her headache became quite severe and she noted fever for the first time. She was hospitalized in another city and was given penicillin 400 TU q4h and an unknown amount of chloramphenicol over a 36-hour period. Because of persistence of symptoms on this regimen, she was referred to [REDACTED].

Admission physical exam revealed temperature of 102°, BP 140/88, P 82, R 14. ENT exam was normal. There was no papilledema. Except for moderate nuchal rigidity, there was no neurological abnormality. The lungs, heart and abdomen were negative.

Admission WBC was 15,000 with 65 segmented forms. CSF exam revealed a mononuclear pleocytosis, normal sugar, modestly increased protein and negative bacterial smear.

It was felt that the patient most likely had "aseptic" meningitis with partially treated bacterial meningitis being a worrisome possibility. She was placed on supportive care and seemed to gradually improve. A repeat CSF examination on the 4th hospital day revealed a slight diminution in cell count without significant change in other respects. The admission CSF had been found sterile, so the patient was continued on supportive treatment.

On the 6th hospital day the patient's headache became worse and her temperature spiked to 103°. Neurological examination remained unchanged except for possible increase in nuchal rigidity. CSF exam revealed a marked PMN pleocytosis, hypoglycorrhachia, protein of 360 and equivocal gram-positive cocci on smear. On the basis of a presumptive diagnosis of pneumococcal meningitis, she was begun on large doses of penicillin. Over the next 2 weeks her temperature ranged from 102-103°; headache and mild nuchal rigidity persisted. An arteriogram on 9/1 was negative, as were sinus and mastoid x-rays. By the 14th hospital day there was unequivocal papilledema and the patient was somnolent, intermittently irrational. Ventriculography on the 30th hospital day revealed cerebral edema without definite evidence of block between the ventricles. During the 5th week the patient became afebrile despite continuing CSF pleocytosis and evidence of increased intracranial pressure. On [REDACTED], 2-1/2 months after admission, ventriculography revealed internal hydrocephalus and a Torkildsen shunt procedure was performed. There was a brief period of unexplained fever and leukocytosis following surgery and she was given penicillin and polymyxin B as empirical therapy for possible surgical infection. Over the ensuing month, the spinal fluid returned to normal in all respects. The patient, however, continued to manifest bizarre behavior and confusion until discharge on [REDACTED]/60.

At follow-up on [REDACTED] 1961, neurosurgical consultant found no neurological defect.

Date	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
CNS	headache nuch.rig.	same	↑ headache ↑ nuch.rig.	headache somnolence papilledema	irrational stupor	bizarre behavior & vision	same	same
WBC	15.2	9.7	23.0	10.6	10.5	7.5	12.7	8.0
Temp.	102	101	103	103	101	99	102	98
CSF								
Pres. (cm)	24	17	>30	>30	50	33	22	?
Cells	900	450	3500	400	500	50	2	0
% PMN	33	40	90	80	90	50	0	0
Sugar	100	102	134	106	121	120	110	?
bs/csf	47	52	14	27	43	56	48	75
Cl	114	108	119	—	—	—	—	—
Prot.	111	91	360	124	175	150	140	40
Smear	0	0	? gm.+ cocci	0	0	0	0	0
Cult.	0	0	0	0	0	0	0	0
Antib.			Pen ———→ 15 mu/day	Pen ———→ 2.4 mu Benemid Chloro 2u	—————dc'd		Duracillin ———→ 2.4 mu/day Poly B ———→	
					↑		↑	
					Ventriculography Cerebral edema		Torkildsen procedure	

CASE #3: [REDACTED]

This 15-year-old [REDACTED] girl was well until 2 weeks prior to admission, when she developed mild retro-orbital pain and low-grade fever. One week later, because of increased severity of headache, she was seen in [REDACTED], where no physical abnormality was found except temperature of 102°. WBC was 7500 with normal differential. She was thought to have a viral syndrome and was discharged on symptomatic care. Two days prior to admission she was evaluated by her private physician, who administered one injection of penicillin. Fever and headache persisted and the patient was admitted to [REDACTED] on [REDACTED]/62.

Family history revealed that the patient's sister had been admitted to [REDACTED] 1 year ago with arthritis of a knee; biopsy of synovium revealed granuloma and acid-fast bacilli on fluorescent microscopy.

