Caseous necrosis in cutaneous leishmaniasis

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Abstract
A case of late stage cutaneous leishmaniasis with focal caseous necrosis is reported. The patient, a 30 year old Tunisian man, presented with idiopathic bone marrow aplasia. Microscopically, minimal changes were observed in the epidermis: slight hyperkeratosis and moderate acanthosis. Lesions predominated in the dermis. Epi-theloid granulomas were found in the lower dermis. Some of these lesions were clearly surrounded by a ring of lymphocytes and were rarely confluent. A peculiar histological feature was the presence of focal acidophilic and slightly granular necrosis at the centre of some the tubercu-loid lesions. Focal fibrinoid necrosis was found in the upper dermis, outside granulomas. A mild to moderate infiltrate of histiocytes, lymphocytes and plasma cells, with scanty neutrophils, was observed mainly in the upper dermis. No intracellular or extracellular Leishman–Donovan bodies were observed. Acid fast mycobacteria, however, were not detected. Leishmaniasis was diagnosed on culture of skin biopsy specimens. The presence of caseous necrosis could lead to diagnostic confusion and result in an erroneous diagnosis of, for example, tuberculosis, syphilis, acne agrimata, and sarcoidosis with fibrinoid necrosis. This is especially the case when parasites are scanty or absent.

Keywords: cutaneous leishmaniasis, caseous necrosis, pathology.

Cutaneous leishmaniasis, caused by infection with a flagellate protozoon, is endemic in the Mediterranean region. The disease can occur in one of four clinical forms: acute leishmaniasis, chronic leishmaniasis, leishmaniasis recidivans, and diffuse cutaneous leishmaniasis. Ninety per cent of cases of acute cutaneous leishmaniasis resolve without treatment, healing with scar formation. The remaining cases generally evolve into chronic disease.
Acute and chronic leishmaniases can manifest clinically as papular, nodular, plaque-like, or most commonly, ulcerated lesions, usually located on skin exposed to the sun. On histological examination, acute leishmaniasis generally appears as macrophage lysis in the centre of macrophagic granulomas, which are usually associated with numerous lymphocytes and plasma cells. Chronic leishmaniasis—that is, late stage leishmaniasis, has been well characterised histologically and commonly presents as tuberculoid lesions without necrosis. However, there is no fundamental distinction between the tuberculoid lesions of chronic cutaneous leishmaniasis and the later stages of its acute counterpart.

Case report
A 30 year old Tunisian man was referred to our institution for treatment of idiopathic bone marrow aplasia. Physical examination disclosed multiple and confluent cutaneous lesions on the patient's left elbow and back (fig 1). The lesions had been spreading for several months, and were crusted and surrounded by gradually spreading erythema and induration. A diagnosis of cutaneous mycobacteria infection was proposed on the basis of skin biopsy findings and antituberculous treatment was started. A few weeks later, culture of the biopsy specimen yielded promastigote forms of leishmania. Bone marrow aspiration and duodenal biopsy were done. Culture remained negative for leishmaniasis. Skin tissue culture was negative after treatment with amphotericin B, despite the presence of iatrogenic immunodepression. Serological tests were negative for leishmania.

Pathological findings
The skin biopsy specimens were fixed in Bouin's liquid and embedded in paraffin wax. Serial sections, 3–4 μm thick, were stained with haematoxylin–safranin, periodic acid-Schiff (PAS) reagent, Ziehl–Neelsen, Giemsa, and Gomori-Grocott stains. Minimal changes were observed in the epidermis on microscopic examination—that is, slight hyperkeratosis and moderate acanthosis. Lesions predominated in the dermis. Epithelioid granulomas were found mainly in the lower dermis. Some of these lesions were clearly surrounded by a ring of lymphocytes and were rarely confluent. A peculiar histological feature was the presence of focal acidophilic and slightly granular necrosis at the centre of some tuberculoid lesions (fig 2). Focal fibrinoid necrosis was found in the upper dermis, outside granulomas. A mild to moderate infiltrate of histiocytes, lymphocytes and plasma cells, with scanty neutrophils, was observed mainly in the upper dermis. No intracellular or extracellular Leishman–Donovan bodies were seen on haematoxylin–eosin–safranin, and Giemsa stained sections. No acid fast mycobacteria were observed on Ziehl–Neelsen stained sections. No refringent material was detected under polarised light. Microorganisms were not seen in sections stained with PAS and Gomori-Grocott.

