RESEARCH ARTICLE

The clinical characteristics and therapeutic outcomes of *Escherichia coli* meningitis in adults

Wen Neng Chang[1*], Wen-Chiu Hsiao[1], Jun-Jun Lee[2], Wan-Chen Tsai[1], Chun-Chih Chien[3], Cheng-Hsien Lu[1], Chia-Yi Lien[1]

Chang WN, Chiu Hsiao W, Jun Lee J, et al. The clinical characteristics and therapeutic outcomes of Escherichia coli meningitis in adults. J Neurol Clin Neurosci. 2021;5(4):15-19.

ABSTRACT

To examine the clinical characteristics and therapeutic outcomes of *Escherichia E. coli* Adult Bacterial Meningitis (ABM). Demographic, clinical and laboratory data and therapeutic outcomes of 25 *E. coli* ABM patients were examined retrospectively. The 25 *E. coli* ABM patients included 12 women and 13 men, aged 33-78 (mean: 59.9) years, of whom 13 had a post neurosurgical state as the underlying condition. Diabetes mellitus was the most common underlying medical condition (9 of the 25 cases). The clinical manifestations included altered consciousness, hydrocephalus, seizure, acute/subacute cerebral infarct, brain abscess, subdural empyema and spinal abscess. Other clinical features included fever, septic shock, bacteremia and hyponatremia. With treatment, the mortality rate was ≥ 44.0% and the presence of septic shock was a significant prognostic factor. A literature review identified 29 community-acquired and 12 post neurosurgical *E. coli* ABM cases, and severe neurologic manifestations and high mortality rates were also found in these reported patients. This preliminary overview of *E. coli* ABM revealed the underlying conditions, severe neurologic manifestations and high mortality rate. Further large-scale, prospective studies are needed to better delineate this specific infectious syndrome of adult *E. coli* meningitis.

Key Words: *Bacterial meningitis; Post neurosurgry; Community-acquired ABM*

INTRODUCTION

Escherichia (E.) coli is a gram-negative, facultative anaerobic, rod-shaped, coliform bacterium of the genus *Escherichia* that is commonly found in the lower intestine of warm-blooded organisms [1]. *E. coli* is an important pathogen implicated in pediatric bacterial meningitis, especially in neonates [2], but it is an uncommon pathogen of Adult Bacterial Meningitis (ABM) [3-5]. In 2005, we reported a brief analysis of *E. coli* ABM. In recent years, except for a study reported by Bichon, et al. [6] who described two spontaneous cases of community-acquired *E. coli* ABM and performed a literature review, no other study has focused on this specific infectious syndrome. Therefore, in this study we analyzed the clinical characteristics, laboratory data and therapeutic outcomes of 25 adult patients with *E. coli* ABM, and we also reviewed the literature in order to better delineate the clinical features of this specific infectious syndrome.

MATERIALS AND METHODS

We retrospectively reviewed the clinical characteristics, laboratory data and therapeutic outcomes of adult patients (≥18 years) with culture-proven *E. coli* meningitis admitted to Chang Gung Memorial Hospital (CGMH)–Kaohsiung over a study period of 29 years (January 1989 to December 2017). CGMH-Kaohsiung is a 2686-bed teaching hospital providing both primary and tertiary care, and it is also the largest medical center in southern Taiwan. During the study period, a total of 547 patients with ABM were identified, of whom 489 had monomicrobial infections, and the other 58 had mixed infections. A total of 35 ABM patients with *E. coli* infection were identified, of whom 25 had monomicrobial infections and 10 had mixed infections. The clinical and laboratory features and therapeutic outcomes of these 25 *E. coli* ABM patients were included for analysis. This study was approved by the Ethics Committee of CGMH-Kaohsiung (IRB No: 201900553B0).