Pertinent features of the admission physical exam included temperature of 104°, lethargy and mild pain on flexion of neck. Fundi were normal and no neurological defect could be demonstrated. Lungs and heart were normal. Peripheral WBC was 9000. CSF exam revealed OP 120 mm., 300 WBC (90% mononuclears), protein 160, glucose of 44 mg.% with blood sugar of 120. Bacterial smear was thought by ward physicians to show equivocal cocci and on the basis of this finding, she was started on large doses of penicillin. Fever persisted and because of the hypoglycorrhachia found on the 5th hospital day, antituberculous drugs and steroids were begun. Fever continued at 102-103° level until the third week, when temperatures gradually dropped to 99-100°. Dull mentation persisted and during the 2nd hospital week she developed a transient right 6th nerve palsy. During the last 4 weeks of hospitalization, she was asymptomatic and physical exam was unremarkable except for mental dullness — questioning of family reveals this is probably her usual status.

All CSF cultures have remained negative. Fungal agar diffusions and complement fixations were negative, as were the viral CF. Intermediate strength PPD was negative on admission; repeat challenge prior to discharge revealed a 12 mm. reaction.

She is at present being followed on INH and PAS on an out-patient basis.

Date	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Temp.	104	104	104	103	103	99	98
CSF Pressure (cm)	120	400	180		150	130	105
Cells	300	180	400		400	100	80
% PMN	10	10	20		20	50	40
Sugar	120	*170	106		110	84	72
bs/csf	44	51	26		32	34	43
Cl	—	—	97		110	118	120
Prot.	160	—	236		420	79	70
Smear	?	0	0		0	0	0
Routine & AFB Culture	cocci	0	0		0	0	0
Rx	Pen 10 mu/day			Meticort. 40/day Strep, INH, PAS			

* IV glucose running

CASE #4: [REDACTED]

This 44-year-old NM with a 3-month history of productive cough, anorexia and 15 lb. weight loss developed aching pain in his low back 2 weeks before hospitalization. For one week prior to admission, he complained of severe, generalized headache and, on the day of admission, he was observed to manifest bizarre behavior and to speak incoherently.

On admission to a [REDACTED] hospital, salient features of the physical exam included temperature of 101°, mental confusion and nuchal rigidity. There were no localizing neurological signs. Except for evidence of recent weight loss, physical examination was otherwise unremarkable. CSF exam was reported as revealing 224 WBC (88% PMN), protein of 80 mg.%, sugar of 70 mg.% and negative serology. Bacterial smear and culture were negative. He was treated for 4 days with multiple antibiotics including penicillin and chloramphenicol. Because of deterioration in the face of therapy, he was transferred to [REDACTED].

On admission here, the physical exam revealed the patient completely disoriented. BP 140/90, P 86, T 100.8°, R 20. There was marked nuchal rigidity, but no localizing or lateralizing neurological signs. Exam of lungs, heart and abdomen revealed no abnormality. A chest x-ray was thought to be within normal limits. WBC was 10,500 with 70% PMNs. CSF exam revealed OP 200 mm., 46 WBC (33 PMN), protein 126, glucose 26 with blood sugar 115. Blood serologies were negative. CSF and bacterial smears were negative, as was India ink prep. PPD #2 was positive after 24 hours. AFB smears of sputa were negative. A presumptive diagnosis of tuberculous meningitis was made and streptomycin, INH and steroids were instituted. Mental confusion and nuchal rigidity persisted and on the 3rd hospital day he developed diffuse rhonchi throughout the chest, temperature of 102° and leukocytosis of 20,000. Chest x-ray revealed a RUL consolidation and patchy infiltrate throughout the left lung. Tracheostomy was performed and penicillin and tetracycline were added to the regimen. Fever persisted as did evidence of progressive pneumonia. At no time did localizing neurological signs develop. He expired, presumably due to respiratory failure, on the 16th hospital day.

CSF studies on the 4th, 7th and 10th hospital days revealed mild mononuclear pleocytosis (30-40 cells) and glucose levels between 25-30 mg.%. Two studies for malignant cells were performed on CSF and were negative. Complement fixation studies for LGV, LCM, WEE, SLE, EE and mumps were negative, as were fungal complement fixations.

