

Mollaret's meningitis: 65 years of history

Francois Abi-Fadel · Katarzyna Harasiuk ·
Michael Ng

Received: 11 November 2010 / Accepted: 24 January 2011 / Published online: 12 February 2011
© SIMI 2011

Benign recurrent meningitis was first described by Pierre Mollaret in 1944 [1]. It is characterized by greater than three episodes of fever, headache and meningismus lasting 2–5 days [2, 5]. We describe a case of a patient presenting with recurrent aseptic meningitis. The diagnosis was only ascertained after the 4th admission.

A 57-year-old woman presented to the emergency department (ED) for headache and nausea lasting 2 weeks. She had near-syncope, vomiting, chills, neck stiffness and dizziness, but denied any fever. The headache was progressive and bi-frontal. Her past medical history was significant for depression on sertraline, back pain, and previous episodes of meningitis found to be aseptic in nature. Also noted was a history of lupus erythematosus controlled with no ongoing therapy. The social history was negative for smoking, alcohol or drugs.

On admission, the vital signs were stable, there was no fever, and a complete physical examination was normal except for the neurologic examination that was significant for meningismus.

The patient was treated with ceftriaxone and vancomycin in the ED, and a lumbar puncture was planned. Droplet precautions were in place.

Infectious disease, rheumatology and neurology services were consulted. The differential diagnosis was bacterial, viral, or lupus related meningitis.

A chest X-ray study was negative, as well as a computed tomography (CT scan) of the head. Brain magnetic resonance imaging (MRI) and brain magnetic resonance angiography (MRA) were also negative.

The laboratory work-up was significant for a cerebral spinal fluid (CSF) red blood cell count (RBC) of 341, white blood cells (WBC) of 591 with 100% lymphocytes on the differential, clear appearance, glucose of 55 mg/dl, and total protein of 97 mg/dl. A urinalysis was also normal. The WBC in the blood was 11,200 cells/mm³, basic metabolic panel normal, lactate dehydrogenase (LDH) 245, and alanineaminotransferase/aspartate aminotransferase (AST/ALT): 92/105.

With the above picture, the patient was taken off antibiotics and off droplet precautions, and aseptic meningitis was diagnosed. Two days after admission, the nausea, vomiting, dizziness, and chills all resolved. Blood cultures and a hepatitis panel were negative. Lupus anticoagulant, anti-cardiolipin, anti-SSA and anti-SSB, anti-nuclear antibody (ANA), rheumatoid factor (RF), anti-ds DNA, Ig G and Ig M antibody levels, and beta 2 glycoprotein antibodies were all negative. Complement C3 and C4 levels were also normal as well as a routine electroencephalogram (EEG). CSF culture, gram's stain and India ink, cryptococcus antigen, and HSV-1 polymerase chain reaction (PCR) were negative. However, HSV-2 PCR was positive.

The consultants advised only symptomatic treatment, and non-steroidal anti-inflammatory (NSAID) avoidance, concluding that the case was a recurrent benign

F. Abi-Fadel
Department of Medicine, Division of Pulmonary and Critical
Care Medicine, Downstate Medical Center,
State University of New York, Brooklyn, NY, USA

K. Harasiuk
Department of Medicine, Hospitalist Division,
Staten Island University Hospital, Staten Island, NY, USA

M. Ng
Division of Neurology, Staten Island University Hospital,
Staten Island, NY, USA

F. Abi-Fadel (✉)
343 Adams Avenue, Staten Island, NY 10306, USA
e-mail: af_francois@yahoo.com

lymphocytic meningitis (i.e. Mollaret's meningitis). No acyclovir was prescribed, and the patient was discharged 4 days later in a stable condition, completely asymptomatic. The patient had three prior admissions, 2 years ago, 3 years ago, and 4.5 years ago for the same symptoms of recurrent headaches, nausea and neck stiffness, with no focal neurological deficits. During all three admissions, CT head scan and MRI of the brain were all negative. The CSF done on each of these admissions showed a high protein level, normal glucose, and high WBC with lymphocytic pleocytosis. Cultures, gram stains and India ink were all negative, but no HSV PCR was performed on those admissions. As well, on each of these admissions, antibiotics and droplet precautions were first implemented, then stopped after the CSF results. A diagnosis of aseptic meningitis due to NSAID or to SLE was made, and the patient was discharged only a couple of days after each visit, in a stable condition.

