Results: Retrospective data were analyzed in the medical records of 24 patients, 19 males and 5 females. Three of these patients were not included in the sample, for presenting insufficient data for analysis. Of the 21 patients, there were 5 families with 5 pairs of siblings. Three families had a positive family history. Consanguinity was observed in 5 (26%) of 19 couples in the sample. Seventeen (81%) patients had ataxia as the first symptom, beginning between 6 months and 7 years of age (median 18 months). Three patients with symptoms started with a telangiectasia and recurrent infections. The onset of symptoms ranged from 15 days old to 7 years of age (median 17 months). Age at diagnosis ranged from 1.5 year to 17 years old (median 5 years). Intravenous immunoglobulin was given for 16 of 23 patients (69.5%), prophylactic antibiotics were given for 15 (65.2%) and vitamin supplement for 12 patients (52.2%). Comorbidities: asthma was present in 6 patients (26%), allergic rhinitis in 3, and bronchiectasis in 3. Other less frequent comorbidities were diabetes (1), atopic dermatitis (1), sarcoidosis (1) and idiopathic thrombocytopenia (1). In evolution, 11 patients (52%) had dysphagia started between 3 and 18 years (median: 12.5 years). The most common infections were upper respiratory tract (83%), pneumonia (79%), sinusitis (66%), diarrhea (54%), tonsillitis (45%) and otitis (25%). Four patients lost follow-up, of the 20 remaining cases there were 8 deaths occurring between 13 and 18 years old. Causes of death were respiratory failure (3 cases), pneumonia (3), leukemia (1) and lymphoma (1).

Conclusions: Recurrent infections, dysphagia, and ataxia were the most frequent symptoms in our sample, and respiratory problems were the main cause of death among these series.

545 Global Prevalence and Types of Autoimmune Diseases Found in Children with Primary Immunodeficiencies: A Single-Center Experience

María Guadalupe Ramírez Vázquez,1 Saul Lugo-Reyes, MD,2 Yamazaki-Nakashimada Marco Antonio, MD,3,4 Francisco Javier Espinosa Rosales, MD, MSc,5 and Sara Elva Espinosa Padilla, MD.1 1Immunología y Alergia clínica, Instituto Nacional de Pediatría, Mexico city, Mexico; 2National Institute of Pediatrics, Immunodeficiencies Research Unit, Mexico City, Mexico; 3National Institute of Pediatrics, México City, Mexico; 4Clinical Immunology, Mexico City, Mexico; 5Research on Primary Immunodeficiencies Unit, National Institute of Pediatrics, Mexico city, Mexico.

Background: Autoimmune manifestations in primary immunodeficiencies (PIDs) are not uncommon, and they are more frequently observed in defects affecting lymphocytes and their regulatory mechanisms. There is a wide variability in prevalence, ranging from immune defects in which autoimmunity defines the syndrome, others with a very high prevalence of autoimmune manifestations, defects with a moderate prevalence, and those in which autoimmunity is rather an exception than the rule.

Objective: We aimed to determine the prevalence of autoimmune in children with PIDs from our hospital, to delineate their clinical features.

Methods: An internal record was consulted to identify autoimmune diseases in our patients with PIDs. Their clinical files were then reviewed for diagnostic workup, age of presentation and outcome.

Results: We identified a prevalence of 18.8% (47 out of 250 patients, 68.1% male patient), within a period of 40 years (1970–2010), with autoimmune manifestations in the context of PID. Of which most are still alive: 35 (74.5%); lost to follow-up: 3 (6.4%); Dead: 9. Known or probable consanguinity was reported in 25.4%, 36.2% had a positive family history. 12.8% also had an allergic disease; none had cancer. The most frequent AI type was Systemic Autoimmune disease (11 case, 23%), followed by Organ-specific autoimmunity (15 cases, 32%), cytopenias (8 cases, 17%), and just antibodies (6 cases, 13%). Other than Autoimmune lymphoproliferative syndrome (ALPS), in which autoimmunity is a case-defining feature, the group of well defined (Hyper-IgE Syndrome (HIES), and Wiskott-Aldrich Syndrome (WAS)) were the PIDs with more cases of autoimmune disease, followed by phagocytosis deficiencies and antibody deficiency.

Discussion: The overall prevalence of autoimmune disease is relatively high PID syndromes such as ALPS, moderate levels in HIES, WAS and defects of phagocytosis and antibody interestingly. Interestingly, most of our patients with HIES have an autosomal-recessive pattern of inheritance and no identified mutational diagnosis; nearly all of our patients with CGD are receiving chronic subcutaneous therapy with human recombinant interferon gamma. Regular follow-up visits are justified for surveillance for complications and frequent treatment adjustments, given the delicate balance between immunosuppression and infection prophylaxis that is required in the care of these patients.

546 Malignancies Associated to Primary Immunodeficiencies. A 40 Year Review

Corin España, MD,1 Saul Lugo-Reyes, MD,2 and Marco Antonio Yamazaki, MD.3 1National Institute of Pediatrics, Pachuca, Mexico; 2Allergy & Clinical Immunology, National Institute of Pediatrics, Mexico City, Mexico; 3National Institute of Pediatrics, Mexico D.F., Mexico.

