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Cytomegalovirus Infection: Not So (H)armless

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Abstract

Presentation
A 23-year-old man presented with a 10-day history of bilateral upper limb weakness and pain.

Diagnosis
Nerve conduction studies demonstrated a mononeuropathy multiplex affecting both upper limbs, confirmed by magnetic resonance imaging (MRI) to affect these structures at brachial plexus level. Cytomegalovirus (CMV) serology demonstrated positive IgM and IgG with low avidity, suggestive of recent infection. The patient had a detectable CMV viraemia.

Treatment
This was treated as CMV-related mononeuropathy multiplex with intravenous ganciclovir followed by oral valganciclovir. The patient's CMV PCR is now undetectable.

Conclusion
CMV-related mononeuropathy multiplex in immunocompetent patients is rare.

Introduction

Cytomegalovirus (CMV) is a double-stranded DNA virus.[3] It traditionally causes transient and subclinical infection in the immunocompetent, rarely leading to more severe manifestations.[1] Central nervous system disease usually occurs in profoundly immunocompromised hosts.[6]

CMV-related mononeuropathy multiplex in an immunocompetent patient is rare.[2,4,5,6] We describe a case of CMV mononeuropathy multiplex in an immunocompetent adult, affecting the brachial plexus bilaterally.

Case Report

A 23-year-old man presented following pain, numbness and weakness affecting predominantly his left arm.

Three weeks prior he experienced a mild flu-like illness with myalgia, tonsillar enlargement and lymphadenopathy, which resolved after four days. Subsequently he began to develop pain in his arms, predominantly left-sided, starting in the elbows. This progressed to numbness, then weakness. Clinical exam showed absent reflexes and asymmetrical weakness in his arms, worse on the left, mainly affecting shoulder abductors, elbow flexors and intrinsic hand muscles. Sensory exam revealed a non-dermatomal band of numbness over his left humerus.

Haematological investigations demonstrated lymphocytosis, mildly raised c-reactive protein (CRP) and a transaminits. Magnetic resonance imaging (MRI) of the brain and cervical spine was unremarkable. A lumbar puncture was performed which showed a white cell count of 8/cmm (0-5) - 60% lymphocytes, protein of 0.69 mg/dl (15-45) and matched oligoclonal bands (both in the serum and CSF).

Nerve conduction studies (NCS) confirmed bilateral mononeuropathy multiplex in the upper limbs, involving left radial & axillary nerves and right ulnar, median & radial nerves. This was particularly severe in the bilateral posterior, lateral and medial cutaneous nerves which showed no sensory response (table 1). Needle electromyography (EMG) showed neurogenic changes in the left deltoid, triceps brachii and right biceps brachii muscles.

Table 1: Nerve Conduction studies, abnormalities highlighted in bold.

	Right			**Left**		
Motor nerve (muscles)						
	Latency (msec)	**Amplitude uV**	**Velocity m/sec**	**Latency (msec)**	**Amplitude uV**	**Velocity m/sec**
Median (APB): Wrist	2.7	***7600***		3.3	12100	
Elbow	7.5	***7200***	52			
Ulnar (ADM): Wrist	2.6	***5000***		2.5	13700	
Below Elbow	6.1	***4800***	59			
Above Elbow	8.4	***4500***	58			
Radial (EIP): Forearm	2.6	3700		2.0	***1000***	
Upper arm				4.6	***1000***	58
Sensory nerves						
Median (Dig III – wrist)	2.0	10	67	2.4	***8***	61
Ulnar (Dig V – Wrist)	2.9	11	61	2.1	6	60
Radial (Forearm – Wrist)	1.2	***13***	68	1.4	***6***	60
Medial Cutaneous Nerve	***No response***			***No response***		
Lateral Cutaneous Nerve	***No response***			***No response***		
Posterior Cutaneous Nerve	***No response***			***No response***		

Computed tomography (CT) of the thorax abdomen and pelvis demonstrated splenomegaly. Positron Emission Tomography (PET) CT (done to out rule evidence of malignancy or lymphoma) showed cervical, axillary and inguinal FDG-avid lymphadenopathy. Lymph node biopsy showed no evidence of malignancy. The patient was started on steroids empirically at this point, with minimal clinical benefit.

Viral serology confirmed CMV IgM and IgG positive (with low avidity of 0.34). He had a detectable CMV viraemia on PCR testing with >600 copies**.** CMV DNA in the cerebrospinal fluid (CSF) was negative. Human immunodeficiency virus (HIV) and hepatitis testing was negative. Lymphocyte subset testing confirmed immunocompetency.

Given the presence of splenomegaly, lymphadenopathy, transaminitis, mononeuropathy multiplex and the positive CMV serology the patient was treated as a primary CMV infection complicated by a mononeuropathy multiplex. It was decided to proceed with treatment, as the patient's neurological deficit was not recovering. Intravenous (IV) ganciclovir was commenced for two weeks, followed by oral valganciclovir. Oral treatment continued for four weeks, ending two weeks following undetectable serum CMV PCR. The patient declined a nerve biopsy.

At six-month follow-up repeat NCS & EMG showed significant partial improvement. At nine months the patient had almost complete clinical recovery except for mild residual weakness in distal finger abduction.

Discussion

The clinical, neurophysiological, serological and imaging findings were all consistent with a primary CMV infection complicated by mononeuropathy multiplex. No evidence of immunodeficiency was found. This confirmed a case of a severe, debilitating CMV infection in an immunocompetent adult.

The neurophysiological findings in this case confirmed a mononeuropathy multiplex affecting the bilateral brachial plexus, more marked on the left. Nerves affected were bilateral and from the medial, lateral and posterior cords of the brachial plexus. Unique features include the unusual neurophysiological finding of complete sensory axonal loss in the forearm cutaneous nerves.

As stated, CMV-associated mononeuropathy multiplex of the brachial plexus in immunocompetent patients is rare.[2,4-6] In the first of cases the patient recovered in six months.[2] In more recent cases the neurological deficit and pain had recovered within 7 months; in another pain resolved in 7 weeks with neurological deficit remaining.[5,6] None were treated with anti-virals or had immunocompetency confirmed via lymphocyte subset testing.

The diagnosis of this condition relies on recognition of the mononeuropathy multiplex pattern, which is determined by pain, neurological findings (motor and sensory loss in multiple territories), clinical course and EMG findings. Infection must always be considered and CMV should not be dismissed in an immunocompetent patient.

In conclusion, we emphasise a significant presentation due to a classically benign infection. This is the first reported case of CMV mononeuritis multiplex in an adult with confirmed immunocompetency via lymphocyte subset testing.

Patient Consent:
A signed consent form from the patient has been obtained and is available for review on request.

Declaration of Conflicts of Interest:
There are no conflicts of interest to declare from any author.

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