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Post-Herpetic Neuralgia

An Essay
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Mohamed Osman Taeimah

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List of abbreviations

5HT	*Serotonin*
AED	*Antiepileptic Drugs*
AIDS	*Acquired Immune deficiency Syndrome*
CMV	*Cytomegalovirus*
CNS	*Central Nervous System*
CSF	*Cerebrospinal Fluid*
DHC	*Dorsal Horn Cell*
DNA	*Deoxyribonucleic acid*
DPN	*Diabetic Neuropathy*
DRG	*Dorsal Root Ganglion*
EBV	*Epstein-Barr virus*
ENF	*Epidermal Nerve Fibers*
FDA	*Food and Drug Administration*
GABA	*Gama Amino Butyric Acid*
HSV	*Herpes Simplex Virus*
Ig	*Immunoglobulin*
IPG	*Implantable Pulse Generator*
KSHV	*Kaposi sarcoma-associated herpesvirus*
LMP	*Lidocaine-Medicated Plaster*
NA	*Noradrenaline*
NICE	*National Institute for Health and Clinical Excellence*
nm	*nanometer*
NMDA	*N-methyl-D-aspartate Antagonists*
NNT	*Number Needed to Treat*
NSAID	*Non-Steroidal Anti-inflammatory Drugs*
PCR	*Polymerase chain reaction*
PHN	*Postherpetic Neuralgia*
RIPG	*Rechargeable Implantable Pulse Generator*
SCS	*Spinal Cord Stimulation*
SNRI	*Serotonin Noradrenaline Reuptake Inhibitor*
TCA	*Tricyclic Antidepressant*
TPRV1	*Transients Receptor Potential Vanilloid 1*

VAS	*Visual Analogue Scale*
VZV	*Varicella Zoster Virus*
*W**HO***	*World Health Organization*

ABSTRACT

Introduction: Shingles (herpes zoster) is caused by the reactivation of a latent varicella zoster virus (VZV) infection, generally decades after the primary infection. The definition of post-herpetic neuralgia varies in the defined time period of the persistence of pain after the resolution of the rash (4-24 weeks) and thus the actual incidence is not known. **Aim of the Work:** The aim of this essay is to improve knowledge about pathogenesis and management of Post-Herpetic Neuralgia. Therefore, it is important to emphasis on the fact that anticipating such disease would be associated with a better outcome. **Conclusion:** Clinical results are dependent on precise lead placement as well as the underlying pathology being treated. However, spinal cord stimulation (SCS) continues to present its own unique set of challenges that must be acknowledged and addressed if this therapy's full potential is to be realized.

Key words: Shingles (herpes zoster), Post-Herpetic Neuralgia, varicella zoster virus, SCS

Introduction

Shingles (herpes zoster) is caused by the reactivation of a latent varicella zoster virus (VZV) infection, generally decades after the primary infection. Primary VZV infection typically occurs during childhood and causes chickenpox (varicella); following primary VZV infection, the virus enters the sensory nerves and travels along the nerve to the sensory dorsal root ganglia and establishes a permanent latent infection. Reactivation of the latent virus leads to the clinical manifestations of shingles, and is associated with immune senescence or suppression of the immune system i.e. immunosuppressive therapy, HIV infection, malignancy and/or increasing age. ***(Van Hoek et al., 2009)***

Post-herpetic neuralgia (PHN) is the most common and feared complication of herpes zoster (HZ); it is mainly reported among the elderly and is described as painful and refractory. It is a complication rather a continuation of acute HZ and is defined as persistent pain in the HZ-involved areas that continues for more than 3 months after disappearance of the vesicles ***(Rowbotham and Fields. 1989)***

Post-herpetic neuralgia, a complication of herpes zoster, is a neuropathic pain syndrome resulting from a combination of inflammatory and viral damage to primary afferent fibers of sensory nerves. ***(Opstetlen, Van Wijick and Stolker. 2004)***

The definition of post-herpetic neuralgia varies in the defined time period of the persistence of pain after the resolution of the rash (4-24 weeks) and thus the actual incidence is not known. ***(Yawn et al., 2007)***

Mixed inflammatory and neuropathic pain is experienced in acute HZ, whereas pain is highly predominant in PHN and the symptoms persist over time ***(Rowbotham et al., 2001)***

The clinical symptoms presented by these patients are very heterogeneous, and some are spontaneous while others are evoked. Spontaneous symptoms frequently include a constant deep and burning pain and an intermittent intense and lacing pain throughout the painful area, leaving it hypersensitive and painful for some minutes. Other disagreeable symptoms are pruritus and painless, but nevertheless disabling sensations of coldness or numbness ***(Treede et al., 2008)***

Unfortunately, no treatment has been shown to completely prevent post-herpetic neuralgia, yet some treatments may shorten the duration or lessen the severity of symptoms ***(Jericho. 2009).***

Aim of the essay

The aim of this essay is to improve knowledge about pathogenesis and management of Post-Herpetic Neuralgia. Therefore, it is important to emphasis on the fact that anticipating such disease would be associated with a better outcome.

