Differential diagnosis of aseptic meningitis syndrome

**Infectious etiologies**
- Viruses
  - Enteroviruses - Polio, coxsackievirus, echovirus
  - HSV types 1 and 2
  - Varicella-zoster virus
  - Adenovirus
  - Epstein-Barr virus
  - LCMV
  - HIV
- Influenza virus types A and B
- Bacteria
  - Partially treated meningitis
  - Parameningeal infection
  - Endocarditis
  - Mycoplasma pneumoniae
  - M tuberculosis
  - Ehrlichiosis - Monocytic, granulocytic
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  - Ehrlichiosis - Monocytic, granulocytic
  - Ehrlichiosis - Monocytic, granulocytic
- Fungi
  - C neoformans
  - Histoplasma capsulatum
  - Coccioidodes immitis
  - Blastomyces dermatitides
- Parasites
  - Toxoplasma gondii
  - Taenia solium (cysticercosis)
  - Sarcoidosis
- Leptomeningeal cancer
- Posttransplantation lymphoproliferative disorder
- Systemic lupus erythematosus
- Wegener granulomatosis
- CNS vasculitis
- Behçet disease

**Noninfectious causes**
- Drugs
  - Nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Trimeprprim-sulfamethoxazole, Vaccination
  - Allopurinol
  - Systemic diseases
  - Sarcoidosis
  - amoxicillin
  - OKT3
  - Azathioprine
  - Intravenous immunoglobulin
  - Isoniazid
  - Intrathecal methotrexate
  - Intrathecal cystine arabinoside
- Systemic diseases
  - Sarcoidosis
  - Leptomeningeal cancer
  - Posttransplantation lymphoproliferative disorder
  - Systemic lupus erythematosus
  - Wegener granulomatosis
  - CNS vasculitis
  - Behçet disease
  - Vogt-Koyanagi-Harada syndrome
- Miscellaneous
  - Arachnoiditis
  - Migraine
  - Postinfectious syndromes

**References:**

1. ^ syd/1537 at Who Named It?
4. ^ Mollaret's meningitis at patient.co.uk
WHAT IS MOLLARET’S MENINGITIS?

Signs / Symptoms / Diagnosis

Mollaret's meningitis is a rare form of recurrent meningitis originally described by Mollaret in 1944. According to Bryun, who further refined the clinical diagnostic criteria, the condition is characterized by (1) recurrent episodes of severe headache, meningismus, and fever; (2) CSF pleocytosis with large endothelial cells (ie, Mollaret cells), neutrophils, and lymphocytes; (3) recurrent attacks separated by symptom-free periods of weeks to months; (4) spontaneous remission of symptoms and signs; and (5) no known causative agent. Cases without fever, with increased CSF gamma globulin and transient neurological signs and symptoms, have been reported. Transient neurological abnormalities, including seizures, diplopia, pathologic reflexes, cranial nerve pareses, hallucinations, and coma, occur in as many as 50% of patients.

Mollaret cells, considered by many to be the hallmark of Mollaret meningitis (although not pathognomonic), are observed early and may comprise 60-70% of cells in the CSF. These cells are usually present for only the first 24 hours and can be missed easily. After the first 24 hours, the CSF shows a lymphocytic predominance with cell counts usually less than 3000/mm³. Hypoglycorrhachia (ie, low CSF glucose concentration) is reported in one third of the patients. CSF protein usually is elevated mildly. Recent data suggest that HSV-2 and, less frequently, HSV-1 may be etiologic in some if not most cases of Mollaret's Meningitis. Hence, acyclovir (intravenous or oral) or valacyclovir (oral only) are worthy of consideration for both therapy and prophylaxis.

Mollaret's Meningitis is suspected based on clinical criteria and confirmed by HSV 1 or HSV 2 on PCR of CSF, although not all cases test positive.

Aseptic meningitis syndrome is not caused by pyogenic bacteria, but can be caused by multiple conditions including infectious viral and nonviral causes and many noninfectious etiologies. Hence, this term is no longer synonymous with viral meningitis, although the two often are used interchangeably.

Drug-induced aseptic meningitis

The incidence of drug-induced meningitis (DIAM) is unknown. Many antimicrobials, such as trimethoprim-sulfamethoxazole, ciprofloxacin, cephalexin, metronidazole, amoxicillin, penicillin, and isoniazid, are causes of aseptic meningitis. In addition, the xanthine oxidase inhibitor allopurinol has been implicated in causing aseptic meningitis. DIAM is a complication in which numerous other drugs, namely nonsteroidal anti-inflammatory drugs (NSAIDs), ranitidine, carbamazepine, vaccines against hepatitis B and mumps, immunoglobulins, OKT3 monoclonal antibodies (ie, directed against the T3 receptor and, therefore, pan T-cell antibodies), co-trimoxazole, radiographic agents, and muromonab-CD3, also have been associated. A high index of suspicion is needed to make an accurate diagnosis of DIAM. Diagnostic accuracy in clinical care depends on a complete history and physical examination.

The clinical presentation does not help in differentiating DIAM from infectious meningitis. The CSF profile (ie, neutrophilic pleocytosis) does not allow DIAM to be distinguished from infectious meningitis. Systemic lupus erythematosus is the single most frequent underlying condition associated with DIAM. Recurrent DIAM is well known; females usually predominate, and the frequency varies with the different underlying conditions.