Background: Cancer has been cited as the second leading cause of death after infection in children and adults with primary immunodeficiencies (PIDs). There seems to be a complex relationship between PIDs, viral infections to which are susceptible, and the development of cancer. Defective immunosurveillance most markedly in cells with strong antigenic potential that have undergone viral induction is a major factor, as support for this the most common cancer subtype is lymphoma. Some estimates suggest that more than 20% of carcinomas in patients with PID are infection induced, Epstein Barr virus being particularly well established cofactor. The risk of cancer in patients with PID is estimated between 4 to 25%, although could be higher in some subtypes of PID. The PIDs most commonly associated to cancer are Ataxia Telangiectasia, common variable immunodeficiency, Wiscott-Aldrich syndrome, severe combined immunodeficiency, and selective IgA deficiency.

Objective: We aimed to determine the prevalence of cancer in children with PIDs, in our hospital, and to determine clinical features and risk factors.

Methods: An internal record was consulted to identify cancer associated in patients with PIDs. The clinical files were reviewed for diagnostic workup, age of presentation, risk factors and outcome.

Results: We identified a prevalence of 1.2% (3 out of 250 patients) within a period of 40 years (1970–2010), with cancer diagnosis in the context of PID. PIDs subtype included, 2 patients with ataxia telangiectasia, both dead, one developed lymphoblastic leukemia and the other patient developed diffuse B cell lymphoma. Third patient with X linked lymphoproliferative syndrome (SAP mutation), with positive family history, developed Burkitt lymphoma, still alive.

Discussion: The overall prevalence of cancer is relatively low to moderate in PID syndromes. Ataxia Telangiectasia continues to be the most highly associated cancer PID. Regular follow-up visits are justified for surveillance for complications. The prognosis in patients with cancer and immunodeficiency is worse than immunocompetent individuals.

547 An Earlier, More Severe Presentation of G6pc3 Deficiency in a Male Infant From Mexico

Alonso Cruz, MD. Pediatric Allergy and Clinical Immunology, National Institute of Pediatrics, Mexico.

Background: Severe congenital neutropenia is a bone marrow failure syndrome characterized by severe neutropenia present from birth. We present
a case of G6PC3 deficiency presenting at an earlier age, with a more severe clinical picture than previously reported.

Case report: A 3-month-old boy, born to nonconsanguineous parents was delivered by C-section at 35 weeks gestation. He was admitted to neonatal intensive care unit for prematurity and poor respiratory effort requiring mechanical ventilation. Aggressive antimicrobial therapy was started for nosocomial pneumonia and severe persistent neutropenia. Physical examination: Poor weight, chest accessory venous vasculature, parasternal systolic murmur grade I left, tachistolia not palpable in scrotal sac. Laboratory workup: Total leukocyte blood count with 2400 mm\(^3\), total neutrophils 200 mm\(^3\). Echocardiogram revealed pulmonary hypertension: 58 mm Hg, foramen ovale with bidirectional shunt. Abdominal ultrasound: kidneys with hydro-nephrosis grade I in the right kidney and grade III left, confirmed by Excretory urography. Esophago-gastroduodenal Series: velopalatal incompetence, pyloric hypertrophy, spontaneous gastroesophageal reflux and upper third of the esophagus. Hearing screening reported bilateral hearing loss. Nissen fundoplication, Stamm gastrostomy and pyloromyotomy were performed. Treatment with Recombinant human G-CSF was started (3–5 mg Kd) with good response. Mutational analysis revealed a single-nucleotide deletion in exon 2, which results in a frameshift and premature stop codon, predicting a nonfunctional trunk protein.

Conclusion: Severe congenital neutropenia type 4 is an autosomal recessive condition, which was defined recently with identification of the causative mutations in G6PC3 and is characterized by congenital neutropenia and variable developmental disorders: cardiovascular (atrial septal defects, pulmonary hypertension) and/or urogenital system (urachal fistulations and cryptorchidism). Some patients show a peculiar variability of subcutaneous veins. Patients with G6PC3 deficiency lack mature neutrophils in the bone marrow and have increased susceptibility to apoptosis in peripheral neutrophils. Recombinant human G-CSF is the first-line therapy. This is only the second case identified in Latin America, and the first one in Mexico. Compared to what has been previously reported, however, our patient presented earlier and with a more severe clinical picture, including bilateral hydrenephrosis. Stem-cell transplantation has never been performed in G6PC3 deficiency, but its being considered in this case given the patient young age and severity.

548 Immunoglobulin a Deficiency, HPV and Oral Cancer

Jorge Álvarez, MD, PhD,1 Emilio Garip, MD,1 Monica Benítez,2 and Luis Guzman, MD2.1 Allergy and Immunology, Instituto de diagnostico y tratamiento Oulton, Córdoba, Argentina; 2Dentistry Department, Córdoba, Argentina; 3Instituto de diagnostico y tratamiento Oulton, Córdoba, Argentina.

