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SYMPOSIA

THE CHALLENGE OF PARASITES AND IMMUNOSUPRESSION: FROM DIAGNOSIS TO TREATMENT

"from the bench to the bed"

PARASITES AND PRIMARY IMMUNODEFICIENCIES

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Background

Primary immunodeficiencies (PIDs) are genetic defects

Affects one or more components of the immune system

Early in infancy and childhood but can be detected later in life

Hallmark: susceptibility to bacterial, protozoal, fungal and viral infections

The French PID study group; Clin Immunol. (2010)

Characteristics >180 different and rare PIDs

Largely misdiagnosed/physicians poorly know about clinical manifestations/laboratory findings

Wide geographical and racial variations in prevalence/type

Although rare, not so uncommon

US: overall prevalence 86.3 per 100.000 inhabitants

Carneiro-Sampaio M; J Clin Immunol. (2013)

X-linked agammaglobulinemia

Common variable immunodeficiency

X-linked hyper IgM syndrome

Selective IgA deficiency

MHC class II deficiency

Severe combined immunodeficiency

Case report

In 2012, a 8 months old boy, native of Dracena county, western region of São Paulo state, was referred to the Regional Hospital of Presidente Prudente, São Paulo, Brazil.

Clinical signs: Fever, cough and vomit for 5 days. In the last 3 months he had 2 acquired community pneumonia.

Physical examination: Pale, febrile, with tachydyspnea, dehydrated, showing hepatomegaly extending to 6 cm below the costal margin and mild splenomegaly.

Epidemiology: The origin and destination of the patient from an emerging visceral leishmaniasis area of São Paulo state as well as symptoms were considered.

Case report

Laboratory findings:

rK rapid test (NEGATIVE), indirect fluorescent antibody test (NEGATIVE) and bone marrow aspirate (POSITIVE) for *Leishmamia* spp.

Immunoglobulins: IgA: <7 mg/dL (0-83); IgG: 42 mg/dL (232-1411); IgM: 29 mg/dL (0-145).

Diagnosis: visceral leishmaniasis and PID (Common Variable Immunodeficiency)

