Treatment failure in cutaneous leishmaniasis in Sri Lanka – Is it for real?
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Abstract
Leishmaniases is a disease spectrum caused by a protozoan parasite of the Genus Leishmania. Leishmaniasis in Sri Lanka (SL) was traditionally known to be caused by Leishmania donovani zymodeme MON-37, with the disease manifesting predominantly as cutaneous leishmaniasis (CL). Intra-lesional sodium stibogluconate (IL-SSG) has been the first-line treatment of CL for over two decades in SL and on average ten IL-SSG injections are required for healing.

In the absence of previous studies on leishmaniasis treatment failure in SL, treatment failure burden was studied in 201 laboratory-confirmed CL patients from southern SL from 2016 to 2018. The majority (151/201, 75.1%) failed treatment with IL-SSG. The randomized controlled clinical trial on safety and efficacy of thermoderapy on antimony failures, conducted from 2017 to 2020 showed a final cure rate of 95% with radio frequency induced thermoderapy. A novel technique of image processing of pre-treatment CL lesion photographs enabled visualizing the underlying inflammatory response in CL ulcers, which differed among the completely healed and the treatment failed.

The in-vitro sensitivity of antimony, amphotericin B and miltefosine on Leishmania promastigotes, tested using the modified MTS-PMS cell viability assay, varied depending on the species and the lesion phenotype, and the IC50 values did not always correlate with the clinical treatment outcome. However, the ex vivo macrophage-amastigote drug sensitivity assay showed significant differences between the IC50 values in treatment failed and healed. Whole genome sequencing of parasites isolated from 26 CL lesions and one mucocutaneous (MCL) lesion identified L. tropica causing CL and MCL for the first time in SL.

In conclusion, treatment failure in leishmaniasis in SL is real and needs urgent attention. Thermoderapy is an effective treatment for antimony failures. Image processing can be developed further into tools to aid in management. Whole genome sequencing provided the first evidence of CL and MCL caused by L. tropica in SL.

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which may contribute to the prevalence of CL in SL and high antimony failure rate. With the possibility of at least three genotypic groups, *L. donovani*, *L. tropica* and *L. donovani* hybrids, causing leishmaniasis in SL, further comprehensive studies on disease pathology, diagnosis and treatment methods are needed for combatting treatment failure in Sri Lankan leishmaniasis patients.