

**ΔΙΑΦΟΡΙΚΗ ΔΙΑΓΝΩΣΗ
ΑΣΘΕΝΟΥΣ ΜΕ
ΛΕΜΦΟΚΥΤΤΑΡΩΣΗ ΣΤΟ ΕΝΥ
ΚΑΙ ΣΥΜΠΤΩΜΑΤΑ
ΔΥΣΑΙΣΘΗΣΙΑΣ ΚΑΤΩ ΑΚΡΩΝ**



Παπαντωνίου Μιχαήλ

Ειδικευόμενος Ιατρός

Νευρολογικό Τμήμα, ΓΝΑ «Ο Ευαγγελισμός»

ΣΥΝΤΟΜΟ ΙΣΤΟΡΙΚΟ

- Από μηνός αναφερόμενες δυσαισθησίες κάτω άκρων
- α/α : Β-ΧΛΛ (άνευ αγωγής), χειρ/θεν χολοστεάτωμα
- Νοσηλεία για διερεύνηση σε ιδιωτικό θεραπευτήριο
- CT εγκεφάλου: χωρίς παθολογικά ευρήματα CT ΟΜΣΣ: σπονδυλοαρθροπάθεια Ο5, ήπια στένωση νωτιαίου σωλήνα και μεσοσπονδύλιων τρημάτων Ο3-4, Ο4-5
- ΚΤΑ/ΑΤΑ/ΗΜΓ κάτω άκρων: κφ
- 2 ΟΝΠ: ήπια λεμφοκυττάρωση ΕΝΥ, με αυξημένο λεύκωμα, φυσιολογικό σάκχαρο, θετική PCR για EBV
- Ανοσοφαινότυπος ΕΝΥ: **Ανίχνευση κλώνου Β-ΧΛΛ (?)**
- Διάγνωση: **EBV Μυελίτιδα**
- Αγωγή: ενδοφλέβια γανκυκλοβίρη, αναγλητικά ΧΝΠΑ



EBV???

Clinical characteristics of patients with Epstein

REVIEW

Pract Neurol 2007; 7: 288-305

Viral encephalitis: a clinician's guide

Tom Solomon, Ian J Hart, Nicholas J Beeching

transplantation, 7 solid organ transplantation and 5 HIV/AIDS. 5 patients had no preceding immunodeficiency. In 8 of the cases, another pathogen was identified in CSF. These were *M. tuberculosis* (2), *T. gondii* (2), *Aspergillus* (1), *Herpes simplex virus 1* (1), *C. neoformans* (1) and *Human herpesvirus 6* (1). Altogether in 15/32 (47%) of the cases the clinician had a strong suspicion of cause other than EBV for the patients' CNS symptoms/findings.

Of note, 7 of 11 (64%) patients with stem cell transplantation had encephalitis (univariate odds ratio 5.6; confidence interval 1.1-27.4). Of these 6 had no other pathogen identified.

Conclusions: EBV DNA was often found together with other microbial findings in CSF of immunocompromised patients. EBV seems to be associated with encephalitis in stem cell transplant recipients.

One problem is that the high sensitivity of some of the recent PCR assays for herpes viruses, such as EBV and CMV, can make positive results difficult to interpret. Most of the adult population have been infected with these viruses and carry them in their lymphocytes. Therefore, there is debate about whether detection of the viruses by PCR of the CSF represents true pathogenic infection, rather than just the presence of infected lymphocytes.³⁹ Where there is uncertainty about the significance of a result, the amount of virus in the CSF compared with the blood (determined by quantitative PCR) usually helps resolve it. For example, in a patient with HIV, a CSF CMV PCR titre that is higher than that in the serum is usually significant.

resolved. It
encephalitis.

PCR positive

em cell

ΜΥΕΛΙΤΙΔΑ???

- ANE: χωρίς εστιακή σημειολογία, χωρίς ορθοκυστικές δ/χες, αναφερόμενη συμπατολογία, χωρίς μυελική συνδρομή
- Αδυναμία διενέργειας MRI λόγω κοχλιακού εμφυτεύματος
- ΚΤΑ/ΑΤΑ/ΗΜΓ: χαμηλό ύψος ΚΤΑ περνιαίου ν. αριστερά, νευρογενείς μονάδες πρ. κνημιαίου ΑΡ Ευρήματα συμβατά με Ο5 ριζίτιδα αριστερά
- ΟΝΠ: 64κκχ (λέμφο-), λεύκωμα 108mg/dl, χωρίς παρουσία ερυθρών, glu ΕΝΥ/ορού 50/89mg/dl PCR ΕΝΥ: αρνητική για βακτήρια/μύκητες/ιούς ΠΛΗΝ EBV: 1.9 x 10000 copies/ml
- Ευρήματα συμβατά με **άσηπτη μηνιγγοριζίτιδα**