Treatment: *Liposomal amphotericin* B and immunotherapy

Discussion

Misdiagnosed in developing and developed countries

Laboratory: Molecular methods, not available in developing countries

Signs and symptoms: from asymptomatic to severe

Type: a broad array of parasites can be diagnosed

Few studies in PIDs compared to HIV symptoms and diagnosis

Giardia lamblia, *Cryptosporidium parvum* and *Toxoplasma gondii*

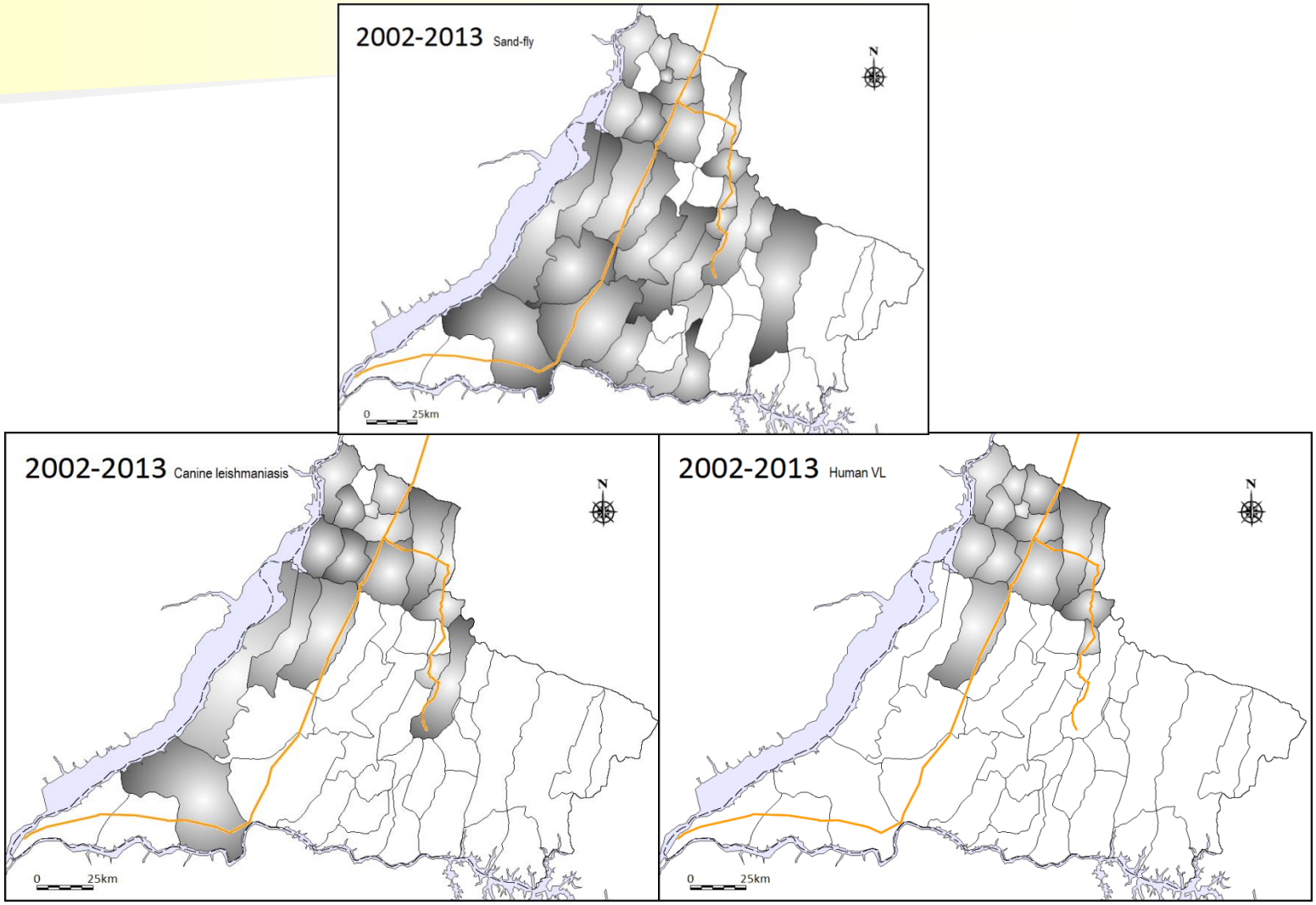
In visceral leishmaniasis the humoral immune response play a role but the parasite is intra-cellular

Most of the immunocomptent patients clear the infection

The cellular immune response play a role and Th1 cytokines are produced

Immunosuppresed patients: defficient immune resonse

The Western region of São Paulo state: a new endemic area of visceral leishmaniasis in Brazil



Prestes-Carneiro *et al.* unpublished data

Conclusion: HIV(-) patients with visceral leishmaniasis must be screened for other immunological diseases, especially Common Variable Immunodeficiency

As far as we know, first case described wordlwide

Case report

A 73 years old woman, living in Presidente Prudente, SP, Brazil, was referred to the Immunodeficiency Ambulatory of the Regional Hospital in February, 2014.

Clinical signs/symptoms: A 2 months history of high grade posterior headache, bilateral cervical, occipital lymphadenopathy. She lost ± 6 kg in body weight in the period.

Physical examination: bilateral cervical, occipital lymphadenopathy characterized by painless, fibro elastic consistency and adhered to the tissues.

