Etiology, Diagnosis, Clinic and Treatment of Cutaneous Leishmaniasis

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ABSTRACT

Cutaneous leishmaniasis can present with localized, chronic, recurrent, diffuse, and sharp forms. For diagnostics, dermatoscopy, microscopy of biopsy material, smears - prints, skin scrapings; inoculation on NNN medium, PCR, serological diagnostics. 4 types of histological manifestations of infection are characteristic: I - abundant amastigotes, II - macrophages, polymorphonuclear neutrophils, plasma cells, necrosis, III – early granuloma with focal accumulation of epithelial cells, lymphocytes and a small number of plasma cells, IV - well-formed epithelioid granuloma in the dermis with Langerhans giant cells, lymphocytes and epithelioid cells. First line drugs for cutaneous leishmaniasis are preparations of pentavalent antimony: sodium stibogluconate intravenously or intramuscularly, meglumine antimonate intravenously or intramuscularly, miltefosine orally.

The second line of therapy includes topical paromomycin, intravenous or intramuscular pentamidine, oral fluconazole, liposomal amphotericin B or amphotericin B deoxycholate, allopurinol. Prevention of cutaneous leishmaniasis is to inform patients, use repellents, window and bedside mosquito nets.

Keywords: cutaneous leishmaniasis, sodium stibogluconate, paromomycin, azoles.

Leishmaniasis is a widespread chronic infection of humans and some animals. Anyone can get sick age, but children and young people are more often affected adults. Clinically isolated skin, mucocutaneous, diffuse cutaneous and visceral (liver and spleen affected) forms of leishmaniasis. According to WHO, about 1.2 million cases of cutaneous leishmaniasis and 400,000 cases of visceral leishmaniasis. Visceral leishmaniasis is second only to malaria as a cause of death from tropical diseases. Most cases of skin leishmaniasis occurs in the countries of the Middle East, Brazil, Peru, Mediterranean, India, Central Asia, Sub-Saharan Africa, Central- southern regions of Texas (USA). Skin- Mucous leishmaniasis is endemic to Central America and northern South America, while visceral leishmaniasis occurs everywhere, but most often in Africa andAsia. In the countries of the central asia eishmaniasis occurs in Uzbekistan and Turkmenistan [1].

Etiology

Leishmaniasis is caused by protozoan intracellular parasites that represented by more than 20 species of Leishmania. The pathogen is transmitted by female mosquitoes, in whose body parasites are in flagellar form (promastigotes). Old World Leishmaniasis is transmitted mosquitoes of the genus

Phlebotomus, and leishmaniasis New World - mosquitoes of the genus Lutzomyia.

Mosquitoes are small in size, which allows them to penetrate standard protective nets on windows and even through nets in protective military helmets. The life span of mosquitoes is 30 days, during the day they rest, are active from dusk to dawn and fly poorly (no more than 2 m). Mosquito bites can be painless and therefore patients often do not indicate the fact of an insect bite. The situation is aggravated by the fact that mosquitoes do not buzz, and therefore do not attract Attention. After being bitten by a mosquito, the parasite invades the host's mononuclear phagocytes and transforms into amastigotes (non-flagellated form).

Clinic

Clinically, cutaneous leishmaniasis can present with localized, chronic, recurrent, diffuse, and acute forms. Localized form of skin leishmaniasis is manifested by papules or nodes that occur at the site of bites, most often it is the face and open areas of the body.

Over time, papules / nodes turn into well-circumscribed painless ulcers with purple corolla . Corolla color due to the destruction of the epidermis and the translucence of the vessels of the dermis. Lymphadenopathy and the presence of satellites are possible. Acute the Old World form of leishmaniasis clinically resembles a boil. ulcers heal with the formation of depressed scars. At localization on the face, a cosmetic defect develops, which leads to serious psychological problems of the patient and is certain stigma of social disadvantage. Chronic relapsing leishmaniasis is characterized by the appearance of new papules along the periphery of scars formed after skin leishmaniasis. This happens due to preservation of single parasites in places of cov, which slowly progress and can spread to the entire skin, although the preferred sites are the face, ears, knees and elbows. Some nodules may have a warty surface or resemble xanthomas, keloid. Some patients are affected nasopharynx or oral cavity, or mucosa nose without destroying the nasal septum.