Parasitological findings
Skin biopsy specimens were submitted for parasitological, bacterial, fungal, and mycobacterial culture.

Cultures on NNN (Novy–MacNeal–Nicolle) medium yielded promastigote forms of leishmania. They were characterised by the electrophoretic analysis of 15 different enzymes. In this patient cutaneous leishmaniasis was caused by infection with Leishmania major, zymodeme MON 25 (MHOM/93/CRE32), which is the usual strain encountered in Tunisia. Cultures for mycobacteria, atypical mycobacteria and fungi were all negative.

Discussion
This present case of late stage cutaneous leishmaniasis is unusual because of the presence of focal caseous necrosis associated with tuberculoid lesions in the lower dermis. The histopathology of cutaneous leishmaniasis has been described extensively and the later stages of acute leishmaniasis and the chronic form of the disease are usually characterised by tuberculoid infiltrates in the dermis. To our knowledge, caseous necrosis has not been described previously in the skin, but has been reported previously in lymph nodes. Septic necrosis has been observed in skin biopsy specimens and attributed to the presence of concomitant infection with Vincent's organisms, Streptococcus viridans, other saprophytic streptococci, or Candida albicans. Bacterial, mycobacterial and fungal cultures were negative in the present case. However, fibrinoid necrosis, which is visually different from caseous necrosis, is common in acute leishmaniasis but less so in the chronic form.

The development of tuberculoid lesions seems to be caused by expansion of a T cell subset producing interleukins 3 and 4 and...
granulocyte macrophage colony stimulating factor.\textsuperscript{16,17} The explanation for the occurrence of caseous necrosis is not clear and we did not find any other aetiological agent that could be responsible for it. Caseous necrosis may have resulted from an imbalance in the immune system of this patient, who presented with a bone marrow aplasia with leucopenia.

The presence of focal caseous necrosis in late stage acute leishmaniasis, in which parasites are scanty or absent,\textsuperscript{8} can lead to difficulties in diagnosis. Tuberculosis,\textsuperscript{20} presenting as the lupus vulgaris or the subcutaneous gumma form with spread into the upper dermis, is the main differential diagnosis. Syphilis at the late secondary stage should also be considered, as well as acne agminata and sarcoidosis with fibrinoid necrosis.\textsuperscript{20} In addition, patients may not have generated antibodies directed against either amastigote or promastigote antigens.\textsuperscript{3} As cutaneous leishmaniasis is being encountered more often because of international travel and the influx of immigrants from areas of the world where this parasite is endemic, expedient diagnosis of this condition may be hampered by the presence of caseous necrosis in skin biopsy specimens.


Carcinosarcoma arising in a dermoid cyst of the ovary

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Abstract

A case of carcinosarcoma arising within an otherwise benign cystic teratoma is reported. The patient, a 78 year old nulliparous woman, presented with right sided abdominal pain of short duration and subsequently underwent a bilateral salpingo-oophorectomy. Slicing of the left ovary revealed a unicocular cyst containing hair admixed with soft yellow material with a thin wall apart from a solid area at one pole. Extensive areas of necrosis and cystic degeneration were present within this mass. Histologically, the large cyst was a typical mature cystic teratoma, containing carcinomatous and sarcomatous elements. Mature cystic teratomas have been reported in association with a variety of malignant ovarian tumours such as mucinous cystadenocarcinoma and malignant germ cell neoplasms. Secondary malignant transformation within a dermoid cyst is a much rarer occurrence, estimated as less than 2% of such lesions. Adenocarcinomas are the second most common malignancies arising within dermoid cysts. Sarcomas alone or in combination with squamous carcinoma have been described arising in a mature cystic teratoma. To the best of our knowledge, no case of sarcoma arising in association with adenocarcinoma has been described before. \(\text{J Clin Pathol} 1996;49:519-521\)

Keywords: ovary, dermoid cyst, carcinosarcoma.

Malignant transformation within a mature cystic teratoma (dermoid cyst) occurs in less than