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Case report

A case of relapsing–remitting facial palsy and ipsilateral brachial plexopathy caused by HSV-1

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ABSTRACT

The etiologies of Bell's palsy and brachial neuritis remain uncertain, and the conditions rarely co-occur or reoccur. Here we present a woman in her twenties who had several relapsing-remitting episodes with left-sided facial palsy and brachial neuropathy. The episodes always started with painful left-sided oral blisters. Repeat PCRs HSV-1 DNA from oral vesicular lesions were positive. Extensive screening did not reveal any other underlying cause. Findings on MRI T2-weighted brachial plexus STIR images, using a 3.0-Tesla scanner during an episode, were compatible with brachial plexus neuritis. Except a mannose-binding lectin deficiency, a congenital complement deficiency that is frequently found in the general Caucasian population, no other immunodeficiency was demonstrated in our patient. In vitro resistance to acyclovir was tested negative, but despite prophylactic treatment with the drug in high doses, relapses recurred. To our knowledge, this is the first ever reported documentation of relapsing-remitting facial and brachial plexus neuritis caused by HSV-1.

1. Why this case is important?

Over the years, several explanations for Bell's palsy (BP) have been given, but the etiology remains uncertain. The reason may be that there is no common etiological factor [1], but a common etiological pathogenesis. Both viral and autoimmune mechanisms have been suggested [2]. Herpes simplex virus type 1 (HSV-1) was postulated as the causative agent over 40 years ago [3], but direct evidence for HSV-1 infection in patients with BP is still lacking. Likewise, brachial plexus neuritis (BPN) is predominantly considered an autoimmune condition, but as with BP it rarely recurs [4]. Herein we present a woman with mannose-binding lectin deficiency (MBLD) who had several relapsing-remitting episodes with left-sided facial palsy and brachial neuropathy associated with ipsilateral herpetic gingivostomatitis. Our case supports existing evidence that HSV-1 may be a direct cause of BP [5]. It also documents HSV-1 as a potential cause of BPN.

2. Case description

A 24-year-old Caucasian woman with polycystic ovary syndrome (PCOS) experienced in mid-August 2012 painful blisters on her tongue (middle lateral part) and inside her mouth (in the posterior part, outside the lower row of teeth in the mandibular gingivae) on the left side. A week later she woke up with an ipsilateral facial palsy accompanied with ear pain, facial numbness, and altered taste on the left side of the tongue. On August 27 she was hospitalized due to slight pain in her anterior left shoulder that had gradually been replaced by weakness and numbness on the lateral side of the upper arm, radial forearm, and the hand. On examination she had a complete peripheral facial palsy with Bell's phenomenon. Sensory loss was found in the distribution of the trigeminal nerve, as well as in several cervical dermatomes (C5-C8). A minor generalized motor deficit in the left upper limb was confirmed, however, most pronounced in the shoulder girdle where muscle power for abduction was graded 4/5. Deep tendon reflexes were depressed, but symmetric. Magnetic resonance imaging (MRI) of the brain, the cervical spine and the brachial plexus was normal. Complete blood count, anti-GM, anti-MAG, anti-GQ1b antibodies and antibodies against *Borrelia burgdorferi* did not reveal underlying pathology. IgG, but

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not IgM, for both VZV and HSV was present. The cerebrospinal fluid (CSF) was also normal, including cells, glucose, protein, IgG index and oligoclonal IgG bands, as well as viral polymerase chain reaction (PCR) assays for varicella-zoster virus (VZV), HSV types 1 and 2. The patient was diagnosed with facial palsy and brachial neuritis, presumably caused by reactivation of VZV, and treated with acyclovir and prednisolone in conventional doses.

At a follow-up-visit 3 months later the patient had almost completely recovered, and a nerve conduction study was normal, but in the following 3 years she experienced 10 stereotype relapses consistently preceded by painful blisters inside the posterior left cheek, often also associated with pain in the angle of the jaw. She was left with minor asymmetry in the left side of her face, a slight reduced sensation in the C8 dermatome and a depressed triceps tendon reflex. Nerve conduction and electromyography showed polyphasic potentials in the left orbicularis muscle due to axonal injury. Neurophysiological examination of the extremities was normal with no signs of nerve conduction block. Except a mannose-binding lectin deficiency (serum level <500 ng/ml and MBL activity <200 U/ml), the patient was totally immune-competent. Work-up, including measurements of serum angiotensin-converting enzyme, genetic testing (*PMP22* duplication), total immunoglobulin as well as subclass levels, immunophenotyping, anti-neuronal antibodies, viral serology, rheumatology tests, bone marrow examination, and repeated CSF-analyses, was normal. The patient was previously exposed to Bacillus Calmette-Guérin (BCG) vaccination, and a Mantoux-test, performed to assess cellular immunity *in vivo*, was positive. In vitro resistance to both acyclovir ($IC_{50} \leq 2\ \mu g/ml$) and foscarnet ($IC_{50} \leq 60\ \mu g/ml$) was tested negative. The patient had no concurrent orofacial edema and fissured tongue which has been reported with recurrent facial palsy due to Melkersson-Rosenthal syndrome.

