

Aseptic meningitis in adults and children: Diagnostic and management challenges



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ABSTRACT

Background: Aseptic meningitis represents a common diagnostic and management dilemma to clinicians.

Objectives: To compare the clinical epidemiology, diagnostic evaluations, management, and outcomes between adults and children with aseptic meningitis.

Study design: We conducted a retrospective study from January 2005 through September 2010 at 9 Memorial Hermann Hospitals in Houston, TX. Patients age ≥ 2 months who presented with community-acquired aseptic meningitis with a CSF white blood cell count > 5 cells/mm³ and a negative Gram stain and cultures were enrolled. Patients with a positive cryptococcal antigen, positive blood cultures, intracranial masses, brain abscesses, or encephalitis were excluded.

Results: A total of 509 patients were included; 404 were adults and 105 were children. Adults were most likely to be female, Caucasian, immunosuppressed, have meningeal symptoms (headache, nausea, stiff neck, photophobia) and have a higher CSF protein ($P < 0.05$). In contrast, children were more likely to have respiratory symptoms, fever, and leukocytosis ($P < 0.05$). In 410 (81%) patients, the etiologies remained unknown. Adults were more likely to be tested for and to have *Herpes simplex virus* and *West Nile virus* while children were more likely to be tested for and to have Enterovirus ($P < 0.001$). The majority of patients were admitted (96.5%) with children receiving antibiotic therapy more frequently ($P < 0.001$) and adults receiving more antiviral therapy ($P = 0.001$). A total of 384 patients (75%) underwent head CT scans and 125 (25%) MRI scans; all were normal except for meningeal enhancement. All patients had a good clinical outcome at discharge.

Discussion: Aseptic meningitis in adults and children represent a management challenge as etiologies remained unknown for the majority of patients due to underutilization of currently available diagnostic techniques.

1. Introduction

Aseptic meningitis is defined as an acute community-acquired syndrome with cerebrospinal fluid (CSF) pleocytosis in the absence of a positive Gram stain and culture, without a parameningeal focus or a systemic illness, and with a good clinical outcome [1]. This case definition has remained relatively unchanged since its initial description in 1925 by Wallgren. The clinical syndrome has since been further characterized and understood to include multiple types of infectious and non-infectious etiologies, although up to 71% of those cases remain with uncertain etiology, especially when PCR testing is not completed. [2]. The most common etiologies of aseptic meningitis in the United States (US) are viruses such as Enterovirus, Herpes simplex type 2, and West Nile virus. Varicella zoster virus and Cytomegalovirus have also

been described as causes of aseptic meningitis [2]. Several prior studies have sought to develop clinical models to try to differentiate this diagnosis from other urgent treatable conditions such as bacterial meningitis and encephalitis [3,4]. To standardize the case definition, a recent international working group defined aseptic meningitis as patients with meningitis symptoms, a CSF white cell count of > 5 cells/mm³, and a negative CSF Gram stain [5]. The diagnostic certainty of this syndrome was further stratified into three levels: Level 1 if the patient had negative CSF cultures without previous antibiotic exposure, Level 2 with negative CSF cultures with previous antibiotic therapy and Level 3 with concomitant encephalitis.

Despite such tools, evaluation of this clinical syndrome in the present day clinical setting remains variable representing a diagnostic and management dilemma to clinicians. As such, the purpose of this study

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was to characterize and compare the baseline characteristics, management strategies, etiologies of adult and pediatric patients with aseptic meningitis and to uncover the frequency and yield of the use of available diagnostic techniques and cranial imaging in this syndrome.

2. Methods

2.1. Study design & case definitions

A retrospective observational cohort study was completed spanning from January 2005 through September 2010. Cases were defined in a similar method to those cited by Tapiainen et al. using only Level 1 and 2 diagnostic certainties [5]. Patients above 2 months of age presenting to the emergency department from the community with acute symptoms of meningitis, CSF white cell count of > 5 cells/mm³, negative Gram stain and culture, and no identified parameningeal focus of infection were included by reviewing all cases with an ICD9 discharge code of meningitis. The cohort was composed of patients presenting to nine Memorial Hermann hospitals, all within the greater Houston metropolitan area. Patients aged 18 years or older were considered adults for the purposes of this study. Baseline patient characteristics at time of presentation to the emergency department, use of microbiologic and imaging modalities, and Glasgow outcome scores [6] at time of discharge were evaluated. The study was approved by the University of Texas Medical School at Houston Committee for the Protection of Human Subjects and by the Memorial Hermann Hospital Research Review Committee.

2.1.1. Statistical assessment

Comparisons of baseline and clinical characteristics were made between pediatric and adult patients using the chi square test for categorical variables and ANOVA for continuous variables with significance attributable at $P < 0.05$. All statistical analysis was completed using SPSS for Mac version 21 (SPSS, Chicago, IL, USA).