In this study, the criteria for a definite diagnosis of *E. coli* meningitis were a positive Cerebro Spinal Fluid (CSF) culture for *E. coli*, clinical features of meningitis including fever, altered consciousness, seizures, acute hydrocephalus and signs of meningeal irritation and purulent CSF features, with at least one of the following: pleocytosis with a leukocyte count >0.25 × 109/L and predominant polymorphonuclear cells, lactate concentration >3.5 mmol/L, glucose ratio (CSF glucose/serum glucose) <0.4 or CSF glucose level <2.5 mmol/L if no simultaneous blood glucose level was determined.

In this study, the procedures to identify *E. coli* were as follows. The CSF was inoculated on 5% sheep blood agar, EMB and chocolate agar. Bacterial typing was performed for all positive cultures. The suspected colonies were confirmed to primarily be gram-negative rods. The pure colonies were subjected to conventional biochemical tests using the triple sugar fermentation reaction, citrate utilization test, urease test, indole test and Voges-Proskauer test before June 2013. From June 2013, freshly grown bacterial isolates were selected and smeared onto the target plate for analysis by MALDI-TOF MS. Identification of microbes was performed using MALDI BioTyper 3.0 software (Bruker Daltonik GmbH, Bremen, Germany). One of the limitations of MALDI-TOF MS is its current inability to discriminate pathogenic E.*coli* from *Shigella* spp. [7-9], as *Shigella* spp. and *E. coli* are closely related. The rapid indole test was therefore performed when *E. coli* was identified by MALDI-TOF MS. *E. coli* were then confirmed by a positive indole test. If the indole test was negative, the organisms were inoculated onto a BD Phoenix System for identification [10]. The antimicrobial susceptibility tests were processed using the Kirby-Bauer Disk Diffusion Susceptibility Test Protocol from January 1989 to July 2008 [11-16], and the BD Phoenix System from August 2008.

In this study, the patients who developed meningitis related to head trauma with skull fractures or neurosurgical procedures were classified as having "postneurosurgical" meningitis. In addition, the patients who demonstrated no clear distinctive disease characteristics and who had not undergone any invasive procedures were classified as having "spontaneous" meningitis [17]. A "nosocomial" infection was defined as a positive bacterial infection not present when the patient was admitted to hospital, clinical evidence of an infection no sooner than 48 h after admission, or clinical evidence of meningitis within a short period of time (usually < 1 month after discharge from the hospital where the patient had received an invasive procedure, especially a neurosurgical procedure). Otherwise, the patients were considered to have a "community-acquired" infection.

During the study period, the intravenous administration of third or fourth-generation cephalosporins (ceftriaxone, ceftazidime, cefepime) combined with vancomycin were the initial empiric antibiotics used for the treatment of ABM. Further antibiotics were adjusted according to the results of susceptibility tests. For the analysis of therapeutic outcomes, the patients were divided into survivor and non-survivor groups, and their prognostic factors were analyzedusing the χ^2-test for the underlying diseases and clinical manifestations, and the Student's t-test for CSF profile, Glasgow coma

[1]*Department of Neurology, Chang Gung University College of Medicine, Kaohsiung, Taiwan;*[2]*Department of Information Management, National Sun Yat-sen University, Kaohsiung, Taiwan;* [3]*Department of Laboratory Medicine, Chang Gung University College of Medicine, Kaohsiung, Taiwan*

Correspondence: *Chang WN, Department of Neurology, Chang Gung University College of Medicine, Kaohsiung, Taiwan, E-mail: cwenneng@ms19.hinet.net*

Received: *October 01, 2021,* **Accepted:** *October 15, 2021,* **Published:** *October 22, 2021*

scale scores and age [18-23]. The Modified Rankin Scale (MRS) was used to analyze the prognosis, and the patients with a MRS score 0-2 were considered to have a good therapeutic outcome, while those with a MRS score ≥ 3 were considered to have a poor therapeutic outcome.

To better delineate the clinical features of *E. coli* ABM, we also reviewed the literature on adults with *E. coli* meningitis. For this purpose, we searched PubMed using the keywords "bacterial meningitis", "*Escherichia coli*" and "adult", and the clinical features of the reported *E. coli* ABM cases were collected for analysis. Articles were excluded from this study if they lacked information on demographic data and those that were not in English. Articles concerning children were also excluded from this study [24-28].

