J Neurol (2002) 249 : 884–887
DOI 10.1007/s00415-002-0754-9

ORIGINAL COMMUNICATION

A. O. Rossetti
K. Meagher-Villemure
F. Vingerhoets
Ph. Maeder
J. Bogousslavsky

Eosinophilic aseptic arachnoiditis
A neurological complication in HIV-negative drug-addicts

Received: 24 October 2001
Received in revised form: 15 January 2002
Accepted: 21 January 2002

A. O. Rossetti, MD (✉) · F. Vingerhoets, MD · J. Bogousslavsky, MD
Service de Neurologie BH-13
CHUV
Lausanne, Switzerland
Tel.: +41-21/3 14-12 20
Fax: +41-21/3 14-12 44
E-Mail: Andrea.Rossetti@chuv.hospvd.ch

K. Meagher-Villemure, MD
Institut de Pathologie
CHUV
Lausanne, Switzerland

Ph. Maeder, MD
Service de Radiologie
CHUV
Lausanne, Switzerland

Abstract The finding of an eosinophilic aseptic meningitis in IV drug abuse is usually suggestive of an opportunistic infection or an allergic reaction. However, HIV-negative patients are at lower risk for developing these complications. Two young HIV-negative patients, with previous intravenous polytoxicomany, developed cystic arachnoiditis over the spinal cord associated with eosinophilic meningitis. Histology of the meningeal spinal cord lesions revealed a vasculocentric mixed inflammatory reaction. In one patient prednisone led to marked clinical improvement. Since infection, vasculitis, sarcoidosis and previous myelography were ruled out, we believe that the syndrome of eosinophilic aseptic arachnoiditis may be related to an hyperergic reaction in the meniges toward drug-adulterants inoculated through the intravenous route.

Key words IV drug abuse · eosinophilic meningitis · arachnoiditis

Introduction

Neurological complications of drug abuse are related to a wide spectrum of entities: infections, cerebral infarction or hemorrhage, transverse myelopathy, seizures, myopathy, rhabdomyolysis, neuropathy and psychiatric symptoms [2, 7, 10]. As drug addicts are known to show compromised immunocompetence, the finding of eosinophilic aseptic meningitis or spinal arachnoiditis may be the expression of an underlying opportunistic infection or of a CNS vasculitis; however, in HIV-negative subjects these complications are relatively infrequent.

We report two HIV-negative patients known for previous intravenous-polytoxicomany and on methadone substitution, who presented with an eosinophilic aseptic meningitis related to a spinal cord arachnoiditis.

Patient 1 (1990)

A 34-year-old man, with previous IV-addiction (benzodiazepines, cocaine, heroine) and on methadone substitution for the past 2 years, reported a several months history of low back pain which progressed to leg weakness associated with sphincter disturbances. Myelography had never been performed. Neurological examination revealed bilateral papilledema, spastic paraparesis, and hypoesthesia of the lower legs. Spinal MRI disclosed some thickening of the arachnoid with cystic cavitations and compression of the lumbar roots and the conus (Fig 1); brain MRI showed a pial contrast enhancement around the brainstem. Chest radiographs, WBC (no eosinophilia), RBC, sedimentation rate and blood chemistry were normal. A lumbar puncture revealed CSF containing an elevated protein level (5000 mg/l), and 21 leucocytes/mm3 (10 % eosinophils). A bilateral L1-L2