3. Results

We identified a total of 907 adults and children with meningitis above the age of 2 months. We excluded 398 patients for the following reasons: positive Gram stain for bacteria or yeast ($n = 113$), nosocomial meningitis ($n = 101$), encephalitis presentation ($n = 86$), and

positive CSF or blood culture ($n = 84$), and incomplete medical records ($n = 14$). A total of 509 patients met the inclusion criteria. Fig. 1 shows the age distribution for all the cases in decades with the majority of patients being between 20 and 40 years old. Fig. 2 shows the distribution by month of presentation with the most common time between May and October. As shown in Table 1, adults composed the majority of patients at 404 (79%) while 105 (21%) patients were children; the median age in the adults was 34 years (18–89) and in the pediatrics it was 4.9 years (2 months–17 years of age). The majority of patients were 20–40 years old (see Fig. 1). Male gender was more common in pediatric patients (59% vs 42%, $P = 0.002$). There were also significant differences in the ethnicity with adults and children having more Caucasian and Hispanics, respectively ($p < 0.001$). More adults were immunocompromised than children (22.5% vs 4.7%, $P < 0.001$). Previous antibiotic therapy was used more commonly in pediatrics than adults (37.1% vs. 7.2%, $P < 0.001$). The majority of the patients with aseptic meningitis presented between the months of May and October (see Fig. 2).

There were several differences between adults and children in the baseline clinical and laboratory presentations (see Table 1). Adults were more likely than children to complain of headache, nausea or vomiting, stiff neck, malaise, photophobia, and have nuchal rigidity present on exam ($p < 0.05$). Fever, concurrent respiratory illness, and rash were more commonly seen in the pediatric population ($p < 0.05$). On initial CSF evaluation, adult patients had a trend to have a higher CSF WBC count ($p = 0.066$) and also had higher CSF protein ($p < 0.001$) than the pediatric group. Children also had higher median CSF neutrophilic pleocytosis than adults ($P < 0.001$). Children had higher serum leukocyte counts than adults ($p < 0.001$).

Diagnostic testing differed between adults and children (see Table 2). Adults were more commonly tested for HIV (30% vs. 5.7%, $P < 0.001$) with only 10 (8.1%) of adults testing positive for HIV. Virological studies such as polymerase chain reaction (PCR) for *Herpes simplex virus* (HSV), Enterovirus and *Varicella Zoster virus* (VZV) and serologies for *West Nile virus* (WNV) were done in the minority of patients. Out of the 509 patients in the cohort, only 175 (34.4%) had PCR for HSV sent, 165 (32.4%) for WNV studies, 138 (27.1%) for enterovirus PCR, 6 (1.2%) for VZV PCR, and 1 patient each for *Cytomegalovirus* (CMV) and *Mycoplasma pneumoniae* PCR. Furthermore, 182 (35.8%) of the patients had no viral studies sent at all. When done, the yield of an enterovirus PCR was 35.5% and for HSV PCR it was 20.6%.

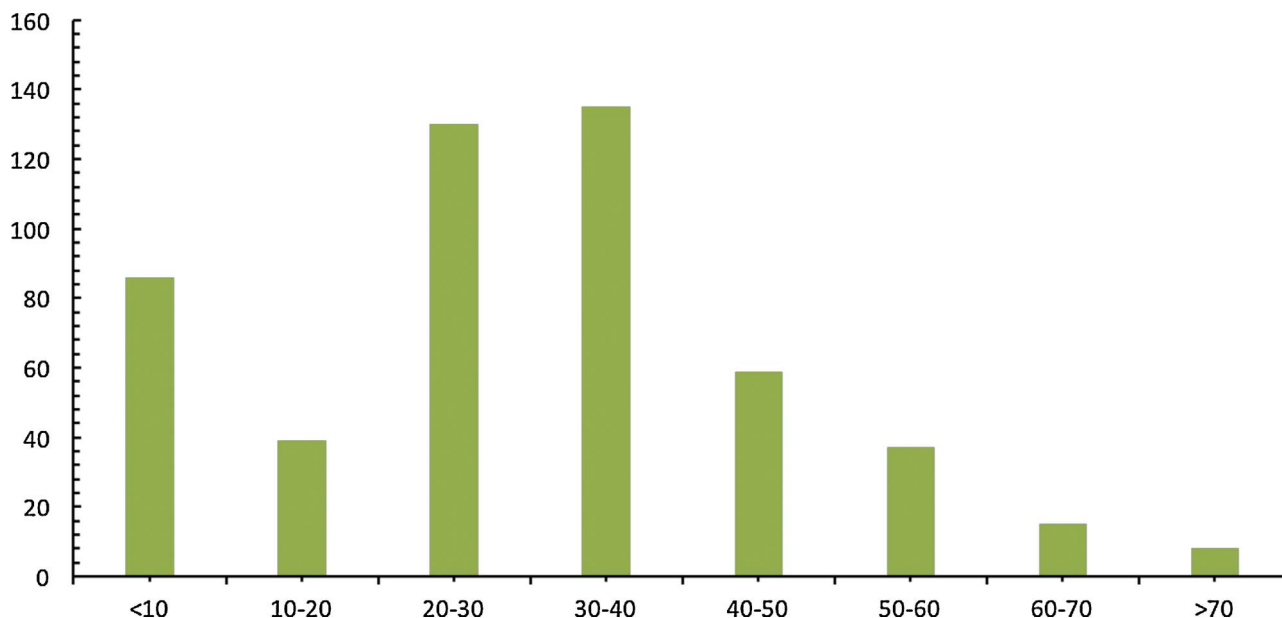


Fig. 1. Age distribution in years of 509 adults and children with aseptic meningitis.

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