6. RESPIRATORY SYSTEM

6.1 Introduction

Salivary glands and the respiratory system appear to constitute primary targets for HHV-6 infection and persistence, yet HHV-6 associated diseases in these tissues are rather rare in immunocompetent persons. A summary of HHV-6 associated disorders in the respiratory system is presented in Table 3. A comprehensive review of such diseases was recently prepared by Sebastian Schmidt and colleagues (2006).

<table>
<thead>
<tr>
<th>Pathologic Entity</th>
<th>Patient</th>
<th>Immune Status</th>
<th>HHV-6 Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinopharyngitis</td>
<td>children</td>
<td>nl</td>
<td>serology</td>
</tr>
<tr>
<td>katarrheic tracheobronchitis</td>
<td>children</td>
<td>nl</td>
<td>serology</td>
</tr>
<tr>
<td>obstructive bronchiolitis</td>
<td>children</td>
<td>nl</td>
<td>serology</td>
</tr>
<tr>
<td>interstitial pneumonitis NIP</td>
<td>children, adults</td>
<td>nl, AIDS, post-transplant</td>
<td>serology, IHC, ISH, PCR</td>
</tr>
<tr>
<td>interstitial pneumonitis LIP</td>
<td>adults</td>
<td>AIDS</td>
<td>serology, IHC, ISH, PCR</td>
</tr>
<tr>
<td>dual infection pneumonitis</td>
<td>adult</td>
<td>immune deficient</td>
<td>serology, IHC, ISH, PCR</td>
</tr>
</tbody>
</table>

Table 3: Rare cases of respiratory diseases caused by HHV-6 infections. The first 3 entities in children may accompany exanthema subitum. Most other cases occur in some kind of immune deficiency including AIDS and transplant recipients. Dual infections in the latter patients consist of reactivated HHV-6 plus pneumocystis carinii, Legionella
pneumophila, human cytomegalovirus or adenovirus infections. Abbreviations: nl = normal; 1HC — immunohistochemistry (HHV-6 p41 antigen); ISH = in situ hybridization; PCR = polymerase chain reaction.

We have observed two patients with classical bronchioloalveolar cell carcinoma, in which tumor cells focally contained HHV-6 antigens (figure). Other adenocarcinomas, small cell carcinomas or squamous cell carcinomas were negative. The observation may further support the notion that pneumocytes or terminal bronchus cells are infectable by HHV-6, yet does not imply a causal relationship between tumor and HHV-6.
6.2 Figures

Immunohistochemistry for HHV-6 p41 on frozen section of lung biopsy

X-ray (left) and gross lung (right) of patient with interstitial pneumonia following bone marrow transplant and HHV-6 reactivation.

Non-specific interstitial pneumonitis (NSIP) following HHV-6 reactivation
Immunohistochemistry of HHV-6 positive cells (red) and lymphoid interstitial pneumonitis (LIP) in a patient with AIDS and HHV-6 reactivation.

Two cases of alveolar cell carcinoma of the lung in patients with HHV-6 reactivation

Immunohistochemistry (left & center) and in situ hybridization (right) for HHV-6 antigen and DNA (pZVH14) in atypical pneumocytes of alveolar cell carcinoma.

NOTE: replication of reactivated HHV-6 is probably supported by atypical pneumocytes rather than causing the cancer *per se*
6.3 Further Reading


Cone RW. Human herpesvirus 6 as a possible cause of pneumonias. Semin Respir Infect 10: 254-258, 1995
