

## Brief Communication

### An outbreak of aseptic meningitis in Hatay Province, Turkey

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Aseptic meningitis is an inflammation of the meninges with sterile bacterial cultures of CSF.<sup>1</sup> Enteroviruses are the most commonly identified cause of aseptic meningitis worldwide. These viruses appear throughout the year, but in temperate climates they are strikingly more prevalent in the summer and fall. Because viral shedding from the gastrointestinal tract is more prolonged than is shedding from the upper respiratory tract, the fecal-oral route is the predominant mode of enteroviral transmission.<sup>2</sup> The most severe clinical syndrome caused by enteroviruses is due to infection of the CNS with signs of aseptic meningitis or, less frequently, encephalitis. Although the outcome of enteroviral meningitis is usually favorable in otherwise healthy and immunocompetent patients, rapid diagnosis and differentiation from bacterial meningitis is imperative because the latter may cause severe neurologic sequelae or even fatal outcome and therefore necessitates immediate antibiotic treatment.<sup>3</sup> In this study, we report an unusual community outbreak of aseptic meningitis with a total of 688 patients involved, in the southern region of Turkey, in summer 2005.

To determine the possible viral cause of this outbreak, as our hospital is the only reference hospital in the province the specialists and general practitioners dealing with such infections were recommended to transfer the CSF samples of the patients to our clinic for proper storage before their transfer of samples to the Virology Department of Refik Saydam Central Institute of Hygiene (RSCIH) in Ankara. For recording the clinical and laboratory findings with CSF examination results and demographic data of the patients a record form was prepared. Data of the rest of the patients whose CSF samples could not be transferred to our clinic were accessed through medical records of the centers dealing with these patients in the region. The collected CSF samples were transferred at +4°C however, storage conditions before their transfer to our center were not clear. All samples were collected in the acute phase of the disease. The CSF samples of patients were stored at -70°C before transport to the Virology Department of RSCIH in Ankara for viral cultivation. Diagnosis of aseptic meningitis was based on the clinical symptoms indicative of meningitis accompanied by a leukocyte count in the CSF of  $\geq 3/\text{mm}^3$  in the absence of bacterial growth in culture, or any alternative nonviral causes and/or detection of the viral agent in the CSF. Cell counts of CSF and peripheral blood, CSF analyses for protein and

glucose, bacterial cultures, and serum analyses of glucose were performed. Isolation of echovirus was performed by conventional cell culture and micro neutralization methods according to standard procedures as described previously.<sup>4</sup>

An outbreak of aseptic meningitis in 688 patients occurred in the southern area of Turkey, Hatay between 1 May, and 30 September 2005. Although 688 patients were diagnosed as aseptic meningitis by examination of CSF in the region within this period, only CSF samples of 100 patients could be collected in our center. The highest incidence was in August, 2005, when 354 cases occurred, which accounted for 51.5% of all patients (Figure 1). The patients' age ranged between 3 months and 46 years with a mean of  $8.70 \pm 6.88$  years. Most of the patients (87.8%) in this outbreak were under 16 years of age. Four hundred and twenty-one (61.2%) patients were male and 267 (38.2%) were female (male:female ratio of 1.58:1). All patients were hospitalized, and the mean hospitalization duration was  $5.26 (\pm 2.61)$  days and minimum one, maximum 21 days. All were discharged without sequelae. During the same period of 2004, only 79 aseptic meningitis cases occurred and most of the cases were in May. The most common clinical manifestations were fever (100%), headache (96%, in older than 4 years old), nausea or vomiting (85%), and neck stiffness (77%, in older than 4 years old). There was a wide variation in the white blood cell (WBC) counts, ranging from 10-1680 cells/mm<sup>3</sup> (mean:  $192.8 \pm 296.4$  cells/mm<sup>3</sup>) and most CSF WBC counts (61%) were less than 100 cells/mm<sup>3</sup>. The CSF WBC counts between 100-500 cells/mm<sup>3</sup> were found in 29% cases, and were over 500 cells/mm<sup>3</sup> in 10%. Lymphocyte cell predominance was observed in 91% cases. The mean CSF value of protein was 42.1 mg/dl (range, 20-58 mg/dl), and hypoglycorrhachia (CSF/serum glucose ratio  $< 2/3$ ) was observed in 12% cases. All of 100 CSF samples collected in our center