Diffuse cutaneous leimshaniasis may present as large, hypopigmented patches, resembling tuberculoid disease leprosy of the rare forms of cutaneous leishmaniasis (up to 5% of cases), the following: lupoid, psoriasiform, zosteriform, verrucous, palmar-plantar, chancriform, resembling paronychia, erysipeloid, mycetoma [4, 5].

Diagnosis

Leishmaniasis should be suspected in any person living/visiting epidemically dangerous countries, since in the case of visceral leishmaniasis, a late diagnosis can be the cause of death of the patient. Special attention is needed given to HIV-infected patients, in whom leishmaniasis is more severe and may be resistant to treatment. Considering that the treatment of leishmaniasis is long and toxic, the diagnosis of leishmaniasis should be confirmed by laboratory tests. The following methods are used to diagnose cutaneous leishmaniasis: have different degrees of sensitivity: dermatoscopy, microscopy (research on slide, Giemsa stain) biopsy material, smears - prints, skin scrapings and aspiration material by the methodmfine needle puncture, culture, PCR, serological diagnostics. Collection of material for examinations (biopsy, aspiration) carried out under sterile conditions, samples it is necessary to receive from new, most active rashes.

Skin biopsy

Punch - a skin biopsy is performed on the entire skin thickness, under local anesthesia, sterile treatment is best done 70% alcohol solution, since iodine solution can inhibit the growth of the culture. The skin is taken from the edge of the ulcer with the capture of unaffected skin.

The sample is divided into three parts: one part is sent for culture and PCR (PCR method also excludes other infections), the second for smears - prints and the third for histological examination (Giemsa stain, hematoxylin with eosin and specific stains to exclude other infections). Biopsy sensitivity for Old World cutaneous leishmaniasis about 60%. The formation of an infectious granuloma is characteristic of cutaneous leishmaniasis. Four types of histological manifestations of infection have been described (Table 2) Amastigotes are best found in macrophages under the epidermis. They are tiny, 2 to 4μm in diameter, which requires high magnification (x1250) to detect them. When painting hematoxylin eosin

amastigotes pale gray-blue color and are determined in the cytoplasm of skin macrophages. Amastigotes can also be found in epidermal Langerhans cells.

Skin scraping

Before starting sampling, it is necessary to ensure good homeostasis to exclude blood entering the sample, which is achieved squeezing the element. The best fence site - in the immediate vicinity of the ulcer or its active border. Make with a sharp scalpel a superficial incision 1–2 mm deep, 5–8 mm long, and with the end of a scalpel, tissue elements and tissue fluid are scraped off. Stained according to Romanovsky - Giemsa [7, 8].

Table 2 - Histological signs of leishmaniasis (M. Z. Handler et al., 2015) [6]

Type	Frequency	Histological features occurrence
I	I 45%	Abundant amastigotes
II	27.5%	Presence of macrophages, polymorphonuclear neutrophils, plasma cells and necrosis
III	15%	Early granuloma with focal accumulation of epithelial cells, lymphocytes and few plasma cells
IV	5%	Well-formed epithelioid granuloma in the dermis with giant Langerhans cells, lymphocytes and epithelioid cells Smears-imprints

Imprint smears are obtained from biopsy material, trying to exclude the presence of blood in the smear as much as possible, but getting wet gauze material can remove amastigotes that are located on the surface sample. The sample is touched carefully, circular rotation of the glass slide, make two samples on one glass, dry, fix in methanol and stain Giemsa.

Cultural study

The ideal option for preparing a sample for cultivation is the presence of a medium before sampling and its rapid transportation to the laboratory after inoculation on Wednesday (within 24 hours after sampling). In the absence of medium, the material placed in a test tube with a buffer solution and neutral pH or in a sterile tube. Sample temperature control (cooling) is required to prevent growth of microflora skin. Culture growth is assessed within 4 weeks, and only after that a conclusion is made about its negativity. For a long-term infection the number of pathogens decreases, they are difficult detect and then the test can be applied Montenegro, based on the ability of the Leishmania antigen to induce cellular - mediated immune response (skin reaction of a delayed type). Suspension of the dead promastigot is administered intradermally on the palmar surface of the forearm. The reaction will be considered positive when forming papules >5 mm in diameter at the site of inoculation after 48–72 hours. The test is positive in 90% of cases with cutaneous and mucocutaneous leishmaniasis lasting 3 months and negative with a diffuse form (anergic) form of cutaneous leishmaniasis. Because of it is impossible to distinguish between previous and real infection (test positive, when there are active manifestations of the disease and remains positive after recovery), it is not recommended in some countries to application.

