Polyradiculopathy in an AIDS patient with cytomegalovirus infection

Vítor Augusto*, Alberto Leal**, Carlos Araújo***. J. Luís Champalimaud****

Abstract

The authors report a case of an HIV1 seropositive homosexual male developing an axonal progressive and ascendant subacute polyradiculopathy, polymorphonuclear pleocytosis compatibly associated with a clinical diagnosis of cytomegalovirus nervous system infection. This entity is rare, and it is of difficult laboratorial confirmation and resistant to therapy measures as reported in the literature.

Keywords: polyradiculopathy, CMV, AIDS, ganciclovir, polymorphonuclear pleocytosis.

Introduction

The cytomegalovirus (CMV) is a frequent opportunistic infection agent in AIDS and appears associated with multi systemic manifestations as chorioretinitis, adrenalitis and gastrointestinal lesions.[1]

Infections by CMV in any location represent 90% of the diagnoses in the autopsy of seropositive patients for the human immunodeficiency virus, [1,2] being the involvement of the central nervous system around 30% in identical circumstances.[1,3]

The clinical manifestations of urinary retention, flaccid paraparesis, crural myalgia and "saddle" anaesthesia in AIDS patients should suggest the diagnosis of polyradiculomyelitis due to CMV.[1]

Such a rare syndrome only occurs in 2% of all AIDS patients and subsequent neurologic complication.[1,4]

The diagnosis is based in the clinical findings associated with persistence neutrophil pleocytosis, being extremely difficult to establish the CMV as etiologic agent, as usually CSF and nervous tissue cultures are negative.[1,5]

Serology has a limited usefulness, due to the fact that most HIV1 seropositive patients is also seropositive for CMV, and the specific IgM antibody can be found without a matching active infection.[1,6]

Recently, the PCR technique (polymerase chain reaction) has proven to be useful to establish a CMV quick and definite diagnosis.[1]

The early recognition of such distinct clinical entity should lead to the start of therapy as early as possible with ganciclovir.[1,7,8,9]

Due to its rare character, with a mainly clinical diagnosis and potentially treatable of such syndrome, our proposal is to present this clinical case aiming to strengthen and make available knowledge in such medical area.

Case report

33 years old patient, male gender, Indian race, graduated in Geography, civil servant, single, born in Lourenço Marques and residing in Loures, homosexual, HIV-1 seropositive known since May 1992, with a previous history of oral candidiasis, pulmonary and ganglionary tuberculosis (*M. tuberculosis*) for two years, at present being medicated with prophylactic isoniazid, zidovudine, co-trimoxazole; with a CD4 value of 38. Admitted in the Infectious and Parasitology Diseases Unit of Egas Moniz Hospital from the 18th October to the 17th November 94 due to lower limb myalgia, febrile syndrome and asymmetric paraparesis.

This is a patient who at the beginning of September 1994 started a clinical condition featured by febrile syndrome (38 – 38.5°C), non-purulent rhinorrhoea, bilateral nasal obstruction and nasal voice, along with complains of lower limb myalgia, diffuse and of moderate intensity, persistent, resistant to analgesic therapy as an outpatient with lysine clonixinate and paracetamol, and paresthesia in the tights and feet, reason why he was hospitalised from the 4 to 12th

*Resident to the Supplementary Internal Medicine Internship

**Resident to the Supplementary Neurology Internship

***Internal Medicine Hospital Assistant

****Head of Service

Unit of Infectious Diseases of Egas Moniz Hospital, Lisbon

October 94 in the same service. He was discharged with a clinically documented diagnosis of exudative pan-sinusitis medicated with oral ciprofloxacin, after symptomatic improvement, pyrexia regression, absence of suggestive laboratorial signs suggesting myositis and persistence of the normal neurological exam.

On the 18th October 94 he was readmitted for worsening myalgia identical to the previous ones associated to muscle weakness in the lower limbs with gait claudication of right predominance, fever (38 – 38.5°C) and paresthesia in the tights and feet.

On admission, the physical exam highlighted a undernourished condition (weight= 44 kg and height= 177cm), dry and scaling skin, axillary temperature= 37.2°C; blood pressure= 110/60 mmHg; radial pulse=84 ppmrar; oral candidiasis. Without any other change worth of note.

