Cutaneous Leishmaniasis in Gozo

Peter Muscat
Medical Officer, Gozo General Hospital

ABSTRACT

Cutaneous Leishmaniasis is caused by a vector borne protozoan parasite known to be endemic in Malta and Gozo. The disease normally produces skin ulcers on the exposed parts of the body such as the face, arms and legs. It is often underdiagnosed and presentation to the doctor tends to be late. If left untreated it may leave the patient permanently scarred, a stigma which can cause serious social prejudice.

There were 68 (49%) cases of cutaneous Leishmaniasis in Gozo as compared to 71 cases in Malta notified between 1983 to December 1998. It is thought that a substantial number of cases are never recorded. 82% of the cases notified in Gozo originated from only 3 villages, namely Nadur, Ghajnsielem and Qala with decreasing order of incidence.

The disease is equally distributed among sexes (50% in both males and females). It is primarily a disease of the young with 59% of cases being under 10 years of age when diagnosed.

INTRODUCTION

Leishmania parasites get their name from W.B. Leishman who developed in 1901 one of the earliest stains specific for this type of parasite. They are widespread in the New World and Old World (but not in S.E. Asia), and human infections are still found in many parts of Europe such as Malta, Spain, Portugal, Southern Italy, France, Greece, Turkey and Southern USSR.

For many years it was not realized just how serious leishmaniasis was. Over the last ten years endemic regions have been spreading further afield and there has been a sharp increase in the number of recorded cases of the disease. 2 million new cases of leishmaniasis (both cutaneous and visceral) are estimated to occur worldwide annually, only 600,000 are officially declared. Presently, declaration is obligatory in only 32 of the 88 countries affected worldwide (Bresson, 1995).

Notification of cases of leishmaniasis was made compulsory in Malta in 1946.

Spread of Infection

Most forms of leishmaniasis are originally infections of small mammals (known as reservoir hosts) which play a major role in the epidemiology of this disease. The disease is spread when the female sandfly of the genus *Phlebotomus* ingests amastigotes while taking a blood meal from an infected reservoir host or from human beings. These transform into promastigotes within the insect's gut, migrate to the salivary glands and are deposited on the skin of the new host when the insect next engorges and the transmission cycle is complete.

The female sandfly

Phlebotomus perniciosus is believed to be the only one species of sandfly to transmit the infection in the Maltese islands. In a sandfly survey that was carried out on Gozo in 1988, it was found that this species, a known vector of visceral leishmaniases (VL) and cutaneous leishmaniases (CL) accounted for 94% of the 3181 flies of the genus *Phlebotomus* that were caught (Leger *et al*, 1991).

External morphology

Adult phlebotomine sandflies can be recognised by their minute size (1.3 - 3.5 mm in length) sand-coloured hairy, appearance, relatively large black eyes and their relatively long and stilt-like legs. The antennae are long and composed of small head-like segments with short hairs. Wings are lanceolate in outline. The abdomen is moderately long and in the female rounded at the tip. In males it terminates in a prominent pair of claspers.

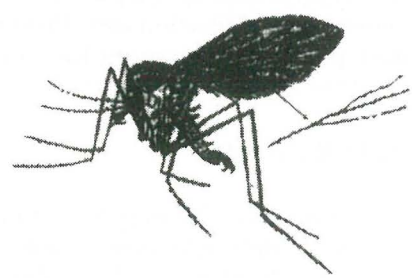

Figure 1. Adult male phlebotomine sandfly and diagrammatic representation of double branching of wing vein.

Adult behaviour

Both sexes feed on plant juices but females in addition suck blood from a variety of vertebrates, including livestock, dogs, urban and wild rodents, snakes and amphibians.

Biting is usually restricted to crepuscular and nocturnal periods but man may be bitten during the day in darkened rooms or in forests during overcast days. Adults are weak fliers and do not usually disperse more than a few hundred meters from their breeding places. Consequently biting may be localised to a few meters. Because of their very short mouthparts they are unable to bite through clothing.

During the day adult sandflies rest in sheltered, dark and humid sites such as tree trunks, on ground litter and foliage of forests, caves, rubble walls, cracks in ground and inside human and animal habitations.

The Parasites

In the Maltese islands, Leishmania infantum is the only known cause of the human visceral leishmaniases and cutaneous leishmaniases and of canine infection (Fenech, 1997). As part of a general survey on leishmaniases and sandflies of the Maltese islands, 22 leishmania stocks were isolated from infected islanders, dogs and sandflies (Gradoni et al, 1991). They were characterized by the analysis of 15 enzymes.

The isolation of Leishmania infantum zymodeme MON-1 from 3 specimens of P. perniciosus suggests that this sandfly species is the principal and perhaps the sole vector of human leishmaniasis in the Maltese islands (Gradoni et al, 1991).

The Reservoir Host

It is thought that the domestic dog is the only known reservoir of infection in Malta. There is no evidence that other mammals such as rats are involved (Fenech, 1997). As early as 1911, Critien demonstrated leishmania in the spleen of 53 Maltese stray dogs. In a door to door survey of dogs residing in 5 villages in Gozo, prevalence of canine leishmaniasis was estimated at 18.5% (Amato Gauci, 1992).