ΔΙΑΦΟΡΙΚΗ ΔΙΑΓΝΩΣΗ ΑΣΗΠΤΗΣ ΜΗΝΙΓΓΟΡΙΖΙΤΙΔΑΣ

Infectious

Tuberculosis and atypical mycobacterial
Fungal (cryptococcal, coccidial, histoplasma, blastomyces, etc.)
Nocardia
HIV
Herpes type 2 (recurrent Mollaret meningitis)
Lyme disease
Syphilis
Brucellosis
Epidural abscess or hematoma
Incompletely treated bacterial meningitis

Granulomatous and vasculitic

Sarcoidosis
Wegener granulomatosis
Behçet disease
Vasculitis
IgG-4 pachymeningitis

Neoplastic

Carcinomatous
Lymphomatous
Leukemic

Allergic

Nonsteroidal antiinflammatory drugs
IVIg
Antibiotics
Other medications

Chemical

Leakage from epidermoid tumor, dermoid cyst, craniopharyngioma, or teratoma
Instillation of irritative substances by lumbar puncture, spinal anesthesia, or surgery

Idiopathic

Vogt-Kayanagi-Harada disease
No cause determined in one-third of cases



ΛΟΙΜΩΞΕΙΣ

Infectious

Tuberculosis and atypical (nonbacterial
Fungal (coccal, etc., histoplasma, blastomyces, etc.)
Nocardia
HIV
Herpes type (Mollaret meningitis)
Lyme disease
Syphilis
Brucella
Epidural abscess or hematoma
Incompletely treated bacterial meningitis

- Κ/α αίματος –ENY: Αρνητικό
- PCR ENY: Αρνητικό για βακτήρια, μύκητες
- PCR Brucella, Borrelia: Αρνητικό
- HIV, HBV, HCV, RPR, FTA-ENY: Αρνητικό
- EBV???



EBV ΜΗΝΙΓΓΟΡΙΖΙΤΙΔΑ

- Ελάχιστα περιστατικά άσηπτης μηνιγγοριζίτιδας από EBV

[Infez Med.](#) 1997 Jul;5(3):182-5.

[Neurological disorder associated to EBV: three case reports].

[Article in Italian]

[Luchi S¹](#), [Del Bono L.](#), [Vincenti A.](#), [Messina F.](#), [Scasso A.](#)

⊕ Author information

Abstract

Epstein-Barr virus (EBV) is associated with a wide range of clinical manifestations. Neurological involvement (NI) during Infectious Mononucleosis occur in 1-5% of the cases, the only NI is more rare. From January 1995 to December 1996 three patients with NI and EBV infection have been observed in our department. The diagnosis were: meningoradiculitis (1 case), meningoencephalitis (1 case), aseptic meningitis (1 case). The diagnosis was based on the results of the lumbar puncture and on the serology: IgM VCA positive at the onset of the symptoms and a significant increase of the IgG VCA after three weeks. No other etiology was apparent. All the patients have been treated

[Brain.](#) 2002 Jan;125(Pt 1):159-65.

Epstein-Barr virus myeloradiculitis and encephalomyeloradiculitis.

[Majid A¹](#), [Galletta SL](#), [Sweeney CJ](#), [Robinson C](#), [Mahalingam R](#), [Smith J](#), [Forghani B](#), [Gilden DH](#).

⊖ Author information

1 Department of Neurology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA.

Abstract

We provide a comprehensive clinical, radiological and virological analysis of four patients with Epstein-Barr virus (EBV) infection of the nervous system. One patient developed acute myeloradiculitis, one had acute encephalomyeloradiculitis, one had acute meningoencephalomyeloradiculitis and one had a subacute meningomyeloradiculitis. The ability of EBV to affect multiple parts of the entire

- Σε όλα τα επιβεβαιωμένα περιστατικά είχαν αποκλειστεί τα λοιπά αίτια



ΑΥΤΟΑΝΟΣΑ ΑΙΤΙΑ

Granulomatous and vasculitic

Sarcoidosis

Wegener's granulomatosis

Behçet's disease

Vasculitis

IgG4-related angitis

- SACE ορού και ENY: Αρνητικό
- Ανοσολογικός έλεγχος: Αρνητικός
- Κλινική εικόνα ΜΗ συμβατή με αγγειίτιδα ΚΝΣ ή νόσο Αδαμαντιάδη - Behcet
- Βιοψία κροταφικής αρτηρίας: Αρνητική
- IgG4 ορού και ENY: κφ