The neurologic exam revealed flaccid paraparesis of distal predominance on the right (grade 4) and proximal on the left (4+); left patellar and right Achilles tendon hyporeflexia; symmetric algic hypoesthesia in the anterior-internal face of the thighs. Analytically, it could be highlighted: high ESR (125 mm/1st hour); normocytic anaemia (HGB=10,6 g/dL); hyponatraemia (130mEq/L); β-2 microglobulin= 4,7 mg/L. The lumbar puncture performed on the 19th October 94 showed the CSF with a clear, normotensive, neutrophilic pleocytosis, high protein concentration (with a severe destruction of the blood brain barrier); hypoglycorrhachia, without intrathecal IgG synthesis.

The results of the cryptococcic antigen, VDRL and TPHA were negative, similarly to the bacterial exam, both mycology and mycobacteriology (direct and cultural). Liquor ADA was equal to 8.5U I/L (serial = 33,5 UI/L). Total anti-CMV serology and IgM were negative. The CSF pathologic-anatomical exam has revealed a presence of abundant granulocytes, neutrophils and absence of neoplastic cells. P 24 antigen was equal to 64 pg/microlitre in the liquor. Mantoux test (PPD = 2UI) has revealed cutaneous anergy. The CE TC has showed a diffuse cortical-subcortical atrophy of moderate grade and signs of pan sinusitis exudative, without reference to lesions taking space.

In the needle EMG denervation signs were found in all the studied muscles both in the lower as in the upper limbs; potentials of motor unit of neuropathic features or absence of voluntary muscle activity and a pattern of reduced recruitment in the muscles where there is involuntary activity.

TABLE I

Cell	616/pmn	104/pmn
Glucose	39	45
Proteins	107	166
Pandy	positive	positive
ADA	8.5	
Cryptococcus	negative	
RTHA	negative	
VDRL	negative	
AgP 24	74,6	
Beta 2 mic	6.2	
CMVT/IgM	negative	
HTLV I/II	negative	

In a study of the nervous motor and sensitive transmission almost normal were recorded, except on the study of F waves, where there was an absence of those while stimulating the motor nerves of the lower limbs. Such electrophysiological findings are compatible with the diagnosis of polyradiculopathy of crural predominance and of sensitive motor polyneuropathy of axonal type.

During the hospitalisation, there was a record of improved myalgia and paresthesia, simultaneous to the emergency of prostrations and gradual decline in the general condition, adding to tachy-/polypnoea, reduced respiratory muscles strength, with subsequent bronchorrhea and breathing difficulties without initial stetho_acoustic, radiological or even gasometry changes.

On the sixth day of admission, he started urinary retention with the need of a permanent vesical probe and on the 15th day faecal incontinence emerged. The transabdominal prostate ultrasound did not reveal any apparent morphological changes.

On the 15th day of admission the second lumbar puncture was performed, confirming the presence of the clear, normotensive, polymorphonuclear CSF with hypoglycorrhachia; high protein concentration and serious destruction of the blood brain barrier (*Table 1*), with samples being sent for viral study at Ricardo Jorge Institute (*Table 2*).

The neurologic re-observation on the 16th day of admission would highlight a flaccid paraparesis (gra-

TABLE II

	Blood	CSF
HTLV (Eliza)	negative	negative
Anti-CMV/IgM	negative	negative
Anti-CMV/ IgG	positive	negative
Anti-HSV/IgM	negative	negative
Anti – HSV/IgG	positive	positive

de 2) predominantly distal and worsen; symmetrical patellar areflexia and Achilles tendon hyporeflexia and cutaneous-plantar reflex in flexion.

Before the clinical and neurological worsening where it should be highlighted a suggestive semiologic condition of sensitive-motor polyradiculoneuropathy with neutrophil pleocytosis, it was decided to start an antiviral therapy com ganciclovir in the diagnosis presumption of likely CMV etiology, on the 4th November 94, with a dose of five mg/kg every 12 hours by endovenous route.

On the 22nd day the condition would evolve for flaccid paraplegia, with segmental muscular strength of grade 4+ in the upper limbs and zero in the lower limbs; sacred anaesthesia on S2-S5 territories and bilateral hypoesthesia in L2 – L3; distal loss of vibration sense in the lower limbs, being the fundoscopy carried out on the 21st October and 9th November normal, namely without cotton like exudates or retinal haemorrhages.

The patient was kept in bed, febrile, prostrated and anorectic with a gradual deterioration of his breathing muscles reduced strength and his state of awareness, manifested through somnolence and mental obnubilation, starting an overall condition of respiratory failure progressing for two days and dying on the 30th day of admission.

No autopsy was carried out.

