INTRODUCTION: Chronic mucocutaneous candidiasis (CMC) is a rare primary T-cell immunodeficiency of unknown etiology characterized by persistent or recurrent Candida infections of the skin, nails and mucous membranes without *Candida albicans* sepsis. There is evidence that the immune defect could be the result of altering patterns of proinflammatory cytokine production, resulting in insufficient interleukin-2 and interferon-release in response to Candida infections.

Histoplasmosis is one of the most common endemic mycosis causing human infection throughout the world. Similar to the other fungi in this category, initial exposure to *Histoplasma capsulatum* occurs through the respiratory tract and, once inhaled, the organism readily spreads in macrophages throughout the reticuloendothelial system. The ability to contain infection is almost entirely mediated by cell-mediated immunity. In most patients, infection is associated with no symptoms or with only mild pulmonary symptoms. People who have either intrinsic or secondary defects in cell-mediated immunity, however, are at risk for development of severe disseminated histoplasmosis.

CASE REPORT: RAAR is a 40 years-old female who presents chronic mucocutaneous candidiasis since the age of 6 months. After the age of 21, she has been presenting recurrent episodes of pneumonia (20 episodes) leading to the development of bronchiectasis. Recently, she presented an asthmatic episode followed by persistently symptomatic pneumonia despite many antibiotic treatments. She was hospitalized after worsening of clinical symptoms and hemoptysis, with the identification of a severe pneumopathy with pleural effusion and multiple cavities in the medium pulmonary lobe. She was submitted to pulmonary biopsy, lobectomy and pleural drainage. Microbiological studies diagnosed a pulmonary histoplasmosis. The patient was discharged after 2 months of hospitalization and treatment with amphotericin followed by itraconazole and cotrimoxazole.

CONCLUSION: Chronic mucocutaneous candidiasis can lead to a defect in cell-mediated immunity that can cause lower or even no production of proinflammatory cytokines. This may be one of the mechanisms leading to an increased susceptibility to *Histoplasma* spp. infections.

PCR 12 – ANHIDROTIC ECTODERMAL DYSPLASIA: POLYMORPHISM WITH NEUROLOGICAL AND RENAL MANIFESTATION IN A BRAZILIAN CHILD.

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Brief Report: Ectodermal Dysplasia Syndrome (EDS) is a group of congenital diseases, some of them with defects in innate immunity, affecting NF-κB protein. We describe a boy, aged five and white, with Anhydrotic Ectodermal Dysplasia (AED). He has congenital alopecia, anhydrosis, small teeth, hypertrophic gums and moderate rhinitis. After age three, the patient developed nephrotic syndrome, with episodes of mild facial edema and normal renal function, despite persistent hematuria and proteinuria. After age four, the patient had intense headaches and papilledema and was investigated with CT, NMR and spinal fluid puncture with no abnormalities found. Six months of acetazolamide and two months of steroid therapies resulted in fewer headaches and the disappearance of papilledema and probably the steroids contributed to an improvement in the nephrotic syndrome.

The patient has normal development without severe infections. The serum levels of IgG were low and IgA and IgM were normal. The number of the lymphocyte subpopulation and the proliferative response to PHA and BCG were normal. Genetic analysis found polymorphisms: 1628a > C3'UTR SNP (homozygote); 1662t > C3'UTR SNP (homozygote); 1729t > C3'UTR SNP (homozygote). We show that this patient has a mutation in the EDAAR gene. New studies of immune functions will be performed to provide more data to further understand this case.

PCR 13 – HEMOPHAGOCYTIC SYNDROME ASSOCIATED TO NK CELLS DEFICIENCY: A CASE REPORT

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INTRODUCTION: Hemophagocytic lymphohistiocytosis (HLH) is a puzzle disease. It may be inherited as an autosomal recessive trait, usually manifested in infancy and early childhood and usually fatal if not treated. The secondary form may be a result of strong activation of the immune system by infection, malignancies or rheumatologic diseases. The main clinical criteria for the diagnosis are: fever, splenomegaly, cytopenias, hypertriglyceridemia, hypofibrinogenemia, hemophagocytosis, low NK-cell activity, hyperferritinemia, and high levels of sIL-2r. NK cell deficiency is a rare disorder clinically manifested by recurrent or severe infections by herpes virus, which can be a trigger to the activation of the immune system, eventually leading to hemophagocytic syndrome.

CASE REPORT: RSS is a 10 month-old, previously healthy female hospitalized for the treatment of urinary tract infection. During hospitalization she developed a febrile hepatosplenomegaly and was referred for investigation. During the hospitalization she presented chronic diarrhea, pancytopenia, digestive bleeding with a positive PCR to CMV, beginning the treatment with Ganciclovir. The bone marrow smear showed hemophagocytosis and the PCR to CMV in the bone marrow was negative. Hyperferritinemia, hypertriglyceridemia, hypofibrinogenemia and sustained pancytopenia supported the HLH diagnosis. The immunological investigation showed very low number of NK cells. No specific treatment for the hemophagocytic syndrome was initiated since the patient experienced spontaneous remission of the signs and symptoms.

CONCLUSION: A high clinical suspicion of HLH is essential to allow early diagnosis and treatment, avoiding severe sequels.