RESULTS

The 25 patients with *E. coli* ABM included 12 women and 13 men, aged 33-78 (mean=59.9, median=61) years. Their clinical and laboratory features and therapeutic outcomes (Table 1). Cases 2 and 3 did not have complete data of the 25 *E. coli* ABM patients, 13 had a postneurosurgical state as the underlying condition, and the other 12 had spontaneous infections. The postneurosurgical states of the 13 patients included Traumatic Head Injury (THI), spontaneous Intracerebral Hemorrhage (ICH) s/p removal of hematoma, spontaneous ICH s/p Ventriculo Peritoneal (VP) shunt, Sub Arachnoid Hemorrhage (SAH) and hydrocephalus s/p ventriculostomy, traumatic ICH and SAH (1), lumbar spondylosis s/p laminectomy, and herniated intervertebral disc s/p laminectomy. Other underlying conditions of the 25 *E. coli* ABM patients included Diabetes Mellitus (DM), liver cirrhosis, old cerebral infarct, alcoholism, spontaneous ICH, myelodysplastic syndrome, multiple sclerosis, brain tumor, non-Hodgkin's lymphoma, and nasopharyngeal carcinoma. Fever was the most common clinical presentation found in 21 patients, followed by altered consciousness, hydrocephalus, septic shock, seizure, Acute/Subacute Cerebral Infarct (ASCI), hyponatremia, brain abscess, subdural empyema, and spinal abscess. Positive *E. coli* blood cultures were noted in six of the 25 enrolled *E. coli* ABM patients. The CSF profiles of the 25 enrolled ABM patients were as follows: white blood cell count: 0.002 to 25.280 109/L (mean=5.105), glucose level: 0.167 to 13.043 mmol/L (mean=3.143); total protein level: 0.04 to 8.00 g/L (mean=3.69) and lactate level: 0.44 to 24.86 mmol/L (mean=11.81).

TABLE 1
The clinical characteristics and therapeutic outcomes of the 25 adults with Escherichia coli meningitis