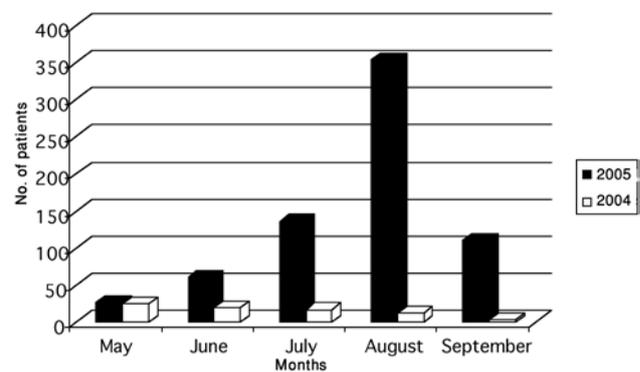


Figure 1 - Monthly distribution of patients with aseptic meningitis in 2004 and 2005.

were negative for bacterial growth. The CSF samples of 100 cases were transported as frozen in an icebox for virus isolation to the Virology Department of RSCIH and presence of enteroviruses was investigated by conventional cell culture and micro neutralization methods. Echovirus type 4 was isolated in 9% of CSF samples. The mean leukocyte count of cases isolated with echovirus type 4 was 188 cells/mm<sup>3</sup> and minimum 16 cells/mm<sup>3</sup>, maximum 845 cells/mm<sup>3</sup>.

The present study documents the occurrence of an outbreak of aseptic meningitis due to echovirus type 4. However, the study has limitations because of difficulties in collection and storage conditions of CSF samples before transfer to our institution, and only a small number of samples yielded a viral isolation. Thus, it does not document the extent of the outbreak or accurately describe the causes of all cases involved in this outbreak. The main method of diagnosis of enterovirus infections is virus isolation from clinical specimens by cell culture. Isolation of enterovirus by cell culture from CSF is frequently less successful because of the low viral titer in clinical specimens, and also because some serotypes grow slowly.<sup>2</sup> Our results were less sensitive when compared with previous reports.<sup>5</sup> Most of our patients (57%) were found to be males and 87.8% were aged between 1-15 years. This indicates that a relative immunodeficiency might account for the male predominance in the incidence of many infectious diseases in children. In this study, all cases occurred throughout the summer and early autumn, which are the typical seasons for outbreaks of enteroviral infections in temperate climates.<sup>2</sup> The similarity in clinical presentation amongst the patients and the higher rates of detection of aseptic meningitis compared with the documents of the previous year in part of our province indicated that we did encounter an outbreak of meningitis. The records of 2005 showed an increase of aseptic meningitis cases up to 688 patients between May 1 and September 30 (rate: 8.11 per 10,000 population) with a peak in August of 354 cases (rate: 4.2 per 10,000 population). The data of the previous year during the same period revealed only 79 cases (rate: 0.94 per 10,000 population) of aseptic meningitis and the number of patients diagnosed in August 2004 was only 13 (rate: 0.15 per 10,000 population). This suggests that there is a significant increase in cases of aseptic meningitis

during summer 2005 in our province. All 688 patients were hospitalized and the mean hospitalization duration was 5.26 days ( $\pm 2.61$ ). No correlation between patient's age and the duration of hospitalization was observed. In this outbreak, no patients experienced sequelae or fatal outcome. Ninety percent of 688 patients in the current study received parenteral antibiotics. This is a high percentage of unnecessary antibiotic usage. Performing CSF polymerase chain reaction for enterovirus on patients with probable viral meningitis may decrease hospitalization times, and decrease prolonged administration of unnecessary antibiotics with considerable financial savings.<sup>6</sup>

In conclusion, although echovirus type 4 was identified in a small part of the cases, it was accused as the main cause of this outbreak.

Received 30th January 2007. Accepted 29th July 2007.

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