JON 754

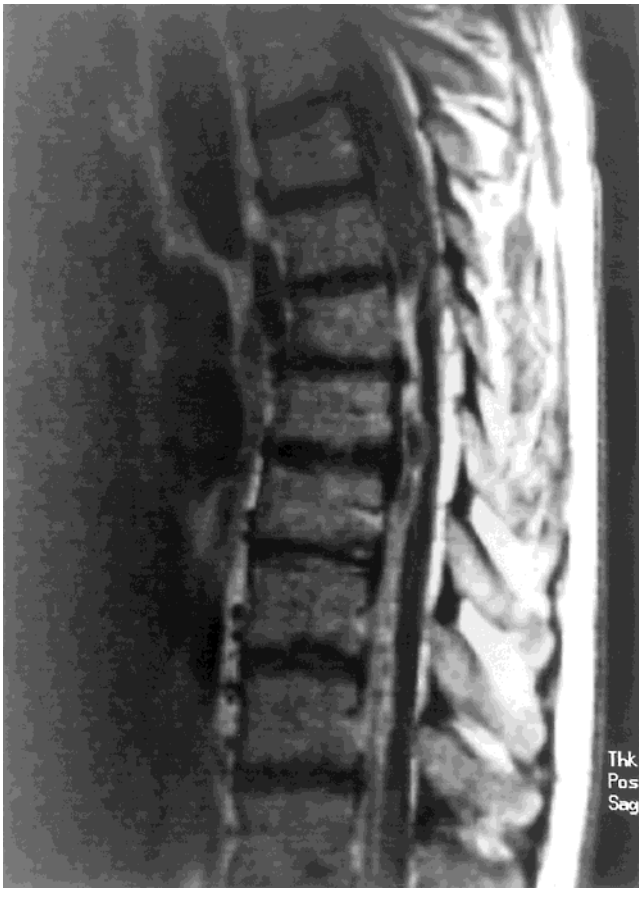

Fig. 1 Sagittal view of the thoracic spine of the 1st patient with contrast enhancement of the meninges and cystic cavitations (T1 weighted MRI with gadolinium).

laminectomy was performed, with slight improvement of the symptoms. Cultures of the material as well as viral and bacterial serology (including HIV) were negative, apart from EBV IgG. After eight months, the patient worsened, a new spinal MRI showed progressive arachnoidal lesions, therefore prednisone treatment was started following a second laminectomy. One month later the patient was found in coma after a heroine overdose; CT of the brain revealed diffuse edema and communicating hydrocephalus. The patient died of pulmonary edema a few hours later. Autopsy was refused by his family.

Patient 2 (2000)

A 26-year-old woman had consumed regularly benzodiazepines, heroine, cocaine, cannabis and methaqualone (mostly intra-venously) in the past, and was on methadone substitution for the past 2 years. She never had myelography, nor experienced low-back trauma. Several months before hospitalisation she developed progressive anorexia associated with worsening leg weakness and sphincter disturbances. Neurological examination revealed a somnolent patient with bilateral papilledema, absent ankle jerks, a distal paraparesis, and hypoesthesia of the right foot. Lumbar MRI revealed a voluminous lesion between the conus and L5 with a central cyst (Fig 2); brain MRI showed meningeal enhancement of the base of the skull (Fig 3). A ventricular derivation and bilateral L3-L4 laminectomy were performed. CSF examination showed 3200 mg/l protein, normal glucose, and 10 leucocytes/mm^3 (4% eosinophils). Thoracoabdominal CT, WBC (no eosinophilia), RBC, blood chemistry and urine analysis were normal. Serology including HIV, Borrelia, syphilis and parasites (cysticercosis, toxoplasmosis, toxocariasis, schistosomiasis, rickettsioses, echinoccocoses), as well as CSF cryptococcal antigens and *Mycobacterium tuberculosis*-PCR were negative, whereas EBV IgG was positive. ACE, rheumatoid factor and nuclear autoantibodies in the serum were in the normal range. Prednisone treatment

