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**Title:** Distribution of increased airway smooth muscle thickness and airway inflammation in asthma

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**Body:** Rationale: A study of 10 cases of fatal asthma (Ebina et al.) identified two types of asthma, based on the site of increased airway smooth muscle (ASM) thickness: large airways only (due to hyperplasia), or both large and small airways (predominantly hypertrophy). Aim: To determine if this site-specific increase in ASM thickness was reproducible in a larger cohort, and was related to remodeling and airway inflammation. Methods: Postmortem cases of asthma (n=43) were categorised as large only (LO, n=15), small only (SO, n=4) and large/small (LS, n=24) if the mean thickness of the ASM layer in their large or small airways was more than one standard deviation above the mean value of controls (n=37). ASM cell size and number, airway dimensions and airway inflammation were compared between LS and LO cases and controls. Results: In LS cases, ASM cell number and volume, thickness of the reticular basement membrane (RBMt), airway wall thickness and eosinophil area density, but not neutrophil area density were increased (p<0.05) in large and small airways compared with controls. In LO cases, ASM cell number, RBMt and eosinophil area density were increased (p<0.05) only in large airways compared with controls. In addition, neutrophil area density was increased (p<0.05) in both large and small airways compared with controls. There were no significant differences in duration, age of onset of asthma or asthma severity between cases. Conclusions: Phenotypes of asthma, based on the distribution of increased thickness of ASM layer are reproducible and associated with ASM hyperplasia and hypertrophy, remodeling and eosinophilia. Neutrophilia was observed only in the LO cases, suggesting a distinct phenotype.