ΝΕΟΠΛΑΣΙΑ

Neoplastic
Carcinomatous
Lymphomatous
Leukemic



- Ιστορικό Β-ΧΛΛ άνευ αγωγής
- CT θώρακος-άνω/κάτω κοιλίας: μη ογκώδης λεμφαδενοπάθεια εκατέρωθεν του διαφράγματος, απουσία οργανομεγαλίας
- Μυελόγραμμα και ανοσοφαινότυπος μυελού: διήθηση μυελού από Β μονοκλωνικό πληθυσμό συμβατό με CLL/SLL σε ποσοστό ~95%



ΕΠΙΝΕΜΗΣΗ ΚΝΣ ΑΠΟ Β-ΧΛΛ

NEUROLOGIA I NEUROCHIRURGIA POLSKA 52 (2018) 228-234

Meningeal Involvement in Early Stage Chronic Lymphocytic Leukemia

JOSEPH CASH, MD, KIM M. FEHIR, MD, PhD, AND MARILYN S. POLLACK, PhD



ELSEVIER

Original

Central

lymphoma

Two patients with early stage chronic lymphocytic leukemia were found to have meningeal involvement. The diagnosis was confirmed by cerebral spinal fluid cytology in the first patient and by flow cytometric analysis in the second patient. Both patients responded well to intrathecal chemotherapy and cranial irradiation. Central nervous system infiltration by tumor cells has rarely been described in chronic lymphocytic leukemia but must be considered in all patients regardless of stage who present with lethargy, dementia, or focal neurologic signs.

Cancer 59:798-800, 1987.

Dariusz Szczepanek^a, Ewa Wąsik-Szczepanek^b, Agnieszka Szymczyk^{b,c,*},
Małgorzata Wach^b, Maria Cioch^b, Monika Podhorecka^b,
Ewelina Grywalska^d, Marek Hus^b

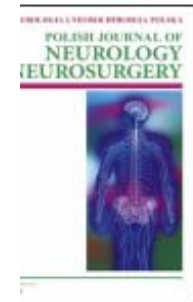
^a Department of Neurosurgery and Paediatric Neurosurgery, Medical University of Lublin, Poland

^b Department of Haematology and Bone Marrow Transplantation, Medical University of Lublin, Poland

^c Independent Clinical Transplantology Unit, Medical University of Lublin, Poland

^d Department of Clinical Immunology, Medical University of Lublin, Poland

patients with CNSi, documented by lymphocytic infiltration either by flow cytometry of the cerebrospinal fluid (CSF; n = 29) or CNS biopsy (n = 1). Neurological symptoms were heterogeneous. At the time of CNSi, less than half of the patients had a progressive CLL and 20 had



ΚΑΡΚΙΝΩΜΑΤΩΔΗΣ ΜΗΝΙΓΓΙΤΙΔΑ

Neoplastic meningitis

Beate Gleissner, Marc Charles Chamberlain

Neoplastic meningitis is a complication of the CNS that occurs in 3–5% of patients with cancer and is characterised by multifocal neurological signs and symptoms. Diagnosis is problematic because the disease is commonly the result of pleomorphic manifestations of neoplastic meningitis and co-occurrence of disease at other sites. Useful tests to establish diagnosis and guide treatment include MRI of the brain and spine, cerebrospinal fluid (CSF) cytology, and radioisotope CSF flow studies. Assessment of the extent of disease of the CNS is of value because large-volume subarachnoid disease or CSF flow obstruction is prognostically significant. Radiotherapy is an established and beneficial treatment for patients with neoplastic meningitis with large tumour volume including parenchymal brain metastasis, sites of symptomatic disease, or CSF flow block. Because neoplastic meningitis affects the entire neuraxis, chemotherapy treatment can include intra-CSF fluid (either intraventricular or intralumbar) or systemic therapy. Most patients (>70%) with neoplastic meningitis have progressive systemic disease and consequently treatment is palliative and tumour response is of restricted durability. Furthermore, as there is no compelling evidence of a survival advantage with aggressive multimodal treatment, future trials need be done to determine the effect of treatment on quality of life and control of neurological symptoms.

Lancet Neurol 2006; 5: 443–52

Medical Clinic I, University Hospital of Saarland Medical School, Homburg, Saar, Germany (B Gleissner MD); and Department of Interdisciplinary Oncology, H Lee Moffitt Cancer Center, University of South Florida, Tampa, Florida, USA (M C Chamberlain MD)

Correspondence to: Marc C Chamberlain, Department of Interdisciplinary Oncology, H Lee Moffitt Cancer Center & Research Institute,

J Adv Pract Oncol. 2013 May-Jun; 4(3): 155–160.

Published online 2013 May 1.

