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Case Report

The First Case of Basal Cell Carcinoma in the Scar Fifty Years After Leishmanization

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Abstract
Cutaneous leishmaniasis (CL) is a self-curing skin infection distributed in tropics and subtropics. Up to one million cases of CL appeared in endemic areas a year. Leishmanization (artificially controlled infections) was widely used to control cutaneous leishmaniasis in the past. Basal cell carcinoma (BCC) is the most common epithelial neoplasm of the skin. Cases of BCC developing in a leishmanial scar have been documented. We present the first case of confirmed basal cell carcinoma arising in 2020 in an 81-old physician working in Moscow (Russian Federation) in a leishmanial scar. It was 50 years after the primary lesion due to a successful leishmanization, widely used to control cutaneous leishmaniasis in the past.

Introduction

Leishmaniasis is a neglected disease caused by protozoan parasites of the genus *Leishmania*. The most common form of leishmaniasis is cutaneous leishmaniasis (CL), which is estimated to affect 600,000 to 1 million new cases worldwide, annually (1). Since antiquity, individuals who had healed their skin lesions of CL were highly resistant to secondary infections. Since the beginning of the 20th century, Russian scientist E.I. Martsinovsky has used artificial inoculations of live *Leishmania* for vaccination against the disease (2). Live organisms started to be used for vaccination (or, to be precise, for controlled infections or leishmanization) for prophylaxis of

CL (3). There were 50000 leishmanizations performed in the Soviet Union, 15000 in Israel, and over 2 million in Iran (4). The use of live vaccines has had some problems, including the development of large uncontrolled skin lesions, exacerbation of psoriasis and other skin diseases, and even immunosuppression. Some individuals in Iran developed non-healing lesions, hard to resolve with chemotherapy. Although this complication was very rare, WHO did not recommend performing leishmanization as a control measure against CL (5)s.

Natural CL infections sometimes had resulted in retarded complications. Humans with healed *Leishmania* cutaneous infection maintain robust cell-mediated immunity and are T helper 1 (Th1) $CD4^+$T cells are particularly important to naturally acquired immunity by releasing IFN-γ that activates infected macrophages to kill the parasite (6). While Th1 immunity results in recovery from CL, there is no sterile cure and parasites never disappear completely, since, in situations where the immune system was compromised, *Leishmania* can suddenly reappear (6).

The prolonged presence or periodical reappearance of *Leishmania* in the place of healed lesions may be a predisposition to epithelial malignant neoplasms at the site of post leishmanial scars. Usually, CL became a risk factor for basal cell carcinoma (BCC). Several BCC cases after CL had been described in Egypt (7), Saudi Arabia (8), Turkey (9), and other Middle East countries (10). An association BCC with a scar after leishmanization was not documented before.

Here we report the first case of confirmed BCC arising in a leishmanial scar, fifty years after the primary lesion due to a successful leishmanization.

Case presentation

Dr. K., an eighty-one-year-old physician has been leishmanized at the age of 29 in Martsinovsky Institute of Medical Parasitology and Tropical Medicine (Moscow) before a departure to Turkmenia – a highly endemic territory for CL (the risk of contracting the disease for newcomers more than 50%).

The consent of the patient participating in the study was taken. A typical lesion had appeared at the site of inoculation of live virulent *Leishmania.* A scar approximately 2.5 cm in diameter had been formed at the site of the lesion after seven months. There were no local activities in the Leishmanization scar during the next 15 years.

Later on, small recurrent ulceration appeared in the leishmanial scar. The lesion was painless, self-curing with spontaneous epithelialization, and reappeared several times. Periods of ulceration became more prolonged with time, and periods without erosion shorter.

The patient had two surgical operations due to a peptic ulcer and a papillary malignant tumor of the thyroid gland during the period after the leishmanization. The latter surgery had followed by X-ray therapy. He also has received prostate brachytherapy in 2012.

