

The Mystery of Williams–Beuren Syndrome Associated With Pulmonary Dysfunction, Sudden Death, and Kounis Syndrome

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TO THE EDITOR:

Williams–Beuren syndrome (WBS) is recognized as the result of deletion of approximately 1.5–1.8 Mb of chromosome 7q11.23 that includes the entire elastin gene in 97–98% of the cases [Lowery et al., 1995; Rodriguez-Revenaga et al., 2005; Del Campo et al., 2006]. The result is an arterial media with increased number of hypertrophied smooth muscle cells, increased collagen content, and reduced amounts of elastin in the form of disorganized and broken elastin fibers [Burch et al., 2008].

Clinically, WBS is characterized by mild-to-moderate intellectual disabilities, characteristic facies, distinctive behavioral and emotional traits, and vascular abnormalities including supra-valvular aortic stenosis (SVAS), peripheral pulmonary stenosis, mitral valve prolapse, mitral valve regurgitation, ventricular septal defect, and supra-valvular pulmonary stenosis [Collins et al., 2010].

In the important paper by Wan et al. [2010] it was found, for the first time, that respiratory impairment manifesting as wheezing, coughing, and dyspnea was evident in 12 patients despite FEV₁ normal measurements. In one nonsmoking patient subclinical emphysema was also detected. The authors of this paper concluded that while significant respiratory impairment is not common finding among young adults with WBS, subclinical emphysema may exist and more in depth searching may shed light on the pathogenesis of this disease and other unexplained events accompanying WBS.

In experiments comparing early and late responses to antigen of sensitized guinea pig parenchymal lung strips [Lanças et al., 2006], it was found that increased collagen content attracts eosinophils and is significantly correlated with base line resistance and elastance in lung strips of ovalbumin sensitized guinea pigs suggesting hypersensitivity inflammation. On the contrary, elastic content and actin are not significantly correlated. These experiments showed that lung parenchyma is involved in late hypersensitivity responses and the constriction responses in this late phase is related to eosinophilic inflammation. But increased collagen content and reduced amounts of elastin are the main characteristics in WBS.

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Research elaborating on perioperative and periprocedural pathophysiology and problems in resuscitation that anesthetists, surgeons, and cardiologists face during anesthesia, surgery, or cardiac catheterization leading to sudden cardiac arrest and death of patients with WBS is lacking. Sudden onset of myocardial ischemia has been implicated in the majority of cases of death during anesthesia and sedation in cases of WBS [Horowitz et al., 2002]. Several drugs that are mast cell stimulators are given during anesthesia [Kounis et al., 2008] and in a recent report [Gupta et al., 2010] of sudden death in WBS, postmortem tryptase was increased suggesting hypersensitive reaction and electrocardiographic changes were of those of Kounis syndrome [Kounis, 2006]. This condition is defined as the concurrence of hypersensitivity reactions with acute coronary events and is applied in both patients with clinically normal and diseased coronary arteries. In cases of WBS associated with SVAS, the majority of cases of sudden death occurring during sedation or anesthesia, myocardial ischemia is the main cause. However, significant myocardial ischemia with associated fatal coronary events has been reported in both the presence and absence of hemodynamically significant SVAS [van Pelt et al., 2005].

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The above events encountered in cases of WBS, namely, pulmonary impairment, myocardial ischemia, sudden death during anesthesia and sedation associated with increased eosinophilic inflammation in lung strips with increased collagen content and Kounis syndrome seem to have a common pathophysiologic basis. Further research is necessary to elucidate these clinical mysteries associated with WBS.

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