

THERAPEUTIC ASPECTS OF CUTANEOUS LEISHMANIASIS

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Cutaneous Leishmaniasis is a chronic disease, endemic in Middle East Africa and Central Asia.

Historical Notes: Thousand years ago the great Iranian physician and philosopher Avicenna denotes a chronic cutaneous ulcer difficult to treat, his description of the lesion is relevant to cutaneous leishmaniasis; in 15th century Al Razi the Persian physician describes clearly this lesion in his book "The Comprehensive Experiments" Pocock in 1755, Cunningham in 1885, Borosky in 1898, Wright, Leishman and Donovan in 1903 describe the lesion and organism in Kala-Azar and Cutaneous Leishmaniasis.

Epidemiology:

The insect vector is sandfly of Genus Phlebotomus with many species (Ph.papatasii, Ph.sergenti, Ph.caucasicus, Ph. alexandri) The life span of Phlebotomus is 30 days, fly

short distance (1000 meters) to heights of 2 meters, their activity is at night in summer months.

Organism

A Flagellata protozoan of the family Trypanosomidae and genus *Leishmania* with species (*L. tropica*, *L. donovani*, *L. brasiliensis*) The agent is *Leishmania Tropica* exists in two forms: in tissue as leishman form (amastigote) an elliptical mass of protoplasm measuring 1.5 to 5 micron containing a spherical vesicular nucleus and a kinetoplast complex; the amastigotes multiply within the cells of the reticuloendothelial system.

Organism in the leptomonad form is elongated, with vesicular nucleus in the middle of the cell, a distinctive flagellum in front which is evolved from kinetoplast; this form is seen in cultures and in the insect vector.

Transmission

The two reservoirs from which phlebotomus obtains its infection are man and animals, the leishman form is taken by insect vector from active lesion in man or animals, (dog, cat, gerbil, rat and rodents); in the stomach of phlebotomus leishman form transforms into the leptomonad; the parasites plug the mouth parts of the sandfly and released in the puncture wound, the cycle requires ten days and in the host the organism assumes the leishman or tissue form.

Immunology

The observation of the self-limited nature of the infection (one year) denotes the development of immunity, vaccination which has the nomadic and historic origin supports the immunological concept of Leishmaniasis; cell-mediated immunity is confirmed by leishman-test (Montene-

gro) and its negativity in Disseminate Cutaneous Leishmaniasis which is seen in cases with impaired cell-mediated immunity. Humoral immunity is evaluated by demonstration of circulating antibodies in the sera of infected individuals with Indirect Fluorescent Antibody Test, Direct Agglutination Test, Prausnitz-Kustner and Anti-leishmania activity of normal animal sera.

Clinical Manifestation

The clinical manifestation of cutaneous leishmaniasis in man is classified: I-Localized: acute, chronic, recidiva

2- Generalized: disseminated, leishmanid

There are two types of acute leishmaniasis: wet (zoophilic) which is seen in rural areas producing ulcerated

lesions and lymphangitis in man; dry (anthropophilic) types are encountered in urban areas: the incubation period is about six months, primary lesion is a 3 to 4 mm papule, after several weeks develops into infiltrated nodule with ulceration and adherent grey crust, before one year heals with permanent and disfiguring scar.

Chronic Cutaneous Leishmaniasis: the lesion shapes granulomatous reaction mimics lupus vulgaris, erythematous and scaly plaques with follicular prominence.

Disseminated Cutaneous Leishmaniasis: is seen in individuals with defect in the cellular immune response and characterized by lesions similar to lepromatous leprosy, widely disseminated and abound with organisms, there is no involvement of internal organs, the leishmanin skin test is negative.

Pathology

In acute leishmaniasis in the dermis there is a mas-

sive infiltrate of histiocytes and mononuclear, intracellular bodies are seen in abundance in the histiocytes; in chronic leishmaniasis the prominent feature is the presence of tubercles in the dermis, composed of epithelioid cells and of giant cells of Langhans type, leishman bodies are scarce; the lesions of disseminated leishmaniasis show an infiltrate of histiocytes and tubercles with abundant leishman bodies.

Therapy of Cutaneous Leishmaniasis

There has been nomadic and indigenous treatments in every part of the world that cutaneous leishmaniasis is endemic. Treatment of cutaneous leishmaniasis is divided in two forms: local and general; local treatment is produced with different methods: a) surgical b) physical c) chemical. Surgical treatment is an old procedure, in the case of small papule without infiltration or tumor in suitable position, the removal must be complete considering the recurrences.

Physical treatment: a) high temperature by use of diathermocoagulation is profited in parts of body that scar formation is unregardable. b) infra-red light is used for single chronic and ulcerative lesions. c) cryotherapy, snow carbon dioxide and liquid nitrogen is profitable for long term treatment.

d) radiotherapy, superficial X-R and Grenz ray is not used today.

Chemical treatment: a) topical application of Zinc Chloride, after curettage of lesion the saturated zinc chloride is applied on the ulcer. b) local infiltration of emetine, 2% emetine hydrochloride solution is infiltrated between 1 to 8 Cgr. in each session which depends

with the size of the lesion.

c) local injection with mepacrine, 5% mepacrine solution is infiltrated into the lesion, 0.3 to 2 cc is used for each injection.

d) local injection of Solustibosan, 4% cc per Kg to Mx 2 cc of the solution of Solustibosan is infiltrated at the base of the lesion.

General Treatment of Cutaneous Leishmaniasis

(Biscatechol-3 : 5-disulphonate)

1- Trivalent derivative of Antimony; Fouadin, in adult begins with a dose of 3.5 ml, then the full dose of 5ml can be given at all further injections, for the children 1 ml per 10 Kg bodyweight, a course of 15-20 injections is necessary.

Stibophen, is the English trade mark in ampoules of 5 ml; the first injection 1.5 ml, the second 3.5, then every other day 5 ml with the total dose of 40 ml.

2- Pentavalent Derivative of Antimony: Glucantime (Meglumine Antimoniate) in 5 ml ampoules contain 1.5 gr., daily dose is 100 mg. per Kg. via IM injections, the course of treatment is two weeks, the interval for next treatment is two weeks.

Pentostam: (sodium stibogluconate) is given 10mg per Kg for 15 days. Neostibosan (Ethylstibamine): is given 100 mg every other day for 15 injections, total dose is 2 gr.

Solustibosan: 3cg injected every day for 12 IM injections

3- Cycloguanil paomate (Camolar): is a repository antimalarial injection in flacons of 50 ml, each ml contains 140 mg of drug, dose of single injection is between 1

to 2.5 ml.

- 4- Metronidazol (Flagyl) : the dose of this drug is 750 mg daily for the course of 15 days, the interval is 10 days, 2-3 courses is necessary.
- 5- Pyrimethamine (Daraprim): is an anti-acidfollic drug used for malaria; dosage is two 25 mg tablets is given for two weeks, the interval for the next treatment is 10-15 days.
- 6- Manomycin: is an antibiotic of neomycin group, is given 600000 to 800000 units every day for 12-14 days.
- 7- Rifampin: is given 600 mg two times daily for 10 days, in children 20 mg per Kg. is administered.
- 8- Dihydroemethine(Ciba): two tablets daily for 30 days.
- 9- Chloroquine: 600 mg two times for two days and then reduced to 300 mg for 2-3 weeks.
- 10-Steroids: injection of steroids into the lesion or systemic administration with other modalities is proposed.
- 11-Transfer factor: in patients with compromised immunity system, the specific or non-specific transfer factor is advocated.

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