Past history: compensated hypothyroidism

Case report-laboratory findings

Laboratory test	Results	Normal range
HIV	negative	
Epstein-Barr Virus	negative	
Citomegalovirus IgM	negative	
Toxoplasmosis IgG IgM IgG affinity	 >250 IU 2.75 IU 75%	 Negative Negative Negative

Case report-diagnosis/treatment

Treatment: Sulfadiazine, pyrimethamine, folinic acid

The patient improved but a persistent lymphocytosis in hemogram remained several months

A biopsy was conducted and a non-Hodgkin lymphoma was diagnosed

Diagnosis: Lymphadenopathy, acute/reactivated toxoplasmosis?, non-Hodgkin lymphoma

At the moment, conservative approach for NHL

Discussion

T. gondii obligate intracellular protozoan

Worldwide distribution

Disseminate throughout the body during the acute phase

Acute infection in immunocompetent, usually asymptomatic

In chronically infected, may induce reactivation

In immunossuppressed neurotoxoplasmosis is a risk

T cell-mediated immunity controls but does not eradicate

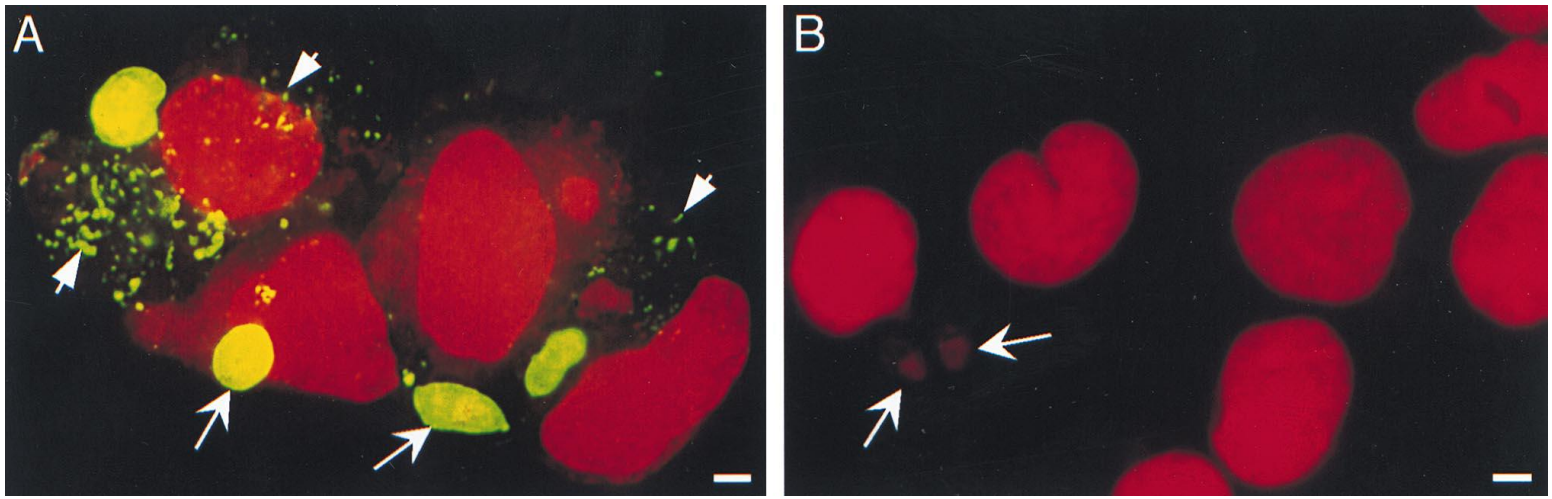
Different T-cells subsets and Intra Epithelial Lymphocytes are involved

IFN-γ/IL-12: resistance in acute and chronic phases

B-cells and humoral immune response also play a role although the parasite is intra-cellular

Antibodies block infection of host cells by tachyzoites

Binding of anti-SAG antibodies to the surface of infected monocytes causes a decrease in cells that become infected with *T. gondii*



JACQUELINE Y. CHANNON, Infect.Immunit., 1999

Conclusion: Individuals with underlying malignancies/organ transplantation or on immunosuppressive drugs are increasing worldwide. In these patients, elevated risk factors for acute disseminated toxoplasmosis may be considered

Lessons for home

Acquired immunosuppresed patients are increasing

New PIDs are being identified

Patients are misdiagnosed also in developed countries

Infectious diseases hallmark of immunossuppression

Parasite infection diagnosis and treatment is a challenge

Clinicians should be aware for diagnosis and treatment not only for PIDs but also for induced immunosuppressed patients

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