Discussion

The case we are assessing presents an example of a unique polyradiculopathy in patients affected by the human immunodeficiency virus (HIV).[8]

The rare descriptions published in the medical literature described it as a diagnosed clinical entity in male patients, within an age range from 30 to 42 years old, homosexuals in a context of acquired immunodeficiency syndrome.[8]

Simultaneously when the neurologic impairment onset symptoms emerge all patients present marked weight loss and muscular emaciation,[8] what in whole also happens in this patient.

The treatment with zidovudine this patient have been subject to is not an impeditive of such kind of complication, as can be assessed by the series previously described, each with a CD4 lymphocytes count usually lower than 50 cell per cubic millimetre at the beginning of the complaints.[9,10]

The number of symptoms and signs present in this clinical case is within the conventional description of CMV polyradiculopathy. The syndrome consisting at the beginning in bilateral diffuse crural pain, followed by feet paraesthesia and afterwards by the quick development of ascending flaccid paraparesis of distal beginning, along with an early urinary retention, sensitive changes in the territories of the lumbar and sacred dermatomes, "saddle hypoesthesia", lower limbs areflexia,[1,7,8,11] happens in this case. The featuring fact in the disease evolution being the upper limbs are spared or lightly committed when the paraparesis or paraplegia is set[1,8] and this is well highlighted in this patient, as well as the absence of proprioceptive vibratory sensitivity deficits of the cranial pairs.[1,8]

The occurrence of pneumonia or breathing failure represents the usual cause of death in such affection, being around six weeks the average time between the symptomatology onset and death in one of the series described by Robert G. Miller et cols.[8]

Laboratorially, the diagnosis of CMV polyradiculopathy is based on the observation of a typically abnormal liquor with polymorphonuclear pleocytosis,[1,7,8] moderate hypoglycorrhachia and marked increase on protein concentration [8,9,11] being the cultures for bacteria, fungi, parasites, other opportunistic infections and VDRL all negative.[1,8] In this clear example, we found in the two lumbar punctures carried out neutrophilic pleocytosis as a more relevant particular, supplemented by the remainder of elements excluding all other hypothetic differential diagnosis.

Among the last ones, can be counted the inflammatory demyelinating polyradiculopathy (IDP) and the distal symmetrical polyneuropathy.

The first of such entity has the specificity of emerging as an onset manifestation on the HIV infection and can be differentiated from progressive CMV polyradiculopathy due to a late occurrence of urinary retention and early involvement of the cranial pairs, as well as the simultaneity of areflexia and paresis both

in the upper limbs as in the lower limbs.[1,7,8]

Under no circumstance there is sensitivity at medullar level in the inflammatory demyelinating polyradiculopathy by CMV,[8] which did not happen while our case was evolving. The same way these pathologies can be differentiated through the electromyographic data and CSF constants, namely absence of neutrophilic pleocytosis, presence of a marked decrease in the speed of nervous conduction, regarding the demyelinating features of IDP, [1] in contrast with the axonal type found in the CMV sensitive-motor polyradiculopathy[1,8] similar to the one recorded in our patient.

To be considered in terms of differential diagnosis it emerged with particular relevance the secondary demyelinating polyneuropathy which is different essentially due to its predominantly sensitive feature, seldom motor and slowly progressive, without sphincter dysfunction or liquor anomalies. [1]

The infiltrative lymphoma of nervous roots can be presented clinically in an overlapping way, being useful on the moment, the non-existence of neutrophilic pleocytosis and the cytology positivity. [1,7,8,11] negative in our description for neoplastic cells and for all purposes confirming the abundance of polymorphonuclears in the CSF.

Diabetic and luetic polyradiculopathy are clearly excluded by the absence of clinical and laboratorial endpoints supporting it. [1,8] being VDRL and CSF TPHA negative in serum as well as the glycaemia, glycorrachia and pleocytosis contradictory of such diagnoses.

As a last analysis, it is opportune to quote some described myelopathies in AIDS patients, although the differences in the syndromatic presentation relating to the situation presented should be weighed. The vacuolar myelopathy and the progressive multifocal leukoencephalopathy (PMLE) are defined by the onset of ataxia and progressive spastic paraparesis to which should be added, in the in case of PMLE, the occurrence of a dementia condition and an Imagiology pattern characteristic in the nuclear magnetic resonance image of widespread demyelination without sphincter or sensitive commitment. [1,8]

The herpetic myelopathy is reproduced by an acute transversal myelitis where there is a predominance of semiologic elements as pyramidal signs below the level of the lesion and lymphocytosis in the liquor.[1,8]

Finally, the tropical spastic paraparesis has a more prolonged course with a positive serology for the HTLV-I antibodies, negative in our assessment. This is a growing prevalence myelopathy where the CSF exam is usually normal. [1,8,12]