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PCR 14 – NEW MUTATION IN EXON FIVE OF CD40 LIGAND DEFICIENT PATIENT WITH SEVERE NEUTROPENIA

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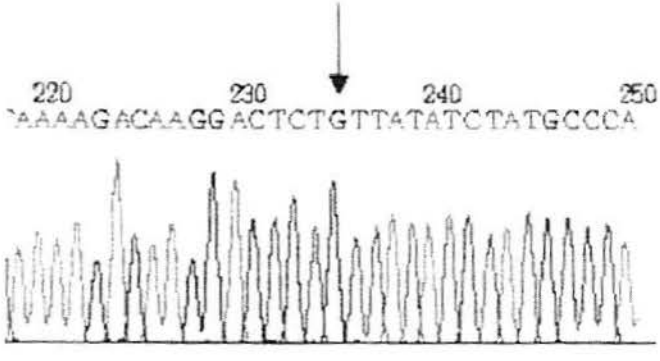
Introduction: Hyper-IgM syndromes (HIGM) is the term used to describe a group of diseases with immunoglobulin deficiencies related to class-switch recombination and somatic hyper mutation. The patients have normal number of B lymphocytes and low concentration of IgG, IgA, IgE, but with normal or high IgM levels.

The most common type of inheritance is the X-linked recessive which is considered a combined form of immunodeficiency disease. The main defect is related to mutations in the CD40 ligand gene (CD40L or CD154).

The CD40L deficiency is considered to be a disease resulting in the failure of T-cell signaling to B cells in order to complete their maturation program by undergoing (Ig)-isotype switching. In normal individuals this contact induces the production of specific antibodies after the class switch from original IgM to IgG, IgA and IgE immunoglobulin. In patients with mutations in the CD40L gene, the immunoglobulin production could be affected leading to an immunodeficiency state

Case Report : T.C is a 2 years old boy, from Brazil, that came to our Immunology Service at an age of 8 months, when presenting since birth, recurrent bacterial infections. At that time, he presented with cyclic neutropenia and low levels of IgG and IgA, and high levels of IgM. We suggested the possibility of primary immunodeficiency and he started immunoglobulin infusion.

Methods: We continued the investigation with bone marrow biopsy showing no alterations. HLA typing was also done (A02, A30, B42, B49, HLA-DRB1 030201, DRB1 110201). DNA sequencing showed a new and rare mutation in exon 5 (A to G) in Y169C, for CD40L



Conclusion: The interest of this case report is the diagnosis of a CD40L patient with severe neutropenia and low immunoglobulin levels. The DNA sequencing showed a rare mutation in exon 5 (A to G) in Y169C. We found an HLA identical donor in the family, and the patient recovered well after a bone marrow transplant.

PCR 15 – ANTI-TNF THERAPY FOR SEVERE AUTOIMMUNE ENTEROPATHY ASSOCIATED WITH COMMON VARIABLE IMMUNODEFICIENCY.

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A 17-years-old man, presenting with chronic diarrhea and malnutrition was investigated with peroral jejunal biopsy and quantitative analysis of serum immunoglobulins. The results have shown villous atrophy and crypt hyperplasia in the small intestine and low IgA levels, respectively. Minor clinical improvement was seen after gluten-free diet. Several months later he developed steatorrhea and insulin-dependent diabetes mellitus, with marked weight loss. Progressive recovery was achieved after glycemic control, empiric therapy for giardiasis and proper enteral nutrition. Six years later he was referred for immunological evaluation due to recurrent infections (extensive cellulitis, pneumonias, sinusitis and sepsis). The laboratory evaluation showed reduced levels of IgG, IgA and IgM was well as low CD4+ T-cell counts in peripheral blood. The clinical picture and laboratory data were consistent with common variable immunodeficiency and IVIG was started (400-600 mg/Kg/month). The patient remained well for several months but gastrointestinal cytomegalovirus (CMV) infection was disclosed during an investigation for daily low grade fever. Conventional therapy with ganciclovir was used for several cycles, due to relapses. In 2009 (27-years-old) he presented chronic diarrhea and significant weight loss. The investigation protocol revealed chronic pancreatitis, gastric CMV disease and conspicuous inflammation of the esophagus, stomach, duodenum, ileum and colon. The most striking histopathological features were the absence of goblet cells throughout the gastrointestinal tract, the atrophic changes in the gastric mucosa and duodenal mucosa (particularly villous atrophy with crypt hyperplasia) and the presence of increased numbers of apoptotic epithelial cells. The initial therapy consisted of ganciclovir, enteral nutrition with oligomeric formulas and aminoacids and steroids (methylprednisolone, 2 mg/Kg), besides IVIg and supportive care. After two weeks of treatment, no significant clinical response was found in spite of negative PCR for CMV. Infliximab (5 mg/kg, every two weeks) was then added, with gradual steroid tapering, with excellent clinical response, as judged by weight gain, control of diarrhea, lowered serum levels of pancreatic enzymes and reduced inflammatory infiltrates in gastric and duodenal biopsies. These results suggest that anti-TNF therapy is a valid option for generalized autoimmune gut disorder in common variable immunodeficiency patients.

PCR 16 – AORTIC ANEURYSM IN A PATIENT WITH AUTOSOMAL-DOMINANT CHRONIC MUCOCUTANEOUS CANDIDIASIS

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Background: Chronic mucocutaneous candidiasis (CMC) is a rare disease, characterized by persistent and refractory infections of the skin, nails and mucous membranes, with yeasts of the genus Candida, infrequently evolving to systemic disease or septicemia.

Case report: We report a family with three CMC patients of a non-consanguineous family beginning in childhood, with lesions in skin, nails and mucosa, improving with time, being the mucosal lesions refractile to therapy. The family members affected by CMC are the mother (propositus), and her two daughters that have classical CMC, one of them with autoimmune thyroiditis.

Patient 1: Female, 38 years old, Caucasian, born to non-consanguineous