No.	Age (years)/ Sex	Antibiotics or managements	Underlying disease	Infection pattern	Clinical manifestation	Bacteremia	MRS
1	57 / F	Aq-penicillin G	Diabetes mellitus, old cerebral infarct	Spontaneous	Fever, altered consciousness, seizure, septic shock, brain abscess	Yes	6
2	60 / F	Olfloxacin	Diabetes mellitus	Spontaneous	Fever	Yes	Unknown
3	66 / M	Ceftazidime	Diabetes mellitus, old cerebral infarct, alcoholism	Spontaneous	Fever, altered consciousness, seizure, septic shock	Yes	Unknown
4	45 / F	Aq-penicillin G	Diabetes mellitus, traumatic head injury	Post-NS	Fever, altered consciousness, septic shock	Yes	6
5	72 / F	None	Spontaneous ICH s/p removal of hematoma	Post-NS	Fever, altered consciousness	No	5
6	67 / F	Imipenem	SAH and hydrocephalus s/p ventriculostomy	Post-NS	Fever, altered consciousness, seizure, septic shock, SIADH	Yes	6
7	66 / M	Aq-peniclilin G	Spontaneous ICH s/p removal of hematoma	Post-NS	Altered consciousness, septic shock, hydrocephalus	No	6
8	53 / M	None	Traumatic head injury	Post-NS	Fever, altered consciousness, septic shock, hydrocephalus	No	6
9	55 / M	Ceftriaxone	Myelodysplastic syndrome	Spontaneous	Headache	No	2
10	48 / M	Revision of VP shunt + Ceftazidime	Traumatic head injury, spontaneous ICH and hydrocephalus s/p VP shunt	Post-NS	Fever	No	0
11	58 / M	Ceftriaxone	Diabetes mellitus, traumatic head injury	Post-NS	Fever, altered consciousness	No	5
12	48 / M	Meropenem	Traumatic head injury, brain tumor	Post-NS	Fever, altered consciousness	No	5
13	70 / F	Ceftriaxone	Diabetes mellitus	Spontaneous	Fever, altered consciousness, hydrocephalus	No	5
14	57 / M	Ceftazidime	Spontaneous ICH s/p VP shunt	Post-NS	Fever, altered consciousness, seizure, hydrocephalus	No	6
15	71 / F	Ceftriaxone	Diabetes mellitus, HIVD s/p laminectomy	Post-NS	Fever, altered consciousness, seizure, subdural empyema, spinal abscess	No	3
16	62 / F	Ceftriaxone	Diabetes mellitus, spontaneous ICH	Spontaneous	None	No	6
17	59 / M	Cefepime	Diabetes mellitus, traumatic head injury with ICH and SAH	Post-NS	Fever, altered consciousness, hydrocephalus, brain abscess	No	5
18	33 / M	Ceftriaxone	Spontaneous ICH, substance abuser, multiple sclerosis	Spontaneous	Acute / subacute cerebral infarct	No	3
19	52 / M	Cefepime	None	Spontaneous	Fever, altered consciousness, acute / subacute cerebral infarct	No	0
20	78 / F	Ceftriaxone	Non-Hodgkin's lymphoma	Spontaneous	Fever, altered consciousness	No	6
21	71 / F	Ertapenem à Cefepime	Liver cirrhosis, lumbar spondylosis s/p laminectomy	Post-NS	Fever, altered consciousness, acute / subacute cerebral infarct, seizure, hydrocephalus	No	6
22	74 / M	Meropenem	Liver cirrhosis	Spontaneous	Fever, altered consciousness, seizure, septic shock, hydrocephalus, hyponatremia	Yes	5
23	62 / F	Meropenem	Liver cirrhosis, lumbar spondylosis s/p laminectomy	Post-NS	Fever, hydrocephalus, acute / subacute cerebral infarct, hyponatremia	No	1
24	61 / F	Ceftriaxone	None	Spontaneous	Fever, altered consciousness, septic shock, hydrocephalus	No	6
25	50 / M	Ceftazidime	Nasopharyngeal carcinoma	Spontaneous	Fever, altered consciousness, hydrocephalus, acute / subacute cerebral infarct, hyponatremia	No	6

Note: NO: Number; M: Male; F: Female; MRS: Modified Rankin Scale; post-NS: Post Neurosurgical; s/p: status post; ICH: Intracerebral Hemorrhage; SAH: Subarachnoid Hemorrhage; SIADH: Syndrome of Inappropriate Antidiuretic Hormone Secretion; VP shunt: Ventriculo-Peritoneal shunt; HIVD: Herniated intervertebral Disc

TABLE 2
The results of the antibiotic susceptibility tests of the 16 isolated Escherichia coli strains (2000-2018)

Antibiotics	Susceptible N (%)	Resistant N (%)	Intermediate N (%)	Not tested N (%)
Ampicillin	4 (25.00)	10 (62.50)	2 (12.50)	0 (0.00)
Ceftazidime	14 (87.50)	1 (6.25)	1 (6.25)	0 (0.00)
Ceftriaxone	12 (75.00)	2 (12.50)	2 (12.50)	0 (0.00)
Cefepime	11 (68.75)	1 (6.25)	0 (0.00)	4 (25.00)
Meropenem	16 (100.00)	0 (0.00)	0 (0.00)	0 (0.00)
Ciprofloxacin	8 (50.00)	3 (18.75)	0 (0.00)	5 (31.25)

Note: N: Number

The data of antibiotic susceptibility tests of the *E. coli* strains isolated from the clinical specimens of Cases 1-9, i.e. before the year 2000, were missing, and therefore only the data of cases 10-25 were available. The antibiotic susceptibility test results (Table 2) revealed that the susceptibility rates to ampicillin, ciprofloxacin, cefepime, ceftriaxone, ceftazidime and meropenem were 25.0% (4/16), > 50% (8/16), > 68.75% (11/16), 75.0% (12/16), 87.5% (14/16) and 100% (16/16), respectively. Despite management, 11 of the 25 patients with *E. coli* meningitis died, and the overall mortality rate was ≥ 44.0% (11/25). Statistical analysis of the clinical manifestations, laboratory data, and underlying conditions between the survivors and non-survivors revealed that the presence of septic shock (p=0.032) was a significant prognostic facto.