Autopsy revealed bronchogenic carcinoma with metastases to brain and meninges.

CASE #5: [REDACTED]

This 33-year-old [REDACTED] [REDACTED] was admitted for evaluation of mental confusion which had been present for 4 days prior to admission. She had been observed to talk incoherently and to have difficulty in walking over the same period. Prior to the onset of these symptoms, she had apparently been in perfect health.

Salient features of admission physical examination included disorientation, temperature of 99°, widely dilated and non-reactive pupils, early papilledema bilaterally and minimal nuchal rigidity. There were no localizing neurological signs and the remainder of the physical was normal.

WBC was 12,000 with 75% PMNs. CSF exam revealed opening pressure of 30 cm., 250 WBC (60% mononuclears), protein of 120 mg.%, and glucose of 32 mg.% with blood sugar 90. Bacterial smear and culture were negative. CSF Wasserman was positive 1:16 dilutions, blood value of 1:64. Second strength PPD was negative. Reinsch test on urine was negative.

Because of the mononuclear pleocytosis associated with hypoglycorrhachia, it was felt she should be treated for tuberculous meningitis; at the same time, penicillin was instituted for therapy of lues. By the 5th day of therapy, the patient's sensorium had cleared remarkably and by the time of discharge on the 15th day, she was considered neurologically normal. She was discharged on INH and pyridoxine and, at follow-up 2 months later, she was asymptomatic and physically normal. Repeat CSF evaluation was not done.

CASE #6: [REDACTED]

This 66-year-old NM was admitted to [REDACTED] in a lethargic, confused state. He had been ill for one month with severe headaches, occasional vomiting and diarrhea, general malaise, somnolence and low-grade fever. Before the onset of his illness, he had been employed at a metal smelting plant for several years. Admission physical exam revealed temperature 99.4°, semistupor, right central facial palsy, slight increase of the right knee jerk and an equivocal right Babinski. There was no apparent sensory deficit. Admission lab revealed hemoglobin 13 without basophilic stippling of RBC, WBC 13,000 with 86% segmented forms. CSF revealed OP 45 mm., 92 lymphocytes, protein 158 with glucose 40 mg.%. Bacterial smears, India ink prep, and routine culture of CSF were negative.

A presumptive diagnosis of lead poisoning with encephalopathy was supported by urine lead values of 2-3 mg./day during therapy with calcium disodium versenate. Multiple CSF examinations revealed pressure of 30-60 mm., few mononuclear cells, protein 150-200, and sugars of 2 mg.% to 40 mg.%. All fluids were examined by smear, India ink preparation and culture without detecting pathogens. Tuberculin and fungal skin tests were negative on admission and on repeat challenge later in the course.

The patient's sensorium and neurological picture remained unchanged and he continued to run low-grade fever. On the 20th hospital day, he developed respiratory distress with physical and x-ray evidence of bronchopneumonia. He was given penicillin and streptomycin in addition to mechanical respiratory assistance. The downhill course was relentless, however, and he became comatose and died on the 22nd hospital day.

Autopsy revealed widespread miliary tuberculosis with meningoencephalitis. Ultimately, several spinal fluid specimens grew out M. tuberculosis.

CASE #7: [REDACTED]

The patient is a 53-year-old [REDACTED] male accountant from [REDACTED] Texas, who has been followed with cryptococcal meningitis.

Present illness: The salient features of the present illness include an episode of pneumonitis in 1950, which was of a rather prolonged nature. In 1954, he developed

a draining sinus in the lumbosacral area which was surgically excised. Culture of this was reported as sterile. In 1954, the patient had a single grand mal seizure and has had none since that time. In the latter part of 1954, he developed multiple draining sinuses in the lumbosacral area. He was seen by Dr. W. Tschumy in [REDACTED] 1955, at which time a diagnosis of cryptococcosis was made and borne out by culture of the organism (Cryptococcus neoformans) from the sinus. At that time the patient had cells in his spinal fluid and a low spinal fluid sugar. He was treated with hydroxystilbamidine and sulfa. Shortly following initiation of therapy, he was transferred to PMH, where therapy was continued. Following a course of therapy, because of the development of skin pigmentation and weakness the patient was evaluated for Addison's disease. 17-ketosteroids were within normal limits.