Two final comments are justified in our view to the framing of the Babinsky sign in the initial neurologic evaluation of this patient and for the absence of a favourable therapeutic answer to ganciclovir. In spite of usually the pyramidal signs of the description of such polyradiculopathy are excluded, it is still justifiable its appearance before the pathological anatomy evidence of a focal myelitis process, occasionally present in the adjacent area to the inflammatory nervous roots, motivating other denominations of such syndrome as Guillain-Barré related with CMV, acute myeloradiculitis or myelitis with radiculopathy, among others.[1,9,11,13,14]

Ganciclovir is an analogous acyclic nucleoside, the structural similar to aciclovir. It penetrates the blood-brain barrier with 40 – 50% of serum levels, leading to a chronic maintenance suppressing therapy due to high rates of recurrence after withdrawal. [8,15] The most frequent side effects are dose-dependent neutropenia and leucopenia.

It is used on the doses of 2,5 mg/kg every eight hours for 10 days or in doses of 5 mg/kg every 12 hours, e.v. route, according to different proposals argued in what refers to induction dose, followed by maintenance with 5-7,5 mg/kg five days a week. [18,13]

However, there are formally described cases of eventual resistance to this drug, as in one of the 1990ties series one of the patients developed CMV polyradiculopathy while in treatment for CMV retinitis, as well as in the first published case of CMV myelitis histopathologically documented treated with anti-viral therapy, described by Jacobson et als., [13] in spite of the proven sensitivity to ganciclovir and foscarnet *in vitro*, the fatal disease progression was inexorable. ■

References

1. Whiteman MLH, Dandapani BK, Shebert RT, Post MJDMRI of AIDS - related polyradiculomyelitis. J Comput Assist Tomog 1994:18 (1): 7 - 11.

2. Reichert CM, O'Leary TJ, Levens DL. Simrell CR, Macher AM Autopsy pathology in the Acquired Immune Deficiency Syndrome. Am J of Pathol 1983; 112:357 - 32.

3. Snider WD, Simpson DM, Nielsen A, Gold JWN, Metroka CE, Posner JB. Neurological complications of Acquired Immune Deficiency Syndrome: analysis of 50 patients. Ann Neurol 1983; 14:403 - 418.

4. de Gans J. Portegies P. Neurological complications of infection with human

immunodeficiency virus type I: a review of literature and 241 cases. Clin Neurol Neurosurg 1989; 91:199 - 219.

5. de Gans J, Tiessens G, Portegies P, Tutuarima J A, Troost D. Predominance of polymorphonuclear leucocytes in cerebro-spinal venal fluid of AIDS patients with cytomegalovirus polyradiculopathy. J AIDS 1990; 3:1155 - 1158.

6. Drew WL. Diagnosis of cytomegalovirus infection. Rev Infect Dis 1988; 10 (Suppl): 468 - 476.

7. Simpson DM, Tagliati M. Neurologic manifestations of HIV infection. Ann Internal Medicine 1994; 121:769 - 785.

8. Miller RG, storey JR , Greco CM. Ganciclovir in the treatment of progressive AIDS-related polyradiculopathy. Neurology 1990; 40:569 - 574.

9. Behar R, Wiley C. Mc Cutchan JA. Cytomegalovirys polyradiculopathy in acquired immune Deficiency Syndrome. Neurology 1987; 37:557 - 561.

10. Peiperl L. Manual of HIV/AIDS therapy, Fountain Valley (CA - USA), Current Clinical Strategies Publishing International 1993:50.

11. Eidelberg D, Sotrel A, Vogel H, Walker P, Kleefield J, Crumpacker IIIC. Progressive polyradiculopathy in Acquired Immune Deficiency Syndrome. Neurology 1986; 36:912 - 916.

12. Roman GC. The neuroepidemiology of tropical spastics paraparesis. Ann Neurol 1988; 23:113 - 120.

13.Jakobson MA, Mills J, Rush J. et al. Failure of anti-viral therapy for acquired immunodeficiency syndrome related cytomegalovirus myelitis. Arch Neurol 1988; 45, 1090 – 1092.

14. Jeantils V, Lemaitre MO, Robert J, Gandown Y, Krivitizky A, Delzant G. Subacute polyneuropathy with encephalopathy in AIDS with human cytomegalovirus pathogenicity? Lancet 1986; 2, 1039.

15. Laskin OL, Use of ganciclovir to treat serious cytomegalovirus infections in patients with AIDS. J Infect Dis 1987; 155:323 – 328.