The literature review identified a total of 41 *E. coli* ABM cases (29 community-acquired infections and 12 postneurosurgical infections) [29-31]. The clinical features and therapeutic outcomes of the reported community-acquired and postneurosurgical *E. coli* ABM cases. Partial data loss was noted among the 41 reported *E. coli* ABM cases.

DISCUSSION

The epidemiology of bacterial meningitis is dynamic [32], and changes in the epidemiology may influence the therapeutic strategies including the choice of empiric antibiotics, which may have prognostic significance [33,34]. In our previous studies of ABM, we demonstrated the frequent changes in ABM epidemiology in Taiwan [35,36]. In these studies, we also reported changes in the relative frequencies of the implicated pathogens and a gradual increase in the number of patients with a postneurosurgical state as the underlying condition. In this 29-year study, *E. coli* infection accounted for 5.1% (25/489) of the ABM patients with monomicrobial infections, and it was found in 17.2% (10/58) of the patients with mixed infections. *Klebsiella pneumoniae* was previously the most common implicated pathogen of spontaneous, community-acquired ABM in Taiwan, however because the number of ABM patients with postneurosurgical infections is now greater than those with spontaneous infections, staphylococcal infection has become the most frequent implicated pathogen. Nevertheless, the incidences of *E. coli* infection in monomicrobial ABM has not changed much, accounting for 2.1%-5.0% of the implicated pathogens.

In the current study, 52.0% (13/25) of the *E. coli* ABM patients had a postneurosurgical state as the underlying condition, and the other 48% (12/25) *E. coli* ABM patients with spontaneous infections had an underlying medical condition as the preceding event (Table 1). This high incidence of underlying medical conditions as the preceding event was also noted in the reported community-acquired *E. coli* ABM cases, of which 69.0% (20/29) had an underlying medical condition as the preceding event. The presence of DM was the most common underlying medical condition in our 25 enrolled *E. coli* ABM patients (9/25, 36.0%). DM is a serious medical disease that causes a heavy burden on medical care systems [37], and more than 10% of the adults in Taiwan have DM [38]. Therefore, in Taiwan, DM is one of the most important underlying medical conditions of ABM, and this specific group of ABM patients have their own epidemiologic trend with a high incidence of *Klebsiella pneumoniae* as the implicated pathogen for spontaneous community-acquired infections, especially in those with a concomitant liver disease such as cirrhosis [39,40]. Nevertheless, further studies are warranted to investigate the relationship between the high incidence of DM and the *E. coli* ABM patients shown in the current study.

Severe neurologic manifestations including altered consciousness, hydrocephalus, seizure and ASCI were noted in 67.9% (19/25), 40.0% (10/25), 28.0% (7/25) and 20.0% (5/25) of our *E. coli* ABM patients, respectively. In addition, fever and septic shock were found in 84.0% (21/25) and 32.0% (8/25) of them, respectively. A high incidence of altered consciousness as one of the clinical manifestations was also noted in the reported *E. coli* ABM cases. Despite the severity of clinical manifestations found in our 25 cases and the other reported *E. coli* ABM patients, these manifestations were not unique and have been reported in ABM caused by other bacterial pathogen infections [41]. Therefore, the diagnosis of *E. coli* infection-related ABM can only be confirmed by positive culture results and/or positive multiplex PCR assay [42,43].

