Cutaneous Leishmaniasis in Southern Africa

A Case Report

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SUMMARY

The microscopical findings in a case of cutaneous leishmaniasis from South West Africa are presented in order to highlight the pathology of this disease and facilitate its recognition, should unsuspected cases occur in the Republic of South Africa. In addition, the ultrastructural findings confirm the presence of typical Leishmania which occur in the cytoplasm of macrophages where they are undergoing destruction. This adds a further dimension to the characterization of this disease in southern Africa.

In 1970 attention was first drawn to the presence of cutaneous leishmaniasis in South West Africa by Grove. He described the disease in both White and Black patients and since then he has documented a total of 18 patients, all of whom appeared to have contracted the disease in the territory. Evidence has been presented that a species of sandfly (Phlebotomus rossi) is the vector responsible and that an animal reservoir of infection exists in the hyrax (Procavia capensis), commonly known locally as the dassie, man being infrequently infected.

As the geographical and physical environment of the north-western Cape Province is similar to that of South West Africa, and as the hyrax exists in both regions, it is quite possible that cutaneous leishmaniasis may exist, as yet unrecognized, within the borders of the Republic of South Africa. In order to highlight this possibility to pathologists and clinicians alike, another case in a patient resident in South West Africa is recorded. The ultrastructure of the lesion is also described because this establishes the aetiology beyond doubt, and further augments the scanty reports that exist on human skin lesions.

CASE REPORT

A 54-year-old White woman residing in Karasburg was referred by her general practitioner to a regional hospital in Upington where a skin nodule on the right side of her neck was removed and submitted for histological examination. No further details are available as to how long the lesion had been present or its rate of growth.

Methods

The tissue was fixed in formol-saline and embedded in paraffin. Sections for light microscopy were stained with haematoxylin and eosin, Giemsa and periodic acid-Schiff. For electron microscopy a portion of the formalin-fixed tissue was washed in phosphate buffer and postfixed in osmium tetroxide. After dehydration in graded alcohols it was embedded in Spurr's epoxy resin. Sections were examined in an AEI 6B electron microscope.

Pathological Findings

The gross specimen consisted of an ellipse of skin measuring 3,0 x 1,5 cm in size. On the surface there was a flattened central nodule, measuring approximately 0,5 cm in diameter, the cut surface of which was bright yellow.

Histologically, the dermis was occupied by a cellular infiltrate consisting of sheets of histiocytes with clear cytoplasm. The cells extended up to the epidermis and downward along the blood vessels and adnexal structures (Fig. 1). Peripherally, chronic inflammatory cells consisting of lymphocytes and plasma cells were also present, as well as focal granulomata of epithelioid histiocytes and Langhans-type giant cells (Fig. 2). A notable feature in the cytoplasm of many cells was the presence of multiple rounded bodies which, by Giemsa staining, showed the nuclei and kinetoplasts of leishmanial amastigotes. The overlying epidermis was not altered in any way.

Ultrastructurally, the predominant cell type was seen to be a macrophage containing oval nuclei with scattered

Fig. 1. The predominant inflammatory reaction in the dermis of sheets of macrophages with clear cytoplasm. The dots present in the cytoplasm of many of the cells are the Leishmania. The epidermis is not remarkable (H and E × 320).

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at the periphery of the lesion macrophages are replaced by scanty granulomata of epithelioid cells and Langhans-type giant cells and a lymphocytic and plasma cell infiltrate. Organisms are scanty in this region (H and E × 320).

Fig. 3. Group of macrophages showing multiple Leishmania lying in clear spaces within the cytoplasm of the cells; these organisms do not appear to be lying in a phagosome (× 5 000). Inset: portion of a macrophage, with organism, showing abundant rough endoplasmic reticulum, mitochondria, polyribosomes and desmosomes, which characterize the cell (× 18 750).

chromatin, and abundant cytoplasm with prominent rough endoplasmic reticulum, moderate numbers of mitochondria and desmosomes linking adjacent cells. Within the cytoplasm of these cells there were leishmanial amastigotes in varying states of disintegration. Up to 8 organisms could be identified in a cell (Fig. 3). These lay in a clear space within the cytoplasm which did not appear to be outlined by a membrane, though the latter observation in formalin-fixed tissue may not be valid. In the intact organisms the nucleus, kinetoplast, basal body with mitochondrion, flagellum, and flagellar pocket could clearly be identified (Fig. 4). At higher magnification the pellicular microtubules of the plasma membrane as well as 9 paired fibrils in a cross-section of a flagellum could be demonstrated (Fig. 4). In many organisms the plasma membrane had partially or completely disintegrated and the cytoplasmic organelles of the amastigotes could only be partially identified or had disappeared completely. This destruction of the organisms occurred entirely within the cytoplasm of the macrophages and did not appear to be related to lysosomes. No organisms could be demonstrated outside the cells.