Six months after the first event, mouth blisters, ipsilateral facial palsy and upper limb sensorimotor dysfunction recurred. HSV-1 DNA PCR from oral vesicular lesions was positive. Standard treatment with acyclovir tablets and corticosteroids was given as before, but this time valacyclovir (500 mg daily) was continued as a prophylactic medication. Again signs and symptoms regressed.

In the beginning of May 2013 she had her second relapse, and acyclovir was given intravenously. The valacyclovir-prophylaxis was increased to 500 mg twice daily, but later stopped due to whished pregnancy that came true after using metformin.

At gestational week 37, previous neurological symptoms reappeared, and she was again treated with acyclovir. Prophylaxis with valacyclovir (500 mg daily) was reinstated. Symptoms slowly regressed, and the patient gave birth to her first child around estimated due date in April.

One month postpartum a new relapse occurred, and again HSV-1 was detected in oral vesicular lesions. Despite increasing the prophylactic valacyclovir dose to 1000 mg three times a day, new episodes were encountered after another 3 and 4 months. A repeat cerebral and cervical MRI in September 2014 did not show any pathology, but findings on T2-weighted brachial plexus STIR images, using a 3.0-Tesla scanner, was compatible with plexus neuritis (Fig. 1). The prophylaxis was removed, but reinstated after one month when the patient's 8th relapse occurred. Three months later, prednisolone was tried immediately when she again got blisters on the left lower gums, but it did not prevent yet another episode of neurological symptoms. In June 2015, the patient experienced her 10th relapse, and presented on the same day as new HSV-1 positive blisters appeared.

3. Other similar and contrasting cases in the literature

There is quite sound evidence that VZV may cause both unilateral peripheral facial nerve palsy [2] and BPN [6], but we found only three cases of BP associated with documented herpes simplex gingivostomatitis in the litterature [7–9]. In a case series presented by Vahlne et al., one of the patients had overt herpes labialis during the BP [10]. Ghonmin reported two cases with bilateral BP following a recent presumed herpetic gingivostomatitis, but viral conformation was not documented [11]. Only one case of BPN due to HSV-1 is reported [12].

4. Discussion

To our knowledge, this is the first reported association between HSV-1 reactivation and facial palsy combined with brachial plexopathy. Documented recurrent intraoral HSV is uncommon. The underlying predisposition to frequent reactivations is unknown, but low cell-mediated immunity probably plays an important role [13], and reduced MBL-mediated complement activation increases susceptibility to viral infections [14], including herpes [15,16]. The patient's PCOS may also be of importance. Experimental works support that ovarian factors, alone or in combination with estrogen, strongly influence susceptibility to HSV-1 infection [17]. In general, estrogen may have protective effects, possibly through macrophage antiviral resistance, but late pregnancy is, despite high levels of estrogen during third trimester, a well-known risk factor for both herpes reactivation and BP. Gestational immunosuppression induced by rise in cortisol levels has been postulated to cause reactivation of a latent herpes simplex virus. The puerperium is also a well-known risk factor for BP [18].

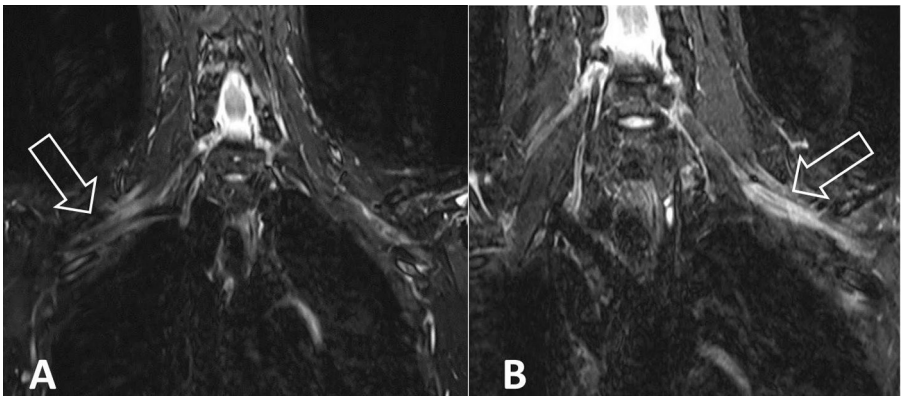

Fig. 1. Coronal T2-weighted fat-suppressed images (TR 3700 msek, TI 230 msek, TE 44 msek, Simens Medical System GMBH, Erlangen, Germany): *A*, Normal right brachial plexus (arrow). *B*, Increased signal in fascicules of left brachial plexus (arrow) consistent with inflammatory edema. Fat-suppressed T1-weighted images post intravenous contrast revealed no enhancement (not shown).