Antimicrobial non-susceptible *E. coli* strains including those which are non-susceptible to carbapenem are known to be increasing in Taiwan [44]. In the current study (Table 2), all 16 isolated *E. coli* strains were susceptible to meropenem, and non-susceptible strains to third and fourth-generation cephalosporins were also noted. In the clinical practice of ABM management, ceftriaxone and ceftazidime are the suggested empirical antibiotics, however meropenem is not currently suggested, and it is usually used in situations in which strains resistant to third and fourth-generation cephalosporins are identified. As shown in Table 2, 12.5% (2/16) and 25.0% of the isolated *E. coli* strains was not susceptible to ceftazidime and ceftriaxone, respectively. Therefore, there is usually a time lag in using the appropriate empiric antibiotic as the initial therapy for ABM, and this may influence the therapeutic outcome. Presently, it is highly suggested to start empiric treatment within 1 hour of arrival for all suspected meningitis cases, and the choice of antibiotics needs to be tailored according to the patient group and local resistance rates of frequently implicated bacterial pathogens to the commonly used antibiotics for ABM treatment. Therefore, further studies are needed to investigate how best to choose appropriate empiric antibiotics to treat ABM, including *E. coli* ABM.

Despite treatment, 11 of our 25 *E. coli* ABM patients died, and the mortality rate (44.0%, 11/25) is higher than that reported ABM overall (25.5%) [3]. In the current study, the presence of septic shock was an important prognostic factor for the *E. coli* ABM patients, and 57.1% (8/14) of the survivors (Table 1) had a poor therapeutic outcome. Although other severe neurologic manifestations such as altered consciousness, hydrocephalus, seizure and ASCI are also known to be important prognostic factors of ABM, they were of no prognostic significance in the current study. High mortality rates were also noted in the reported *E. coli* ABM cases. Because this is a retrospective study, partial data loss in the current study and in the reported *E. coli* ABM cases, is the most important limitation of this study.

In conclusion, in this study conducted in Taiwan, infections accounted for 5.1% of the patients with monomicrobial ABM, and 52.0% of the *E. coli* ABM patients had a postneurosurgical condition as the preceding event. In addition to a postneurosurgical condition, DM was another important underlying condition, accounting for 36.0% of the *E. coli* ABM patients. Severe neurologic manifestations including altered consciousness, hydrocephalus, seizure and ASCI were found in the patients with *E. coli* ABM. The mortality rate of *E. coli* ABM was high in this study (44.0%), and the presence of septic shock was a significant prognostic factor. The survivors of *E. coli* ABM had severe neurological deficits. High mortality and morbidity rates were also noted in the reported *E. coli* ABM cases. This study offers an overview of *E. coli* ABM; however, because of the limited number of cases and the missing data in some of the enrolled *E. coli* ABM cases, further large-scale prospective studies are needed to better delineate the clinical characteristics of this specific infectious syndrome in adults.

CONCLUSION

We conducted this study to report changes in the relative frequencies of the implicated pathogens and a gradual increase in the number of patients with a postneurosurgical state as the underlying condition and in the study periods

of 29 years, the incidence of *E. coli* infection in ABM patients didn't change. Post-neurosurgical state and DM were the important underlying conditions in these patients and not only high mortality rate was noted in the reported *E. coli* ABM cases but the survivors of *E. coli* ABM had severe neurological deficits. For our limited case numbers in this study, further large-scale, prospective studies are needed to better delineate this specific infectious syndrome of adult *E. coli* meningitis.

