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Short communication

Characterizing the thymic lesions in piglets infected with attenuated strains of highly pathogenic porcine reproductive and respiratory syndrome virus

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ABSTRACT

Piglets infected with the highly pathogenic PRRSV (HP-PRRSV) HuN4 strain develop severe thymus atrophy. However, the attenuated strain HuN4-F112 does not lead to lesions in organs. Here, we have characterized the thymic lesions in piglets infected with attenuated strains of HP-PRRSV HuN4 isolated at different passages in the attenuation process to produce HuN4-F112 from the parent HuN4 strain (HuN4-F5, HuN4-F15, HuN4-F23, HuN4-F30, and HuN4-F112). The thymic effects of infection were evaluated in terms of the thymus/body weight ratio, pathological changes, and thymocytes apoptosis. The ability of HP-PRRSV to induce thymus atrophy was reduced following attenuation after 23 passages; the HuN4-F23, but not HuN4-F30, caused thymus atrophy. The ability of the virus to induce thymocyte apoptosis decreased as it became attenuated. In addition, the viral load in the thymus was reduced as the virus was attenuated. The HuN4-F23 and HuN4-F30 strains might provide insight into the molecular mechanisms of HP-PRRSV pathogenesis. Taken together, our results indicate that the ability of HP-PRRSV to induce thymic atrophy is related to its pathogenicity.

1. Introduction

Porcine reproductive and respiratory syndrome (PRRS) was first identified in the 1990s in the United States and Europe (Collins et al., 1992; Rossow, 1998; Terpstra et al., 1991; Wensvoort et al., 1991). It is widely recognized as an important viral pathogen in the swine industry worldwide. PRRS is characterized by reproductive failure in gilts and sows and severe respiratory dysfunction in young pigs. PRRS virus (PRRSV), the causative agent of PRRS, is an enveloped positive single-stranded RNA virus that belongs to the *Arteriviridae* family. In 2006, an outbreak of "high fever" disease caused by highly pathogenic PRRSV (HP-PRRSV) led to substantial economic losses in China (Tian et al., 2007; Tong et al., 2007).

We have previously shown that piglets infected with HP-PRRSV (HuN4) developed significant thymic atrophy (He et al., 2012; Wang et al., 2011). The atrophy observed during HuN4 infection was attributed to the large number of apoptotic thymocytes (He et al., 2012; Li et al., 2014a). Previous study has also shown that piglets immunized with an attenuated strain of HP-PRRSV (HuN4-F112) did not develop lesions in organs and developed a protective immune response against HP-PRRSV infection (Tian et al., 2009). Here, we have characterized the thymic lesions caused by HP-PRRSV and several HP-PRRSV strains isolated at different passages during the attenuation process to modify HuN4 to HuN4-F112. The thymic effects of infection with HP-PRRSV were evaluated in terms of the thymus/body weight ratio, pathological changes in the thymus, thymic viral load, and apoptotic thymocytes.

2. Materials and methods

2.1. Virus strains

The HP-PRRSV HuN4 strain (Genbank no. EF635006) used in this study has been previously described (Tong et al., 2007). The attenuated strains HuN4-F5, HuN4-F15, HuN4-F23, HuN4-F30, and HuN4-F112 are derivatives of HuN4 isolated after 5, 15, 23, 30, or 112 passages through Marc-145 cells, respectively