Serological and immunological diagnostics is used in the diagnosis of visceral and sometimes mucocutaneous leishmaniasis. Indirect immunofluorescence, enzyme immunoassay, Western blot, direct agglutination, immunoprecipitation and isoenzyme electrophoresis.

Due to the weak humoral response, these diagnostic methods are not widely used. When using chemiluminescent ELISA found a significant increase levels of anti-a-Gal IgG when infected with L. tropica or L. major. Of the innovative methods for diagnosing cutaneous leishmaniasis, the effectiveness of a rapid test based on immunochromatographic analysis (CL DetectTMRapid Test), which allows you to

detect all types of pathogens in skin samples [8, 9].

Differential diagnosis of cutaneous leishmaniasis includes infectious and malignancies that closely resemble cutaneous leishmaniasis: insect bites, deep fungal infections, lupus vulgaris, Kaposi's sarcoma, nontuberculous mycobacteriosis, tertiary syphilis, basal cell carcinoma. When localized process on the face, differential diagnosis is carried out with Wegener's granulomatosis and angiocentric NK/T-cell lymphoma [1, 6, 8].

Treatment

The treatment of leishmaniasis is a fairly complex. No method gives 100% results, data on the effectiveness of certain drugs are controversial. When choosing a method of treatment, it is necessary to determine the type of pathogen and the geographical location of the site infections. Without treatment, Old World leishmaniasis reduces in 2-4 months if caused by L. major, or 6-15 months later if caused by L. tropica. New World cutaneous leishmaniasis caused by L. mexicana reduces after 3 months in >75% of cases, caused by L. braziliensis and L. panamensis less than 10% and 35% respectively. Due to the pronounced side effects of drugs, systemic treatment cutaneous leishmaniasis is indicated for numerous rashes (more than 5-10), plaques more than 4 cm in diameter, localization of leishmaniomas on the skin of the hands, feet, face, in the area joints or with rashes existing over 6 months. Medicines first-line therapy for cutaneous leishmaniasis are pentavalent antimony: sodium stibogluconate 20 mg/kg/day intravenously or intramuscularly, antimonite meglumine 20 mg/kg/day for 20 days and miltefosine 2.5 mg/kg/day orally (maximum 150 mg) within 28 days. The second line of therapy includes topical paromomycin twice a day. 10-20 days, pentamidine 2-3 mg IV or intramuscularly daily or every other day 4-7 doses, fluconazole 200 mg/day or 6-8 mg/kg/day day by mouth for 6 weeks or other azoles ketoconazole 600 mg/day or 10 mg/kg/day four weeks (in some countries, ketoconazole, due to side effects in medicine, is not applied), itraconazole 7 mg/kg/day 3 weeks, liposomal amphotericin B 3 mg/kg 1-5 day, 14 and 21 days, amphotericin deoxycholate B 10 mg/kg once or 1 mg/kg every other day 15 IVs, allopurinol 300 mg / day - 3 months (L. tropica), or 300 mg x 3 once a day for 6 weeks (L. mexicana), or 100 mg 4times a day (L. panamensis), or 1.5-2.5 mg / kg / day 28 days (L. donovani).

Local treatment includes the application combined ointment containing 15% paromomycin and 12% methylbenzethonium chloride (New World cutaneous leishmaniasis), paromomycin/gentamicin (Old World cutaneous leishmaniasis), imiquimod. Intralesional administration of sodium stibogluconate 0.2-0.4 ml intradermally 3 times a week for 2 months is effective in the treatment of leishmaniasis Old World.

Physiotherapy includes the use cryotherapy, curettage, radiofrequency, CO2 laser [1, 6, 8, 10, 11].

Conclusion

Cutaneous leishmaniasis is a difficult disease to diagnose and treat. Therefore, it is necessary to take measures to prevent the disease. Our territory, that is, the territory of Uzbekistan, is a bit of an epidemic danger zone. This requires doctors to organize preventive measures well.

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