During the last four years, the indurated skin ulcer with elevated borders persists permanently varying in size from 2 to 3 cm. Surrounding inflammations, regional lymphadenopathies, and general symptoms were absent. The use of antibiotics and antiseptics was inefficient.

BCC was suspected and a standard wide surgical full-thickness excision within healthy tissue limits had been performed in 2019. The patient has recovered completely.

The histopathology was that of a BCC. The microscopic examination has been shown basaloid cells with scant cytoplasm and elongated hyperchromatic nuclei, peripheral palisading with necrotic nests, peritumoral clefting, and mucinous alteration of surrounding stroma (Fig. 1).

Discussion

BCC is the most common malignancy of the skin (11). The occurrence of malignant neoplasms in sites of scars is an infrequent but well-known phenomenon (12). Cases of BCC developing in a leishmanial scar have also been documented (8). Although the coexistence of cutaneous leishmaniasis and BCC may have been coincidental, some studies suggest that an association between these two entities does exist (9). The pathogenesis of BCC is associated with intense and intermittent UV radiation exposure (13).

Our patient holds several of the classical identifiable traits placing him at higher risk of BCC – male gender, upper-middle-age, history of malignancies, previous X-ray radiation, and leishmanization with the leishmanial scar on the site of BCC tumor. In terms of surgical treatment, wide local excision allowed for a successful outcome.

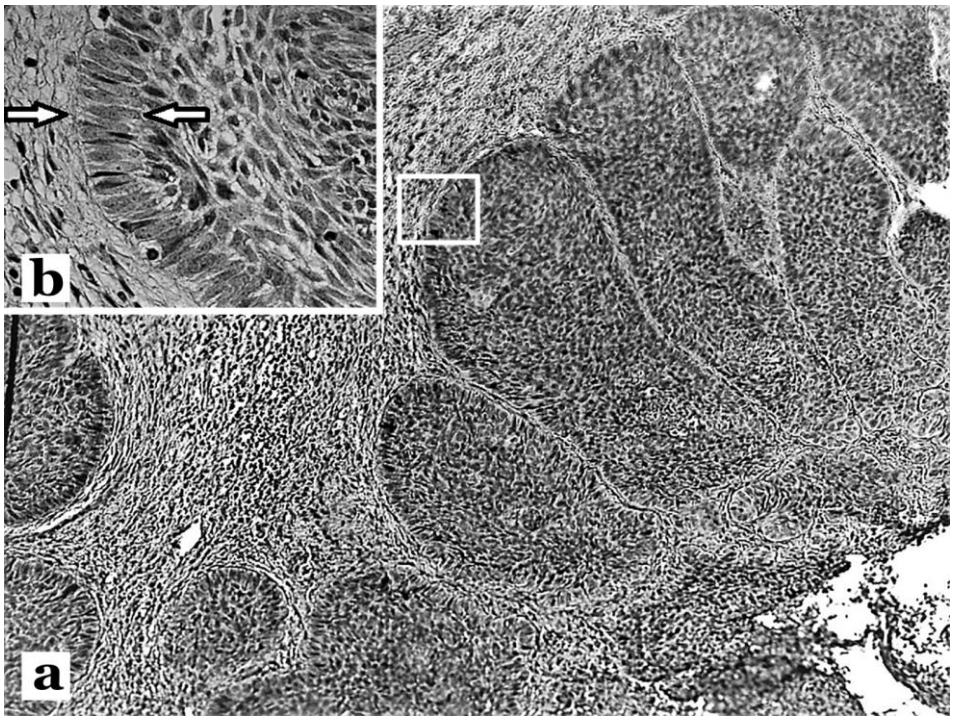

Fig. 1: (a) Hematoxylin and eosin-stained section of infiltrative basal cell carcinoma grows into the reticular layer of the dermis without invading the subcutaneous tissue (×100 magnification); (b) higher magnification (×400) shows the prominent peripheral nuclear palisading (arrows)

Conflict of interest

All contributing authors declare no conflict of interest.

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