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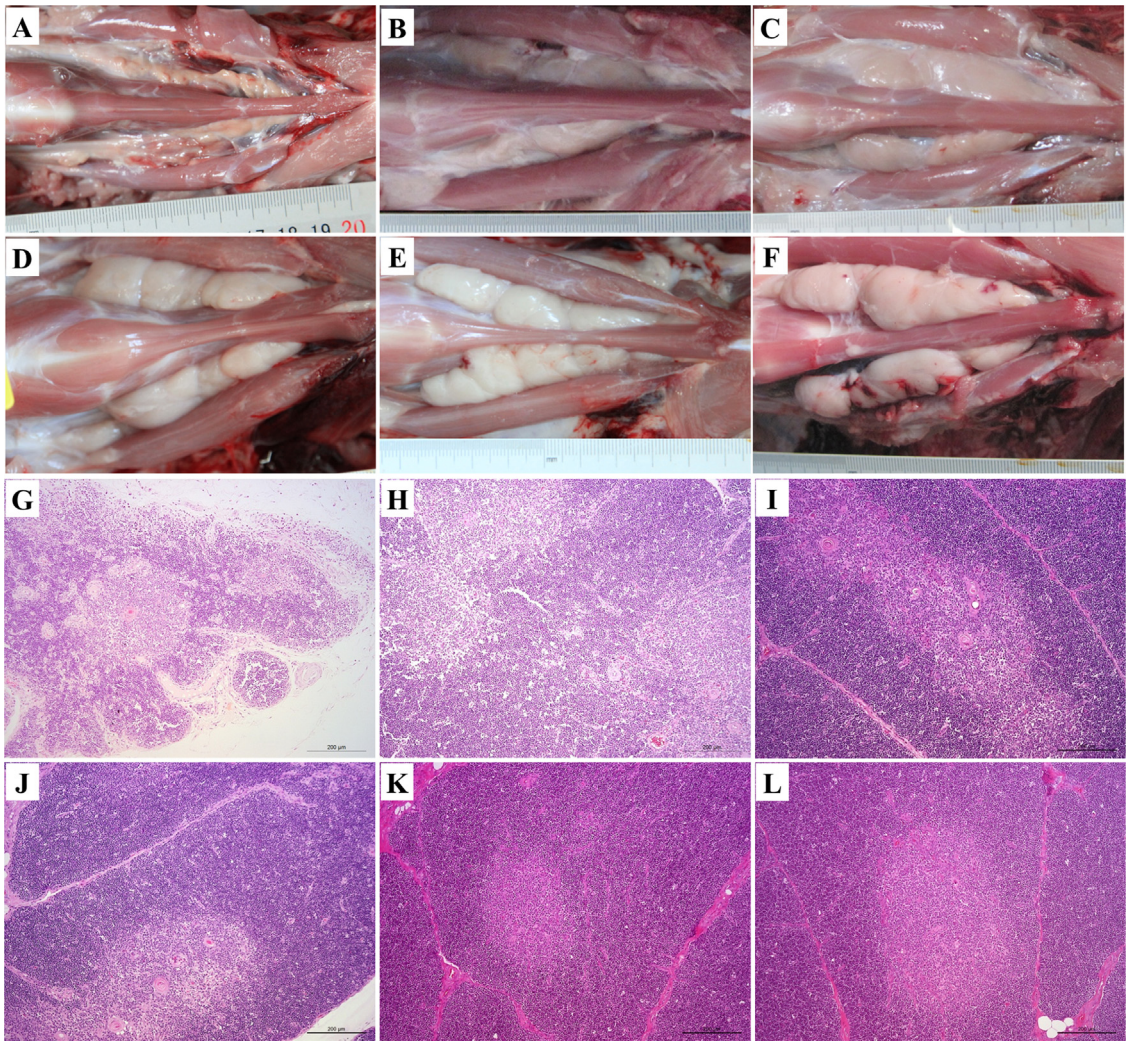

Fig. 1. Representative images showing the pathological changes in the thymus of piglets infected with attenuated strains of HP-PRRSV HuN4. Piglets were infected with attenuated HuN4 strains and necropsied 10 days post-infection. The thymus was evaluated macroscopically (A–F) and sections were H&E stained for histological examination (G–L). The panels showing thymic changes for each attenuated HuN4 strain are: HuN4-F5—(A and G); HuN4-F15—(B and H); HuN4-F23—(C and I); HuN4-F30—(D and J); and HuN4-F112—(E and K). The thymus of an age matched negative control piglet is shown in panels (F) and (L).

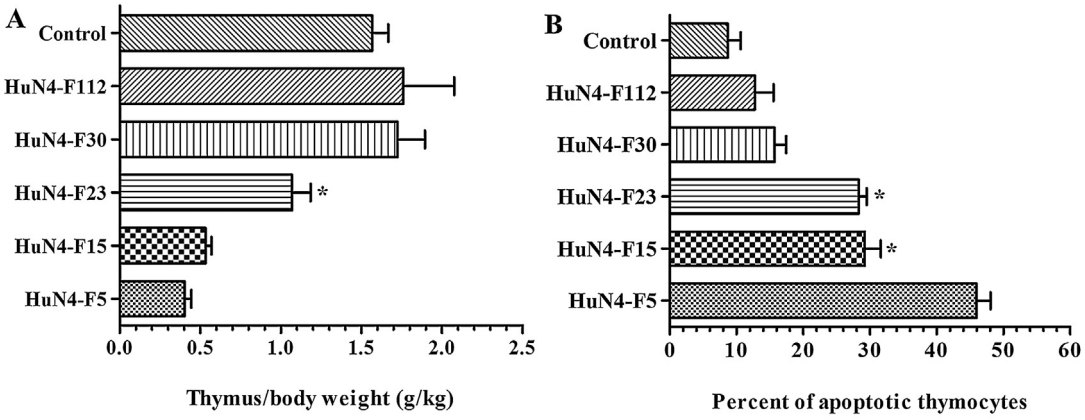

Fig. 2. The mean (±SD) of the thymus/body weight ratio and levels of thymocyte apoptosis at 10 DPI. The thymus was collected from piglets infected with the indicated attenuated HuN4 strains 10 DPI. (A) Thymic atrophy was quantified as the ratio of the thymus to total body weight (g/kg). (B) The percentage of thymocytes undergoing apoptosis or necrosis was assessed by flow cytometry. Statistical analyses were performed using the GraphPad Prism software. The analysis of variance (ANOVA) test was used to compare between groups. A p-value less than 0.05 was considered statistically significant (* $p < 0.05$).