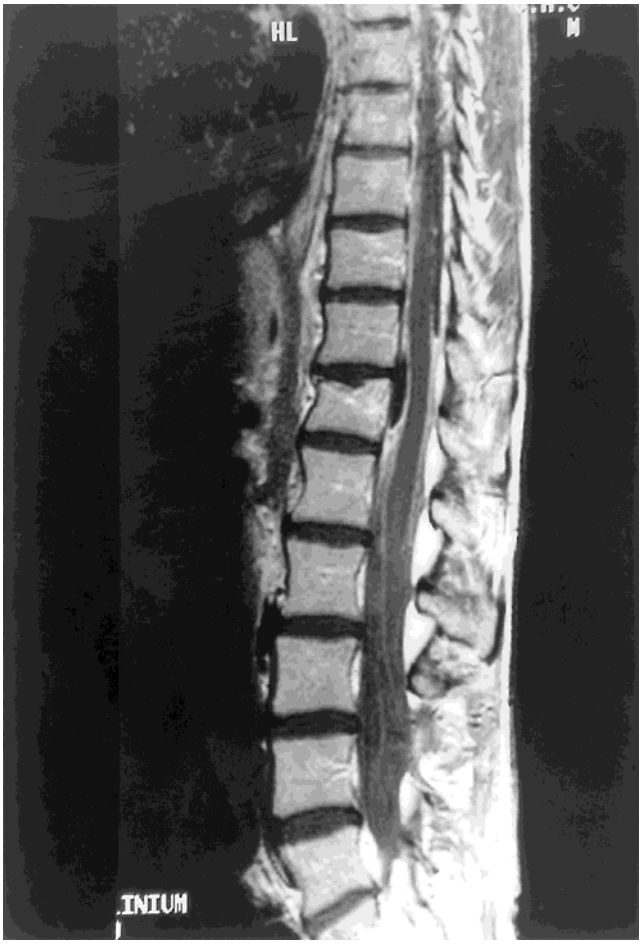

Fig. 2 Dorsolumbar spine of the 2nd patient surrounded by an arachnoditic process with contrast enhancement and cystic cavitations, very similar to Fig. 1 (T1 weighted MRI with gadolinium).

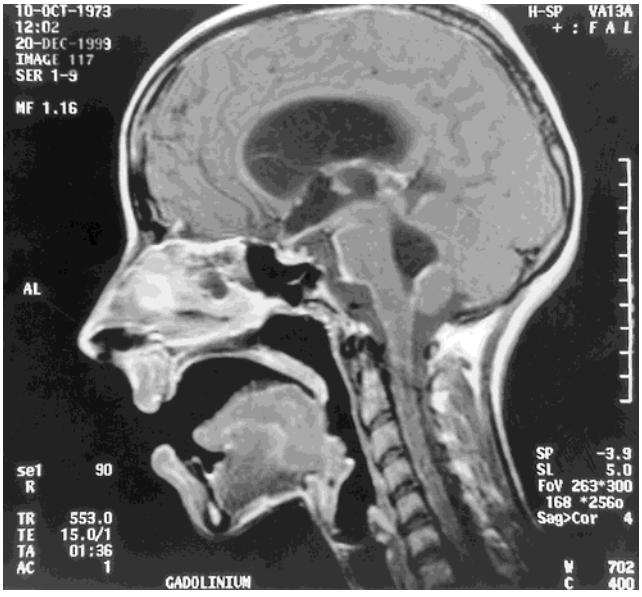

Fig. 3 Sagittal view of the skull of the 2nd patient with marked hydrocephalus and contrast enhancement of the meninges around the brainstem, with obstruction of Magendie's and Luschka's foramina (T1 weighted MRI with gadolinium).

was initiated, under which the patient markedly improved: review at 6 months showed a weight gain, no papilledema, a residual minimal weakness of the legs without sensory deficits and normal sphincter function. Unfortunately, the patient was later lost to follow-up.

Pathology

The histological specimen from the spinal meningeal biopsy in Patient 1 showed a chronic arachnoiditis with fibrosis and an angiocentric lympho-histiocytic infiltration, few eosinophiles, without granulomatous reaction or atypical cell features. After the 2nd laminectomy, the same fibrous changes were found with a mixed type of inflammatory reaction.

The meningeal biopsy of Patient 2 revealed a multinodular inflammatory reaction surrounding predominantly many small vessels (Fig 4). The inflammatory infiltrate was made of lymphocytes, histiocytes, rare eosinophiles and plasma cells (Fig 5). Immunohistochemistry revealed positive cells for CD45 (LCA), CD68 in histiocytes, CD3 (T-cells), rare CD20 (B-cells) and a polyclonal type of immunoglobulins in the plasma cells. A negative CD1A, as well as absence of Birbeck granules in histiocytes on ultrastructure study, excluded the presence of Langherhans cells disease.

