A220 SPONTANEOUS ARTHRITIS IS PROTECTIVE FOR THE DEVELOPMENT OF AORTIC ATHEROSCLEROSIS IN APOE$^{-/-}$ MICE

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Background Inflammatory arthritides, such as rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA), are chronic debilitating disorders characterised by reduced life expectancy. The shortened lifespan in RA is largely due to cardiovascular disease. Alarmingly, premature atherosclerosis is already evident in children with JIA. Representative animal models of this phenomenon are lacking. Thus, the overall goal of this project is to establish a novel model of atherosclerosis in animals that are predisposed toward spontaneous arthritis, that is, the ApoE$^{-/-}$.K/BxA^{g7} mouse. The ApoE$^{-/-}$ mouse is susceptible to spontaneous atherosclerosis, which can be exacerbated by feeding a high fat "western" diet. The K/BxA^{g7} mouse expresses a transgenic T cell receptor (KRN) and a MHC Class II Allele (A^{g7}) that predisposes toward severe, spontaneous and persistent arthritis. Crossbreeding the ApoE$^{-/-}$ and K/BxA^{g7} strains should generate mice that are inherently susceptible to both atherosclerosis and arthritis.

Methods ApoE$^{-/-}$.K/BxA^{g7}, K/BxA^{g7} and ApoE$^{-/-}$ control animals were assessed for the development of arthritis weekly, beginning at 4 weeks of age. Serial measurements of joint width (mm), clinical inflammation score (0–3 scale, 4 paws) and a novel clinical joint destruction index (0–40 scale, paw joints, wrists, ankles) were obtained. To assess atherosclerosis, aortic and carotid arteries from 21 to 23-week-old mice were stained with Sudan IV. Atherosclerotic lesions were quantitated using Image-Pro morphometric analysis, with lesion area normalised to total aortic area (aortic sinus to iliac bifurcation) or total common carotid artery area.

Results All three measures of arthritis were significantly greater in ApoE$^{-/-}$. K/BxA^{g7} and K/BxA^{g7} animals compared to ApoE$^{-/-}$ controls ($p<0.001$). The onset and severity of arthritis was similar in ApoE$^{-/-}$. K/BxA^{g7} and K/BxA^{g7} controls. Aortic atherosclerosis was >5-fold lower in ApoE$^{-/-}$.K/BxA^{g7} animals compared to ApoE$^{-/-}$ mice ($p < 0.05$), whereas carotid atherosclerosis was similar between the two groups. Data regarding the effect of arthritis on the development of diet-inducible atherosclerosis in this model is forthcoming.

Conclusions Our results suggest that ApoE deficiency does not affect the onset or severity of arthritis in the K/BxA^{g7} model of spontaneous arthritis. Arthritis does not exacerbate, and may in fact be protective for the development of aortic atherosclerosis in these animals. Furthermore, this effect may be regional in nature, as demonstrated by similar carotid plaque area, but less aortic atherosclerosis in ApoE$^{-/-}$.K/BxA^{g7} animals compared to ApoE$^{-/-}$ controls.