When first described by Pierre Mollaret [1], the meningitis picture had no identifiable infectious agents, and it was considered an idiopathic aseptic meningitis. Currently, the etiology found is most commonly herpes virus HSV-2 [3]. After a primary genital infection, HSV-2 becomes dormant, within the sensory neurons of the sacral dorsal root ganglia. The retrograde seeding of the CSF, results in recurrent meningitis.

Rare cases are due to HSV-1, EBV, or reactivation of latent cerebral toxoplasmosis [5]. Noninfectious etiologies are also described, such as patients with brain cystic lesions, and intraspinal epidermoid cyst. These abnormalities cause meningeal irritation due to intermittent leakage of squamous material. Furthermore, drug-induced aseptic meningitis such as those due to non-steroidal anti-rheumatic drugs can be causative as well as recurrent meningitis due to systemic lupus erythematosus. This was one of the main differential diagnoses in our case.

Mollaret's meningitis is considered as a syndrome with multiple etiologies. Nevertheless, according to some authors, the term Mollaret's meningitis should be restricted to idiopathic recurrent aseptic meningitis [2].

As previously mentioned, Mollaret's meningitis is characterized by greater than three episodes of fever, headache and meningismus lasting 2–5 days [2, 5]. Individual attacks are sudden, with signs and symptoms reaching maximum intensity within a few hours. The symptom-free time can vary from weeks to years, and recurrent attacks usually resolve after a period of 3–5 years [4]. The longest case described in the literature was a patient with symptoms lasting more than 28 years. Our patient intervals were around 1 year each.

Many people have side effects between bouts that vary from chronic daily headaches to after-effects from meningitis such as hearing loss. However, the longterm health of the patients seems to not be adversely affected. Over 50% of patients have associated neurological signs and symptoms such as seizures, change in mental status, coma, hallucinations and cranial nerve palsies [5]. Our patient did not have any of these. Persistence of the above signs and symptoms, if present, should call for an alternative cause and diagnosis. The pathognomonic finding is large granular plasma cells on Papanicolaou's stain of the CSF. It usually demonstrates large, friable endothelial cells termed Mollaret's cells. These are considered to be large activated cells of monocyte/macrophage lineage. They are usually present only during the first 24 h and can be easily missed. Mollaret described them as 'fantomes cellulaires' (cell ghosts) [2].

After the first 24 h, the CSF shows a lymphocytic predominance with cell counts usually less than $3,000/\text{mm}^3$. Low CSF glucose concentration is reported in one-third of patients. CSF protein, especially the gamma globulin fraction, is usually mildly elevated. Also, there is a transition from a mainly neutrophilic pleocytosis early in the course, to a mainly lymphocytic pleocytosis as the disease progresses. Furthermore, a PCR for HSV DNA in the CSF remains the most crucial diagnostic [2, 3].

Although no randomized trials have been conducted in view of the rarity of this entity, acyclovir (intravenous or oral) or valacyclovir (oral) remain the main treatment.

Other therapies include steroids, indomethacin, and colchicine. A history of recurrent meningitis should lead to a consideration of the diagnosis of Mollaret's meningitis as a potential benign diagnosis. The prognosis is usually excellent.

Conflict of interest None.

References

1. Mollaret P (1944) La meningite endothelio-leucocytaire multi-recurrente. *Rev Neurol Paris* 76:57–67
2. Pearce JM (2008) Mollaret's meningitis. *Eur Neurol* 60(6):316–317
3. Picard FJ, Dekaban GA, Silva J, Rice GP (1993) Mollaret's meningitis associated with herpes simplex type 2 infection. *Neurology* 43(9):1722–1727
4. Stoppe G, Stark E, Patzold U (1987) Mollaret's meningitis: CSF-immunocytological examinations. *J Neurol* 234(2):103–106
5. Prandota J (2009) Mollaret meningitis may be caused by reactivation of latent cerebral toxoplasmosis. *Int J Neurosci* 119(10):1655–1692