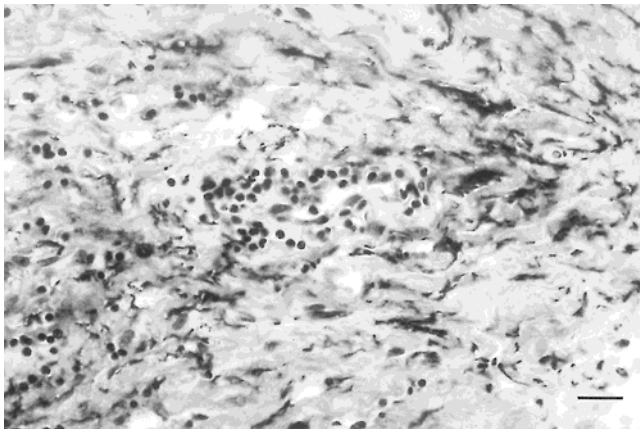

Fig. 4 Dense fibrous tissue with small vessels surrounded by lymphocytes and plasma cells. (HE 250X, the black bar corresponds to 40 µm).

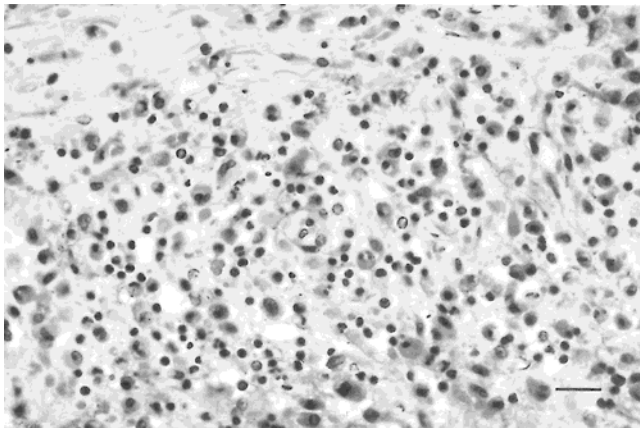

Fig. 5 Inflammatory infiltrate with numerous histiocytes, lymphocytes, plasma cells and rare eosinophiles (HE 400X, the black bar corresponds to 25 µm).

Discussion

Our 2 HIV-negative patients showed an unusual concomitant progressive occurrence of an eosinophilic aseptic meningitis related to spinal arachnoiditis.

Eosinophilic aseptic meningitis, with or without prominent arachnoiditis, has infectious (parasitic, fungal, bacterial, viral) and non-infectious causes (systemic hypereosinophilia, Chürg-Strauss syndrome, lymphomas, sarcoidosis, systemic lupus erythematosus, ventriculo-peritoneal-shunts) [1, 3, 11, 12]. An arachnoidal reaction can further be the consequence of trauma, or of the insertion of foreign material (blood, cytostatic agents, anesthetic drugs, steroids, radiological contrast agents, and antimicrobial drugs) into the subarachnoidal space [1, 3]. Our clinical investigations ruled out an infection, which can be considered the leading cause of neurological complications among drug addicts [2, 7, 10], and an autoimmune process or sarcoido-

sis. Although the ventricular shunt of the 2nd patient could have induced an eosinophilic reaction, the first patient showed an eosinophilia in the CSF previous to surgery. Systemic inoculation of Non-Steroidol-Anti-Rheumatic (Drugs) drugs or antibiotics, which can be found as cut substances in street drugs, may be responsible for an eosinophilic reaction [12]. A similar mechanism, although without CNS eosinophilia, has been reported to involve the spinal cord in drug addicts [5]: in that case a vasculitis was histologically diagnosed in the CNS, whereas in our patients a perivascular inflammatory reaction without signs of vasculitis was found.