Virology Background

Introduction:

The herpesvirus family contains several of the most-important human viral pathogens. Clinically, the herpesviruses exhibit a spectrum of diseases. Some have a wide host-cell range, and others have a narrow host-cell range. ***(Baines.2011)***

The outstanding property of herpesviruses is their ability to establish lifelong persistent infections in their hosts and to undergo periodic reactivation. Their frequent reactivation in immunosuppressed patients causes serious health complications. Curiously, the reactivated infection may be clinically quite different from the disease caused by the primary infection. ***(Baines.2011)***

Herpesviruses possess a large number of genes, some of which have proved to be susceptible to antiviral chemotherapy. The herpesviruses that commonly infect humans include herpes simplex virus types 1 and 2 (HSV-1, HSV-2), varicella- zoster virus, cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpesviruses 6 and 7, and herpesvirus 8 (Kaposi sarcoma-associated herpesvirus [KSHV]). ***(Espy et al., 2006)***

Herpes B virus of monkeys can also infect humans. There are nearly 100 viruses of the herpes group that infect many

different animal species. ***(Huff and Barry.2003)***

PROPERTIES OP HERPESVIRUSES

❖ **Important Properties of Herpesviruses**

- **Virion:** Spherical, 150-200 nm in diameter (icosahedrai)
- **Genome:** Double-stranded DNA, linear, 125-240 kbp, reiterated sequences
- **Proteins:** More than 35 proteins in virion
- **Envelope:** Contains viral glycoproteins, Fc receptors
- **Replication:** Nucleus, bud from nuclear membrane

❖ **Outstanding characteristics:**

- Encode many enzymes
- Establish latent infections
- Persist indefinitely in infected hosts
- Frequently reactivated in immunosuppressed hosts
- Some cause cancer

(Baines.2011)

❖ **Structure and Composition**

Herpesviruses are large viruses. Different members of the group share architectural details and are indistinguishable by electron microscopy. All herpesviruses have a core of double-stranded DNA, in the form of a toroid, surrounded by a protein coat that exhibits icosahedral symmetry and has 162 capsomeres. The nucleocapsid is surrounded by an envelope that is derived from the nuclear membrane of the infected cell and contains viral glycoprotein spikes about 8 nm long. An amorphous, sometimes asymmetric structure between the capsid and envelope is designated the tegument. The enveloped form measures 150-200 nm; the "naked" virion, 125 nm. ***(Baines.2011)***

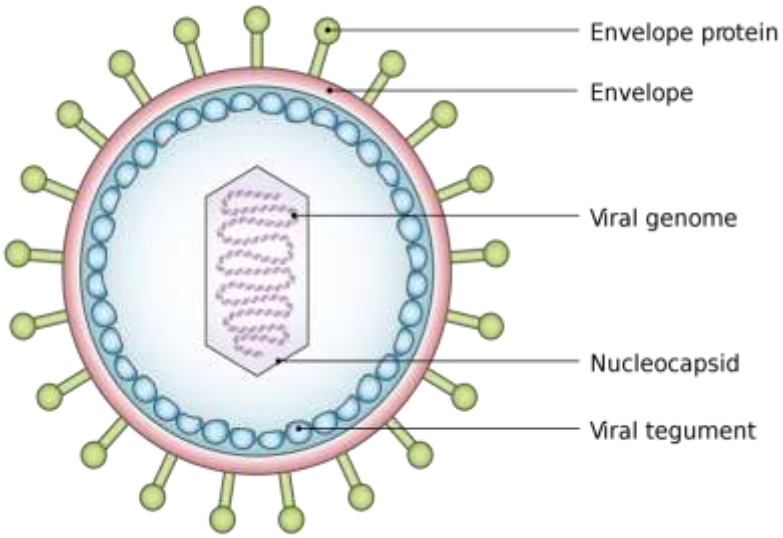

Figure (1): Structure of Herpesvirus.

The double-stranded DNA genome (125-240 kbp) is linear.

A striking feature of herpesvirus DNAs is their sequence arrangement. Herpesvirus genomes possess terminal and internal repeated sequences. Some members, such as the HSVs, undergo genome rearrangements, giving rise to different genome "isomers." The base composition of herpesvirus DNAs varies from 31% to 75% (G+C). ***(Baines.2011)***

There is little DNA homology among different herpesviruses except for HSV-1 and HSV-2, which show 50% sequence homology, and human herpesviruses 6 and 7 (HHV-6 and HHV-7), which display limited (30-50%) sequence homology. Treatment with restriction endonucleases yields characteristically different cleavage patterns for herpesviruses and even for different strains of each type. This "fingerprinting" of strains allows epidemiologic tracing of a given strain. ***(Baines.2011)***

The herpesvirus genome is large and encodes at least 100 different proteins. Of these, more than 35 polypeptides are involved in the structure of the virus particle; at least 10 are part of the viral envelope. Herpesviruses encode an array of virus-specific enzymes involved in nucleic acid metabolism, DNA synthesis, gene expression, and protein regulation (DNA polymerase, helicase-primase, thymidine kinase, transcription factors, and protein kinases). Many herpesvirus genes appear to be viral homologs of cellular genes. ***(Gulley and Tang.2008)***