Background: Selective IgA deficiency is the most common primary immunodeficiency. Serum IgA level lower than 7 mg/dL is considered selective IgA deficiency. Most people with selective IgA deficiency are asymptomatic, with incidental findings. Others may present recurrent respiratory infections, allergic symptoms, other infections and autoimmune diseases. It represents a genetically heterogeneous group of abnormalities. We report 2 cases of IgA-deficiency, HPV, and cancer, which required oral mucosa and tongue surgery.

Methods: Case I: Female patient, 30 years old. Medical history: vaginal HPV and Herpes. No promiscuous conduct. Complaint: recurrent infections. Physical exam: oral white lesions are observed. Laboratory findings: serum immunoglobulin A: lower than 7 mg%, secretory immunoglobulin A: lower than 1 mg%. Both exams were repeated and determinations showed low values. Cytology - Glucose - serum protein electrophoresis - Ig G - Ig M - CD3 - CD4 - CD8 - CD19 - CD56 all determinations showed normal values. HIV I/II: negative. Biopsy of oral mucosa with the following report: severe dysplasia and intraepithelial carcinoma. Signs of HPV. Surgery was performed on oral mucosa with the following pathology report: moderately differentiated squamous cell carcinoma. Microscopic, morphological changes related to cytopathogenic viral effects. The patient presented good evolution.

Case II: Female patient 40 years of age. Medical history: HPV and genital herpes. No promiscuous conduct. Complaint: leukoplakia in tongue edges. Physical examination: oral white lesions. Laboratory serum immunoglobulin A: value obtained: lower than 7 mg%. Cytology - Glucose - serum protein electrophoresis - Ig G - Ig M - CD3 - CD4 - CD8 - CD19 - CD56 with normal values. HIV I/II: negative. Surgery was performed in tongue and regional lymph node. Tongue Pathology: moderately differentiated squamous cell carcinoma with negative edges. HPV (+) PCR.

Conclusion: We report on the possible association between selective IgA deficiency - HPV - Cancer which has not been previously reported in time. We suggest further screening of these possible associations and detailed monitoring of these patients.

QUALITY OF LIFE MEASURES IN ASTHMA AND ALLERGIC DISEASES

549 Management of Twenty-Five Pediatric Patients with Hereditary Angioedema (Hae) Undergoing Home Treatment - A Clinical Surveillance Program

Inmaculada Martinez-Saguer, MD,1 Emel Aygören-Pürsün, MD,1 Eva Rasieke, MD,1 Thomas Klingebiel, MD, PhD,2 and Wolffart Keuz, MD, PhD2.

1Center of Pediatrics III, Department of Hematology, Oncology and Hemostasis, Comprehensive Care Center for Thrombosis and Hemostasis, J-W. Goethe-University Hospital, Frankfurt a. M., Germany; 2Center of Pediatrics III, Department of Hematology, Oncology and Hemostasis, J-W. Goethe-University Hospital, Frankfurt a. M., Germany.

Background: Hereditary angioedema (HAE) is a rare disorder characterized by C1 esterase inhibitor (C1-INH) deficiency. Clinically, HAE is characterized by relapsing episodes of edema at various body sites followed by disease-free intervals of variable duration. Episodes of upper airway obstruction (usually laryngeal edema) are potentially life-threatening and many patients died by asphyxiation in the families. In literature Longhurst et al, Buygun et al and Levi et al showed improvement of quality of life in patients with hereditary angioedema due to home treatment with C1-inhibitor-concentrate.

Methods: We investigated in a cohort study the integration of a clinical surveillance program into home treatment of pediatric patients suffering from hereditary angioedema. Parameters investigated were overall coping of the pediatric patient with home treatment, documentation of efficacy/safety of C1-INH concentrate (Berinert® P, CSL Behring, Marburg), regular control of laboratory parameters (C1-inhibitor (INH) activity, C1-INH antigen, C4, hepatitis A, -B, -C, HIV-1/-2, and parvovirus B19 serology) and quality of life parameters (hospitalization, absence from school).

Results: Twenty-five pediatric HAE patients (6 male, 19 female) have so far been investigated. Twenty-one patients suffer from HAE type I, 4 patients from HAE type II. Median age is 13.7 years (range: 2.8–17.4 years), first diagnosis of HAE took place at the median age of 5 years (range: 0.1–15.9 years) and first manifestation of HAE at the median age of 3.9 years (range: 0.3–11.7 years). Plasma C4 complement was reduced in nearly all patients (median: 2.4 mg/dL; range: <1.4–10 mg/dL) except one patient. All patients coped well with home treatment, compliance was excellent, clinical findings during regular medical control remained in the normal range and all parameters confirmed an improved quality of life, e.g., patients had not been hospitalized nor had they been absent from school. There were no adverse drug reactions due to administration of C1-INH concentrate.

Conclusions: Home treatment might be also a valuable option for pediatric HAE patients not affecting compliance negatively and providing a significant positive impact on health-related quality of life.