Although there is no long-term follow-up, and, owing to the small number of patients, there is the possibility of a coincidental association of drug addiction and the development of the described syndrome, it is tempting to assume that the inoculation of cut substances such as NSAR drugs or antibiotics via the blood circulation into the subarachnoidal space may account for the eosinophilic arachnoiditis. The fact that the immune system of the 2 subjects was probably not severely depressed, thus allowing an hyperergic reaction, and the dramatic improvement of the 2nd patient under prednisone treatment, which points to an inflammatory cause, support this hypothesis. The histology of an angiocentric mixed inflammatory changes in both meningeal biopsies may suggest a reaction related to lymphomatoid granulomatosis (LG), even if the absence of atypical lymphocytes is unusual. This entity shows neurological involvement in 30 % of the cases [6, 8], and has been recorded among immunosuppressed hosts [4, 6], but not especially in HIV-negative drug addicts. Since our patients were both EBV positive, the possible pathogenic role of an excessive polyclonal T-cell reaction following an EBV-related B-cell proliferation may be an explanation for the angiocentric reaction in an already inflamed tissue, in analogy to LG [4, 9].

Conclusion

Since it is unusual to find a CNS involvement in drug addicts whose causation is neither infectious, nor vasculitic, these observations suggest that the occurrence of a spinal eosinophilic aseptic arachnoiditis associated with an angiocentric inflammation in HIV-negative IV-drug addicts could account for a specific, although infrequent entity, adding a new element to the range of neurological damage induced by blood-inoculated drugs. Its rapid recognition allows the introduction of anti-inflammatory treatment leading to clinical improvement of its otherwise potentially lethal course.

References

1. Benini A, Blanco J (1990) Chronische fibroplastische Leptomeningitis von Rückenmark und Cauda equina. Schweiz Arch Neurol Psychiatr 14: 293–343
2. Bernasconi A, Kuntzer T, Labdon N, Janzer RC, Yersin B, Regli F (1996) Complications neurologiques périphériques et médullaires de la toxicomanie intraveineuse à l'héroïne. Rev Neurol (Paris) 152:688–694
3. Esses SI, Morley TP (1983) Spinal arachnoiditis. Can J Neurol Sci 10:2–10
4. Gold JE, Ghali V, Gold S, Brown JC, Zalusky R (1990) Angiocentric immunoproliferative lesion/T-cell Non-Hodgkin's lymphoma and the acquired immunodeficiency syndrome: a case report and review of the literature. Cancer 66:2407–2413
5. Judice DJ, LeBlanc HJ, McGarry PA (1978) Spinal cord vasculitis presenting as a spinal cord tumor in a heroin addict. J Neurosurg 48:131–134
6. Katzenstein AA, Carington CB, Liebow AA (1979) Lymphomatoid granulomatosis: a clinicopathological study of 152 cases. Cancer 43:360–373
7. Koppel BS, Tuchman AJ, Mangiardi JR, Daeas M, Wetzner I (1988) Epidural spinal infection in intravenous drug abusers. Arch Neurol 45:1331–1337
8. Liebow AA, Carrington CB, Friedman PJ (1972). Lymphomatoid granulomatosis. Hum Pathol 3:457–558
9. Myers JL, Kurtin PJ, Katzenstein AL, Tazelahaar HD, Colby TV, Strickler JC, Lloyd RV, Isaacson PG (1995) Lymphomatoid granulomatosis. Evidence of immunophenotipic diversity and relationship to Epstein-Barr-Virus infection. Am J Surg Pathol 19:1300–1312
10. Pearson J, Richter RW (1979) Addiction to opiates: neurologic aspects. In: Vinken PJ, Bruyn GW (eds) Handbook of clinical neurology, Intoxication of the nervous system. Part II, Vol. 37. Amsterdam: North Holland Publishing Company, pp 365–400
11. Strupp M, Pfister HW, Eichenlaub S, Arbusow V (1999) Meningomyelitis in case of toxocariasis with markedly isolated CSF eosinophilia and an MRI-documented thoracic cord lesion. J Neurol 246:741–744
12. Weller PF, Liu LX (1993) Eosinophilic meningitis. Sem Neurol 13:161–168