He was finally discharged in [REDACTED] 1956 and had done remarkably well. He worked as a [REDACTED] until 2 days prior to readmission on [REDACTED] 1958. In [REDACTED] 1958, he began to note generalized ease of fatigue, difficulty in mental concentration and anorexia. His wife also stated that he had difficulty in walking. Physical examination at that time revealed blood pressure 100/60 and he was afebrile. Physical exam was within normal limits except for a palpable liver and spleen. Neurologic examination revealed presence of Romberg's sign with the patient falling to the right. Laboratory findings included hemoglobin 15 gm.%, WBC 3200 with 85% polys. Spinal fluid findings are listed below. A Congo red test revealed 66% of the dye remaining in the serum after one hour. The patient was begun on amphotericin B therapy and received 345 mg. over a period of one month. He failed to show dramatic clinical improvement and was discharged prior to the Christmas holidays.

Following his discharge he did remarkably well, returning to work, which he continued until the time of his readmission in [REDACTED] 1960. In [REDACTED] 1960, he began to note drowsiness, confusion and difficulty with his gait.

On admission on [REDACTED]/60, he seemed more alert than on his previous admission. He had no generalized lymphadenopathy. The liver and spleen were still palpable. There was a draining sinus on the wing of the left ileum. This lesion was biopsied; however, organisms were not noted on special stain or culture.

Other laboratory findings included hemoglobin 14.0 gm.%, WBC 4000 with 87% polys, which persisted in the range of 2-3,000 throughout his hospital course. Albumin 4.0 gm.%, globulin 2.1 gm.%.

He was restarted on amphotericin B therapy and received a total of 1.51 gm. without significant untoward effects.

Following completion of his therapy, he has returned to work and when seen early in 1962 by Dr. Tschumy, was doing very satisfactorily.

Date	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED] 58	[REDACTED] 58	[REDACTED] 60	[REDACTED] 60	[REDACTED] 60
Pressure	nor.	3	—	7.8	—	7.0	11.0	12.6
WBC	49	84	15	16	0	76	10	1
% PMN	22	50	27	80	—	33	100	0
Protein	333	—	352	440	260	435	400	313
Sugar	27	27	16	31	50	27	57	42
Culture	0	+	0	0	0	0		
Rx	x 20H-S			x Ampho B (345 mg.)		x Ampho B (1510 mg.)		

CASE #8: [REDACTED]

A 20-year-old gravida 4, para 1 housewife with 2 previous spontaneous abortions was hospitalized in [REDACTED] 1958 in active labor. Saddle block anesthesia, using 4 mg. tetracaine hydrochloride, was accomplished with some difficulty. Delivery was uncomplicated. Eight hours after administration of the anesthetic her oral temperature was 101.4°, rising to 101.8°. Six hours later severe headache, backache and nuchal rigidity were noted. There were no residual effects of the anesthetic and no neurological changes were detected. On lumbar puncture, the CSF pressure was increased and the CSF contained 5000 cells with 90% PMNs, protein 200 mg.% and sugar 68 mg.%. No organisms were seen on stained smears of the CSF sediment. Blood and CSF cultures were negative. Bacterial contamination was considered and the patient was treated with penicillin, chloramphenicol and polymyxin B. She had clinically recovered and was afebrile in less than 24 hours after onset of the illness. The patient was examined 5 months after the meningitis and was found to have no neurological abnormalities.

CATEGORIES OF CNS DISEASE BASED ON RELATIONSHIP
BETWEEN TOTAL CELL COUNT AND GLUCOSE LEVEL

A. Cells 100's - normal sugar

1. Aseptic meningitis
2. Partially-treated bacterial
3. Brain abscess
4. Rare neoplastic
5. Early bacterial
6. Early granulomatous
7. Poisoning - lead, in children
8. Meningovascular lues

B. Cells 100's - low sugar

1. Granulomatous (TBc, fungus)
2. Neoplastic
3. Meningovascular lues
4. LCU?

C. Cells 1000's - normal sugar - rare

1. Chemical
2. Early bacterial - rare

D. Cells 1000's - low sugar

1. Bacterial meningitis
2. TBc - rare

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