204 Genetic Analysis and Etiology of Angioedema

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RATIONALE: Angioedema (AE) without urticaria is idiopathic in the majority of cases. We studied patients with AE by genetic analysis for novel mutations of proteins interacting with the bradykinin pathway.

METHODS: 126 patients with AE were recruited at a university hospital clinic. Patients were categorized according the proposed pathogenesis of AE: C1 inhibitor deficiency and low C4 levels, autoimmune disease, malignant cancer, angiotensin-converting enzyme (ACE) inhibitor-induced, nonsteroidal anti-inflammatory drug (NSAID)-induced, or idiopathic. In addition, each patient had a blood sample analyzed for a complement profile and enzymes (antigenic and functional C1 inhibitor, C3, C4, CH 50), and immunologic parameters. A subset of 52 patients was tested for specific mutations in factor XII, plasminogen-activator inhibitor-1 (PAI-1), ACE, and aminopeptidase P (APP).

RESULTS: The cause of angioedema was identified in 52 (41%) of the cases: 3 (2%) patients had a low plasma C1 inhibitor and C4; 18 (14%) were ACE inhibitor-induced; 10 (8%) were due to autoimmune disorders; 5 (4%) were associated with malignancy; and 16 (13%) were due to NSAIDs. In the remaining 74 (59%) patients the cause of angioedema was idiopathic. In those with genetic analysis 13 (25%) had a specific genetic variant in APP, 10 (19%) in ACE, 13 (25%) in PAI, and 0 in Factor XII.

CONCLUSIONS: In addition to related diseases and medications causing AE, certain genetic variants encoding proteins in the bradykinin generation and/or catabolism pathways may be implicit in the pathogenesis of AE. Further studies are ongoing.

205 Hereditary Angioedema Type III: Mutation in Factor XII Gene in Brazilian Families

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RATIONALE: Hereditary Angioedema (HAE) type III is a rare familial disorder, described mostly in women, influenced by estrogen exposure. Patients with HAE type III have normal C1-inhibitor (C1-INH) levels and activity. Mutations of the gene encoding Coagulation Factor XII (*F12*) have been identified in some patients with HAE type III. Our aim was to investigate *F12* mutations in patients with clinical characteristics of HAE type III from Brazil.

METHODS: Four families with index cases of female patients who presented history of recurrent angioedema episodes with normal C1-INH and C4 levels, were evaluated for HAE type III by genetic analysis. Genomic DNA was isolated from whole blood from patients and relatives with recurrent angioedema attacks. PCR was performed with 50 ng DNA, and sequencing of exon 9 from *F12* was performed.

RESULTS: Patients' symptoms include episodes of edema of extremities, face, tongue, and lips, abdominal pain, and dyspnea. Episodes are triggered by trauma, stress, and oral contraceptives. After diagnosis, symptoms were controlled with withdrawal of contraceptives and/or Danazol or Tranexamic acid use. Genetic analysis revealed a previously identified missense mutation located in exon 9 of *F12,* c.983C>A, also designated as p.Thr309Lys, in index cases of three of four families. Relatives with history of episodes of angioedema in two of these families (mother, maternal aunt and maternal female cousin; two daughters) also bear the *F12* mutation.

CONCLUSIONS: This study describes the presence of a genetic mutation in the gene coding for Factor XII as a likely cause of HAE type III in three families in Brazil.

206 Oral Food Challenge and Food Allergy Quality of Life in Caregivers of Food Allergic Children

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RATIONALE: Food allergy is associated with increased anxiety and decreased caregiver quality of life (QoL). Little is known about the effect of oral food challenges (OFC) on QoL.

METHODS: Caregivers of children who underwent OFC at the University of Michigan Allergy Clinics between 2000-2012 completed a questionnaire assessing their child's food allergy history, and food allergy QoL using the FAQL-PB. Survey responses were verified through chart review, and results were compared between OFC participants and non-challenged food allergy controls using regression analysis to determine factors associated with food allergy QoL.

RESULTS: 336 children underwent a total of 417 OFCs (372 passed, 45 failed). The most commonly challenged foods were peanut (40%) egg (22%), and milk (15%). 118 parents completed surveys (35%). Undergoing food challenge (1.53; P=0.002) and income >$50,000 (-0.95; P=0.02) was associated with decreased ordered log-odds of a higher QoL score (better QoL). Parent-reported anaphylaxis (+0.64; P=0.04); eczema (+0.74; P=(0.006); and having other food-allergic children (+0.9; P=0.001) were associated with increased ordered log-odds of a higher QoL score (worse QoL). There were no significant differences in QoL scores based on challenge outcome. Adjusted odds of undergoing challenge were significantly lower with increasing FAQL-PB scores (worse QoL) (OR 0.62; P=0.005), if the patient has eczema (OR 0.37; P=0.009), or tree nut allergy (OR 0.06; P=0.14).

CONCLUSIONS: In this population, OFC is associated with improved caregiver QoL. QoL is unaffected by challenge outcome. However, children of caregivers with better QoL have higher odds of undergoing food challenge. This finding merits further study.