REFERENCES

1. Tenaillon O, Skurnik D, Picard B, et al. The population genetics of commensal *Escherichia coli*. Nat Rev Microbiol. 2010;8(3):207-17.
2. Tauzin M, Ouldali N, Lévy C, et al. Combination therapy with ciprofloxacin and third-generation cephalosporin versus third-generation cephalosporin monotherapy in *Escherichia coli* meningitis in infants: a multicentre propensity score-matched observational study. Clin microbiol Infect. 2019;25(8):1006-1012.
3. Lien CY, Huang CR, Tsai WC ME, et al. Epidemiologic trend of adult bacterial meningitis in southern Taiwan (2006-2015). J Clin Neurosci. 2017;42: 59-65.
4. Yang TM, Lu CH, Huang CR et al. Clinical characteristics of adult *Escherichia coli* meningitis. Jpn J Infect Dis. 2005; 58(3): 168-170.
5. Van de Beek D, de Gans J, Spanjaard L. Clinical features and prognostic factors in adult with bacterial meningitis. N Engl J Med. 2004;351(18):1849-1859.
6. Bichon A, Aubry C, Dubourg G et al. *Escherichia coli* spontaneous community-acquired meningitis in adults: a case report and literature review. Int J Infect Dis. 2018;67:70-74.
7. Khot PD, Couturier MR, Wilson A et al. Optiimization of matrix–assisted laser desorption ioniziation–time of flight mass spectrometry analysis for bacterial identification. J. Clin. Microbiol. 2012;50(12):3845-3852.
8. Martiny D, Busson L, Wybo I, et al. Comparision of the Microflex LT and Vitek MS systems for routine identification of bacteria by matrix–assisted laser desorption ionization–time of flight mass spectrometry. J Clin Microbiol. 2012;50(4):1313-1325.
9. Clark AE, Kaleta EJ, Arora A, et al. Matrix-assisted laser desorption ionization-time of flight mass spectrometry: A fundamental shift in the routine practice of clinical microbiology. Clin Microbiol Rev. 2013;26(3):547-603.
10. O'Hara CM. Evaluation of the Phoenix 100 ID/AST system and NID panel for identification of Enterobacteriaceae, Vibrionaceae, and commonly isolated nonenteric gram-negative bacilli. J Clin Microbiol. 2006; 44(3):928-933.
11. Wayne Pa. Performance standards for antimicrobial susceptibility testing; fourteenth informational supplement. National Committee for Clinical Laboratory Standards.M100:S16
12. Kunin CM, Bender AS, Russell CM. Meningitis in adults caused by *Escherichia coli* 04 and 075. Arch Intern Med. 115(6): 652-658
13. Manesis JG, Stanosheck J. *Escherichia coli* meningitis in adults. Arch Neurol. 1965;13:214-216.
14. Crane LR, Lerner AM. Non-traumatic gram-negative bacillary meningitis in the Detroit Medical Center, 1964–1974 (with special mention of cases due to *Escherichia coli*). Med. (Baltimore). 1978;57:197209.
15. Mancebo J, Domingo P, Blanch L, et al. Post-neurosurgical and spontaneous gram-negative bacillary meningitis in adults. Scand J Infect Dis. 1986;18(6):533-538.
16. Mofredj A, Guerin JM, Leibinger F et al. Spontaneous *Escherichia coli* meningitis in an adult. Scand J Infect Dis. 2000;32:699-700.
17. Chang KH, Lyu RK, Tang LM. Spontaneous *Escherichia coli* meningitis associated with hemophagocytic lymphohistiocytosis. J Formos Med Assoc. 2006;105(9):756-759.
18. Miletic D, Poljak I, Eskinja N et al. Giant anterior sacral meningocele presenting as bacterial meningitis in a previously healthy adult. Orthopedics. 2008;31(2):182.
19. Cabellos C, Viladrich PF, Ariza J et al. Community-acquired bacterial meningitis in cirrhotic patients. Clin Microbiol Infect. 2008;14(1):35-40.
20. Weyrich P, Ettahar N, Legout L, et al. First initial community-acquired meningitis due to extended-spectrum beta-lactamase producing *Escherichia coli* complicated with multiple aortic mycotic aneurysms. Ann Clin Microbiol Antimicrob. 2012;11:4.
21. Kangath RV, Midturi J. An unusual case of *E. coli* meningitis in a patient with Marfan's syndrome. BMJ Case Rep. 2013: bcr2013008592.
