PRIMARY IMMUNODEFICIENCY

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Intravenous Immunoglobulin in Leukocyte Adhesion Deficiency
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Background: Leukocyte adhesion deficiency (LAD) is a primary immunodeficiency disease (PID) caused by a defect in neutrophil adhesion, characterized by skin ulcers, poor wound healing and recurrent bacterial infection. Intravenous immunoglobulin (IVIG) is used to treat patients with PID, but in LAD is not routinely used. Treatment consists in prompt antibiotic, G-CSF for chronic ulcers and the only definite therapy is bone marrow transplantation (BMT). We present the case of a child with LAD, who was treated with IVIG with a good response before BMT.

Methods: We present a case report of a 2 year-old male, second child of consanguineous parents (cousins 1st grade). His sister had omphalitis and umbilical abscess and died at 6 months with candidiasis and perianal infection. There were 6 episodes of infectious diseases from birth to 6 months: At 11 days of life presented with omphalitis. At 2 months, upper respiratory tract infection with poor response to antibiotics. At 4 months he presented with suppurative otitis media, and was transferred to our hospital with suspected immunodeficiency, with neutrophilia (up to 95900). He was treated with IV antibiotics, and after resolution with prophylactic antibiotics. At 6 months he had gastroenteritis and 1 week later septic shock. Treatment with intravenous immunoglobulins (IVIG) was started.

Results: After IVIG was initiated there were only 6 episodes of infectious diseases from 6 months to 2 years, including in the cord blood stem cell transplantation (CBSTC) period: at 9 months, gastroenteritis; at 15 months balanoposthitis (ecthyma gangrenosum), at 17 months had cellulitis in the hand and buttocks and oral candidiasis. CBSTC was performed on February 2011, at 1 year 11 months, but didn’t engraft. He was discharged with prophylactic antibiotics and cyclosporine. At 2 years he had catheter associated sepsis. Currently the patient is receiving monthly IVIG, fluconazol, TMP-SMX, Acyclovir and in protocol for BMT and has remained stable.

Conclusions: IVIG is not routinely used in LAD. In our case, monthly IVIG resulted in improvement with less infectious episodes. We suggest the use of IVIG as an adjuvant tool for the treatment of patients with LAD before BMT.

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Descriptive Analysis of the Immunological Behavior of Patients with Ataxia Telangiectasia Attended in the National Institute of Pediatrics in the Past 30 Years
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Background: Ataxia Telangiectasia is an autosomal recessive disease characterized by progressive neurological impairment, ataxia, oculo-cutaneous telangiectasia, immunodeficiency, recurrent infections sinopulmonary and cancer predisposition processes. It does not exist in clinical practice guidelines for boarding and management of these patients, neither a suggestion of monitoring.

Methods: Automated search was requested file to the department of clinical records to identify patients diagnosed with Ataxia Telangiectasia. We included all that had clear and complete information to the variables analyzed.

Results: It was a description of variables by central tendencies and dispersion for continuous and categorical variables that were analyzed for frequencies and/or proportions. Included is determination of immunoglobulins IgG and IgA in 35 patients, 34 of 35 IgM and IgE in 9 patients. We observed in 5 patients hypogammaglobulinemia and 13 patients hypergammaglobulinemia. In relation to IgA, 17 patients had a deficiency and 6 of them high levels for their age, IgM in 13 patients reported figures above the percentile for their age. Altered IgE was found in one patient. IgG subclasses were determined in 9 patients and showed alteration in 9 of them. The IgG1 was not altered in anyone of the patients, low IgG2 was found according to age in 7 patients, 2 patients with low IgG3, and low IgG4 in 8 patients. The presence of lymphopenia was observed from the first test, in 14 from 28 patients. In a second measurement was observed in 17 from 25 patients. In the third measurement was observed in 13 form 21 patients.

Conclusions: In the Ataxia Telangiectasia it has been reported that it could be affected almost all the subtypes and subclasses of immunoglobulins, as hypogammaglobulinemia that could be corrected by exogenous administration. We suggest supervise levels of IgG during follow-up of patients and establish decision-subclasses according to the possibilities of each working group, according to the context of clinical infections. Based on our result we suggested that the monitoring of this disease is through an algorithm of clinical boarding.

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Alteration of Humoral and Cellular Immunity in Patients with Ataxia-Telangiectasia at Reference Center in Sao Paulo, Brazil
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Background: To analyze the levels of immunoglobulins and the number of T and B lymphocytes in patients with ataxia-telangiectasia (AT) followed in outpatient immunology.

Methods: A descriptive and retrospective study of medical records of patients diagnosed with AT followed at Federal University of Sao Paulo, Brazil.

Results: Of 24 patients studied, 5 (21%) had levels of IgG below the age-normal percentile 3 (p3), 3 patients (14%) had values above the 10th percentile. IgA values were below the p3 in 11 (46%) subjects; draws attention to high IgM in 14 (58%) individuals. Anemia was found in only 3 patients (12.5%), in the first case the etiology was probably iron deficiency, the second had a diagnosis of Waldemastrom Macroglobulinemia and the third was with sepsis. Seventeen (70.8%) had total lymphocyte count below the p10, marked leukopenia (below p5) was observed in 5 (20.8%). Neutropenia (<1500 cells /mm3) was observed in only 2 (8.3%) and eosinophilia (>500 cells /mm3) in 6 patients (25%). In 79% (19/24) of patients the lymphocyte subpopulation was analyzed, and 17 (89.5%) of 19 subjects showed low number of CD3+ cells compared with controls of similar age. The number of CD4+ T cells was below the p10 in 21 of 23 evaluated patients (91.3%). Interestingly, in most patients the number of CD4+ T cells was between 200 and 500/mm3, suggesting severe depression of cellular immunity. Only one patient had a high number of CD8+ T lymphocytes, in 15 (65%) of 23 subjects the number of CD8+ T cells was below p10. Eight patients underwent a CD19+ cell count, and all of them showed low values. NK cells were quantified in 7 individuals, 3 (43%) cases showing high levels.

Conclusions: Most patients treated in our department showed dysgamma-globulinemia, and low number of lymphocytes T and B.

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Clinical Features of Patients with Ataxia-Telangiectasia at Reference Center in Sao Paulo, Brazil
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Background: Clinical symptoms of patients with ataxia-telangiectasia (AT) followed in outpatient immunology.

Methods: A descriptive study using chart review of patients diagnosed with AT
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 bronchectasia 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.

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

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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 autoimmunity in children with PIDs from our hospital, to delineate their clinical features.

Methods: An internal register 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.

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Malignancies Associated to Primary Immunodeficiencies. A 40-Year Review

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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 register 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.

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

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Background: Severe congenital neutropenia is a bone marrow failure syndrome characterized by severe neutropenia present from birth. We present...