PMCID: PMC4093424

PMID: [25031995](#)

How to Recognize and Treat Neoplastic Meningitis

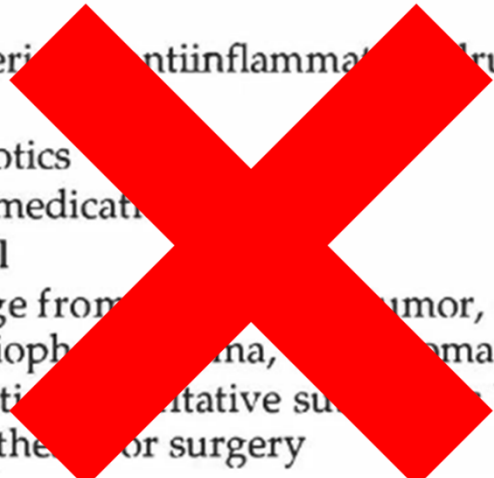
[Margaret M. Fields](#), MSN, ACNP-BC, AOCNP®

From MD Anderson Cancer Center, Houston, Texas

Correspondence to: Margaret M. Fields, MSN, ACNP-BC, AOCNP®, MD Anderson Cancer Center, Neuro Oncology, 1400 Holcombe Boulevard, Unit 431, Houston, TX 77030. E-mail: mmfields@mdanderson.org

Copyright © 2013, Harborside Press

ΙΑΤΡΟΓΕΝΗΣ



Allergic
Nonsteroidal antiinflammatory drugs
IVIg
Antibiotics
Other medications
Chemical
Leakage from meningioma, tumor, dermoid cyst, craniopharyngioma, epidermoid cyst
Instillation of irritative substances by lumbar puncture, spinal anesthesia for surgery

- Δεν αναφέρεται γνωστή αλλεργία
- Δεν αναφέρεται λήψη οποιασδήποτε αγωγής
- Δεν αναφέρεται πρόσφατο χειρ/ο συμβατό με αίτιο



ΙΔΙΟΠΑΘΗΣ

Idiopathic

Vogt-Kayanagi-Harada disease

No cause determined in one-third of cases



- Κλινική εικόνα μη συμβατή με νόσο Vogt-Kayanagi-Harada
- Ιδιοπαθής ?



ΔΙΑΦΟΡΙΚΗ ΔΙΑΓΝΩΣΗ ΑΣΗΠΤΗΣ ΜΗΝΙΓΓΟΡΙΖΙΤΙΔΑΣ

Infectious

- Tuberculosis and atypical mycobacterial
- Fungal (coccal, coccidial, plasmodial, blastomyces, etc.)
- Nocardia*
- HIV
- Herpes type 2 (mollaret meningitis)
- Lyme disease
- Syphilis
- Brucellosis
- Epidural abscess or hematoma
- Incompletely treated bacterial meningitis

Granulomatous and vasculitic

- Sarcoidosis
- Wegener granulomatosis
- Behçet disease
- Vasculitis
- IgG-4 pachymeningitis

Neoplastic

- Carcinomatous
- Lymphomatous
- Leukemic



Allergic

- Nonsteroidal antiinflammatory drugs
- IVIg
- Antibiotics
- Other medications

Chemical

- Leakage from tumor, dermoid cyst, craniomeningocele, meningocele, meningocele, meningocele
- Instillation of irritative substances by lumbar puncture, spinal anesthesia, or surgery

Idiopathic

- Vogt-Kayanagi-Harada disease
- No cause determined in one-third of cases



ΔΙΑΓΝΩΣΤΙΚΗ ΠΡΟΣΕΓΓΙΣΗ

- EBV Μηνιγγοριζίτιδα?
- Επινέμηση ΝΣ από Β-ΧΛΛ?
- Άλλη καρκινοματώδης μηνιγγίτιδα?
- Ιδιοπαθής?



ΠΕΡΑΙΤΕΡΩ ΔΙΕΡΕΥΝΗΣΗ

- Ανοσοφαινότυπος ΕΝΥ ?
- Κυτταρολογική ΕΝΥ και Κυτταρομετρία Ροής ?
- Απεικόνιση με Μαγνητική Τομογραφία ?
- PET SCAN ?
- Βιοψία λεπτομήνιγγας ?
- Ανταπόκριση σε θεραπευτική αγωγή ?

Στην συνέχεια η εξέταση που έθεσε την διάγνωση και η περαιτέρω κλινική πορεία της ασθενούς



ΣΑΣ ΕΥΧΑΡΙΣΤΩ



- *Une leçon clinique à la Salpêtrière* - Pierre Aristide André Brouillet, 1887
Paris Descartes University, Paris, France