Fig. 4. Some of the fine structure of intact intracytoplasmic Leishmania, such as flagellum, kinetoplast, basal body and polyribosomes (× 37 500). Inset: view of plasma membrane with its pellicular microtubules (small arrows) and a cross section of a flagellum with 9 paired fibrils (large arrows) (× 70 000).

DISCUSSION

The presence of cutaneous leishmaniasis in South West Africa is now well known, following the initial and subsequent reports of Grove. In his recent report of 18 cases he has given a full account of the clinical and pathological findings of the disease as encountered in southern Africa. In reporting this additional case we wish to further underline the importance of recognizing the presence of this disease entity within our geographical region where it may go undiagnosed clinically and pathologically.

Grove has indicated that human infections are probably infrequently due to a bite by the sandfly P. rossi, which is infected from a reservoir of Leishmania occurring in the hyrax. The sandfly becomes infected through biting the relatively hairless nose of the animal.

The circumstances under which the disease occurs in South West Africa would appear to be very similar to those that obtain in the highlands of Ethiopia, as outlined by Bray. Here the sandfly P. longipes becomes infected at cliff faces where significant populations of infected hyraxes occur. Herdsmen living in the vicinity are exposed to the bites of the flies. In contrast, in southwestern Ethiopia the focal point of infection would appear to be large, solitary wild fig trees, in the shade of which coffee is grown, and which also harbour hyraxes.

As environmental conditions in the north-western Cape
are similar to those which occur across the Orange River in adjacent South West Africa, cutaneous leishmaniasis may indeed already be established there. The human population here is very sparse; thus, with limited opportunities for infection, the condition may be exceedingly rare. However, along the irrigated regions of the Orange River, further west near Upington, the population density increases, and here one should be on the lookout for clinical cases. Indeed, although the present patient was resident in Karasburg, South West Africa, the specimen for histological diagnosis was submitted from this area.

The lesion consisted of large numbers of histiocytic cells with clear cytoplasm and containing numerous easily recognizable intracytoplasmic *Leishmania*. Peripherally, a mild tuberculoid response of epithelioid cells and Langhans-type giant cells was present. This lesion presented no diagnostic difficulties and would probably be categorized as being of the macrophage/intermediate type of histological reaction, according to the Ridley-Jopling classification; as such it falls within the range of appearances described by Grové. However, once again it should be stressed that the reaction may be nonspecific, with parasites extremely scanty or absent in the lesion. In such an event, with a diagnosis not immediately obvious to the pathologist, an awareness of the possibility of cutaneous leishmaniasis in skin biopsy specimens from patients within the area at risk will reduce the number of undiagnosed cases to a minimum.

The fact that we were able to study the ultrastructure of the lesion adds another dimension to the southern African disease thus far not reported. The trypanosomes and leishmaniae show a constancy of basic structure, and no striking ultrastructural differences have been discerned between the various flagellates and between the pathogenic and non-pathogenic species. According to Sandbank, *L. tropica major*, the causative organism of Oriental sore in humans, had not been studied by electron microscopy before she reported 3 cases. The findings in our case conform very closely with those described by her.

We have confirmed the macrophage character of the predominant inflammatory cell and the presence within the cytoplasm of such cells of leishmanial amastigotes in varying stages of disintegration. The better preserved organisms lay free within the cytoplasm of the cells and showed the typical nucleus, kinetoplast, basal body, mitochondrion, flagellum and flagellar pocket of *Leishmania*, as described by Sandbank in infections of *L. tropica*. While our findings prove beyond doubt the leishmanial character of the organisms and are consistent in appearance with those of *L. tropica major*, they do not permit one to conclude that this specific organism is involved. None the less, much of the evidence accumulated thus far points towards this organism being responsible for the South West African type of cutaneous leishmaniasis. Grové has indicated that identification of *Leishmania* strains isolated from humans, hyraxes and sandflies in South West Africa is under way.

Although we have not demonstrated organisms within phagosomes of the macrophages, as Sandbank has, the frequency of disintegrated form of *Leishmania* within the cytoplasm of the macrophages, with none occurring extracellularly, leaves us in little doubt that the destruction of the *Leishmania* occurs within macrophages.

This case report of cutaneous leishmaniasis underlines the necessity for clinicians and pathologists within the Republic of South Africa to recognize this entity, should they come in contact with it. Further, the ultrastructural findings show the presence of typical leishmanial amastigotes occurring within macrophages of the lesion, and indicate that destruction of the organisms occurs within these cells.

REFERENCES