22. Kohlmann R, Nefedev A, Kaase M et al. Community-acquired adult *Escherichia coli* meningitis leading to diagnosis of unrecognized retropharyngeal abscess and cervical spondylodiscitis: A case report. BMC Infect Dis. 2015;15: 567.
23. Van Veen KE, Brouwer MC, Van der Ende A et al. Bacterial meningitis in solid organ transplant recipients: A population-based prospective study. Transpl Infect Dis. 2016; 18(5): 674-680.
24. Ishida K, Noborio M, Nakamura M et al. Spontaneous *Escherichia coli* bacterial meningitis mimicking heatstroke in an adult. Clin Case Rep. 2016;4(4):323-326.
25. Kasimahanti R, Satish SK, Anand M. Community-acquired Escherichia coli meningitis with ventriculitis in an adult-a rare case report. J Intensive Care. 2018;6:63.
26. Abu-Rumeileh S, Abdelhak A, Foschi M, et al. Guillain-Barré syndrome spectrum associated with COVID-19: An up-to-date systematic review of 73 cases. J. Neurol. 2020;268:1133-1170.
27. Baig AM, Khaleeq A, Ali U, et al. Evidence of the COVID-19 virus targeting the CNS: Tissue distribution, host-virus interaction, and proposed neurotropic mechanisms. ACS Chem Neurosci. 2020;11(7):995-998.
28. Crary MA, Carnaby-Mann GD, Groher ME. Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. Arch Phys Med Rehabil. 2005;86: 1516-1520.
29. Costello F, Dalakas MC. Cranial neuropathies and COVID-19: Neurotropism and autoimmunity. Neurol. 2020; 95(5): 195-196.
30. Gutiérrez-Ortiz C, Méndez-Guerrero A, Rodrigo-Rey S, et al. Miller fisher syndrome and polyneuritis cranialis in COVID-19. Neurol. 2020;95(5):e601-e605.
31. Hutchins KL, Jansen JH, Comer AD, et al. COVID-19-Associated bifacial weakness with paresthesia subtype of Guillain-Barré Syndrome. AJNR Am J Neuroradiol. 2020;41(9):1707-1711.
32. Heckmann JG, Heckmann SM, Lang CJG, et al. Neurological aspects of taste disorders. Arch Neurol. 2003;60(5):19:667-671.
33. Juliao Caamaño DS, Alonso Beato R, et al. Facial diplegia, a possible atypical variant of Guillain-Barré Syndrome as a rare neurological complication of SARS-CoV-2. J Clin Neurosci. 2020;77:230-232.
34. Ogier M, Andéol G, Sagui E, et al. How to detect and track chronic neurologic sequelae of COVID-19? Use of auditory brainstem responses and neuroimaging for long-term patient follow-up. Brain Behav Immun Health. 2020;5:100081.
35. Whittaker A, Anson M, Harky A. Neurological manifestations of COVID-19: A systematic review and current update. Acta Neurol Scand. 2020; 142(1):14-22.
36. Budhram A, Leung A, Nicolle MW, et al. Diagnosing autoimmune limbic encephalitis. CMAJ. 2019;191(19):E529-E534.
37. Dubey D, Pittock SJ, Kelly CR, et al. Autoimmune encephalitis epidemiology and a comparison to infectious encephalitis. Ann Neurol. 2018;83(1):166-77.
38. Hacohen Y, Joseph S, Kneen R, et al. Limbic encephalitis associated with elevated antithyroid antibodies. J Child Neurol. 2014;29(6):769-73.
39. Granerod J, Ambrose HE, Davies NW, et al. Causes of encephalitis and differences in their clinical presentations in England: A multicentre,

population-based prospective study. Lancet Infect Dis. 2010;10(12):835-44.

40. Leypoldt F, Titulaer MJ, Aguilar E, et al. Herpes simplex virus-1 encephalitis can trigger anti-NMDA receptor encephalitis: Case report. Neurology. 2013;81(18):1637-9.

41. Santana LM, Valadares EJA, Rosa-Junior M. Differential diagnosis of temporal lobe lesions with hyperintense signal on T2-weighted and FLAIR sequences: Pictorial essay. Radiol Bras. 2020;53(2):129~136.

42. Eran A, Hodes A, Izbudak I. Bilateral temporal lobe disease: looking beyond herpes encephalitis. Insights Imaging. 2016;7(2):265-74.

43. Granerod J, Davies NW, Mukonoweshuro W, et al. Neuroimaging in encephalitis: Analysis of imaging findings and interobserver agreement. Clin Radiol. 2016;71(10):1050-8.

44. Toledano M, Davies NWS. Infectious encephalitis: Mimics and chameleons. Pract Neurol. 2019 Jun;19(3):225-37.