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Possible role of rhinovirus in Lennox-Gastaut Syndrome exacerbation- Quinonez Jonathan - Larkin Community Hospital

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Introduction:

Lennox-Gastaut syndrome (LGS) refers to a rare form of childhood-onset epilepsy characterized by cognitive dysfunction, generalized multiple type seizures, and slow spike-wave seen on an electroencephalogram (EEG). LGS presents between the ages of 3-5 and can persist into adulthood. LGS is associated with brain tumors and malformations, congenital infections, gene mutations and related disorders not limited to tuberous sclerosis. The management of LGS is limited due to treatment-resistant seizures. Respiratory viral infections are implicated in both protection from, and inception of, allergic airway disease. Severe lower respiratory tract viral infections are associated with recurrent wheeze, asthma and atopy. It is unclear if this association is causal and the underlying mechanisms governing this are unknown. Whilst respiratory viral infections are the major precipitants of acute exacerbations of wheezing illness, early life infections are also clearly associated with protection from allergic diseases. This article aims to review the current understanding of the complex relationship between lower respiratory tract viral infections and their impact upon development of atopy in the airway. Rhinoviruses are a major cause of asthma exacerbations in children and adults. With the use of sensitive RT-PCR methods, respiratory viruses are found in approximately 80% of wheezing episodes in children and in approximately one half of such episodes in adults. Rhinovirus is a member of the family Picornaviridae, and acute rhinovirus infections occur predominantly in the upper airway. This virus has also been identified in the lower airway, and it might cause acute wheezing through the production of proinflammatory mediators with a resulting neutrophilic inflammatory response. Precisely how this process leads to increases in airway hyperresponsiveness and airway obstruction is not fully established. The recent development of PCR for the diagnosis of respiratory viral infections has permitted studies revealing the importance of virus infections in acute exacerbations of asthma. Several studies implicate rhinovirus as the major virus type in mild and severe wheezing illness in children of all age groups, but particularly over 1 year of age. Rhinoviruses have been shown to replicate in the lower airway, suggesting that virus induced asthma exacerbations result from direct inoculation, spread of the virus from the upper to the lower airway. The importance of RS virus infection in bronchiolitis and wheezing in infants has been reaffirmed. Recent studies using PCR to detect C pneumoniae, suggests a high prevalence of chronic infection in asthmatic children, and that the immune response to this organism may play a pathological role in asthma. These studies now require confirmation with larger carefully controlled studies. However, risk factors for wheezing with colds include asthma and atopy, extremes in age, and perhaps having a deficient TH1 response to rhinovirus. With the use of in vitro models and experimental inoculation studies, significant advances have led to a better understanding of the mechanisms by which rhinovirus infections cause asthma exacerbations. Advances in our understanding of this interaction might provide knowledge that could ultimately lead to specific treatment modalities to prevent and/or treat this significant burden of asthma exacerbations. Children with asthma were studied during the Southern hemisphere winter and summer of 2001-2002. Human rhinovirus (hRV) was significantly associated (P=.0001) with asthma exacerbations in winter and spring/summer, but not in intervening asymptomatic periods. Although hRV was also found in children with upper respiratory tract infection (URTI) who underwent sampling at the same time, it was present in significantly higher numbers of

children with symptomatic asthma (P<.0001). Human metapneumovirus was also found in small numbers of children with URTI, but significantly less frequently in children with asthma. Recently a new genogroup of human rhinovirus (HRV) has been described and named HRV-C. The relative importance of HRV-C in viral respiratory tract illnesses is unknown. The prognosis for LGS is poor as mortality rates increase from childhood (5%) to adulthood (90%). Lennox-Gastaut syndrome (LGS) is a severe form of epilepsy that typically becomes apparent during infancy or early childhood. Clinical studies and animal models have further demonstrated that lower respiratory tract viral infections are strongly associated with development of recurrent wheeze and asthma with human rhinoviruses being shown to be the most prevalent cause of lower respiratory tract viral infections in infants, along with associated asthma development. A case-control study provided evidence of a contributory role for respiratory viral infections within this association, whilst recent experimental studies provide a possible mechanistic insight. Affected children experience several different types of seizures most commonly atonic, tonic and atypical absence seizures. Children with Lennox-Gastaut syndrome may also develop cognitive dysfunction, delays in reaching developmental milestones and behavioral problems. Lennox-Gastaut syndrome can be caused by a variety of underlying conditions, but in some cases no cause can be identified. Lennox-Gastaut syndrome can be difficult to treat because it is resistant (refractory) to many kinds of antiseizure medications. Research is ongoing to identify and assess new therapies for Lennox-Gastaut syndrome.There is no consensus in the medical literature on the exact definition of Lennox-Gastaut syndrome. Generally, three findings are necessary for the diagnosis: multiple generalized seizure types; a slow spike-and-wave pattern (less than 2.5 Hz) on EEG; and cognitive dysfunction. The International League Against Epilepsy (ILAE) Task Force most recently classified the disorder as an epileptic encephalopathy. Epileptic encephalopathies are a group of disorders in which seizure activity leads to progressive cognitive dysfunction.

Case:

We present a case of a 3-year-old female with a past medical history of LGS, global developmental delays, epileptic encephalopathy, and multiple chromosomal mutations (VUS-ALG13, CARS2, NF1).She presented to a local hospital after experiencing seven seizure episodes within 24 hoursand experiencedtwo more episodes within a minute. Ativan and Keppra were administered. For further management, she was later transferred to another hospital. Upon arrival, the patient was febrile and experienced two more seizure episodes. She was placed on a multi-drug regiment (Ativan, Onfi, Vigabatrin) of which improved her condition. The EEG demonstrated abnormalities that included diffuse spike/waves as well as multifocal spike/waves. She was later found to have an imposing rhinovirus infection.

Conclusion:

We present a case of LGS exacerbation induced by a rhinovirus infection. While seizures in LGS are usually treatment-resistant, correction of any underlying causes could improve any LGS exacerbations.