In Easter 1985 Killick-Kendrick et al carried out a survey on canine leishmaniasis in Gozo. The point prevalence of the disease in dogs was estimated at 21% (DH File 256/94). Leishmaniasis in domestic dogs is still diagnosed quite regularly by veterinary surgeons.

Clinical presentation

Dogs may be completely asymptomatic but have positive blood serology. Sometimes dogs may have one or more clinical symptoms as shown in the figure below. Treatment of dogs is not very satisfactory, relapse being common. Responsiveness to treatment varies according to the clinical condition of the infected dogs. In a study done by Mancianti et al (1988), 81 dogs naturally infected with Leishmania infantum in the Isle of Elba, Italy, were treated with meglumine antimonate (glucantime). The recovery rates were 47.2% for asymptomatic cases, 33.3% for oligosymptomatic cases and only 11.1% for symptomatic cases. Figure 2 below shows the variable clinical presentations by dogs infected with leishmania parasites.

- *Completely asymptomatic*
- *Crusted sores which bleed*
- *Generalized hair loss with remaining hair becoming stiff and crusty*
- *Flaking of the skin at the tips of the ears*
- *'Lunettes' (skin around the eyes is bare of hair)*
- *Nails grow long extremely rapidly and curl under*
- *Lymphadenopathy especially prescapular (in front of the point of the shoulder) and submaxillary*
- *Ulcers that may break out especially on the paws and legs*
- *Emaciation, poor appetite and weight loss*
- *Anaemia*
- *Vesicles (blisters) on the inside of the ears.*

Figure 2. Clinical presentation of dogs infested with leishmaniasis.

Incidence of Cutaneous Leishmaniasis

There were 139 cases of cutaneous leishmaniasis recorded in the Maltese islands between 1983 and December 1998. (Infectious Disease Register, 1997., Disease Surveillance Branch, 1998). Of these, 68 (49%) of cases originated from Gozo as compared to 71 cases in Malta. It is thought that a substantial number of cases are never recorded. Of the cases notified from Gozo, 82% originated from only 3 villages, namely Nadur, Ghajnsielem and Qala with decreasing order of incidence.

The largest annual number of recorded cases of cutaneous leishmaniasis in Gozo alone was in 1998 when 13 cases were notified, while that for Malta were in 1990 and 1998 where 13 cases each year were notified. The largest annual number of notified cases in the Maltese islands combined was in 1998 when 26 cases were reported (figure 3).

Cutaneous leishmaniasis is primarily a disease of the young, the vast majority of patients being children 2 to 6 years of age when diagnosed (figure 4). The age at presentation of patients varied from 5 months to 66 years. The disease is equally distributed among sexes (50% in both males and females).

Clinical presentation and Diagnosis

The lesion begins as a single,

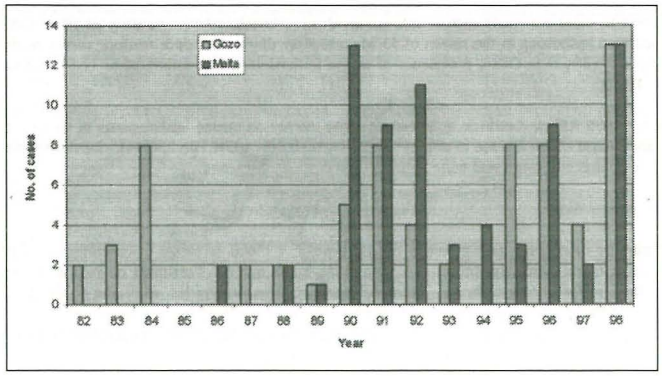

Figure 3. Annual incidence of cutaneous leishmaniasis in Malta and Gozo during the period 1982-December 1998.

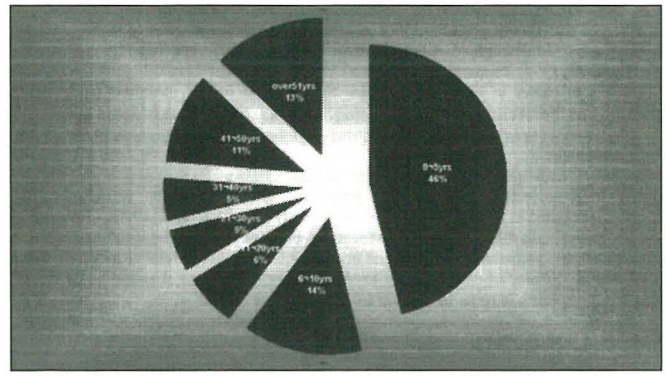

Figure 4. Age distribution of cases of cutaneous leishmaniasis in Gozo during the period 1983 - December 1998.

red, pruritic, crusted module (papule) on exposed parts, usually the face. The central area ulcerates and slowly enlarges centrifugally. Lymphadenopathy is unusual. Occasionally lesions are multiple. Diagnosis is made by demonstrating the protozoa in scrapings from the base of the lesion or in biopsy material.

Presentation to the doctor

The delay in seeking medical advice of Gozitan patients varied from 2 months to 9 months. The mode duration of delay was 4 months. Delay in seeking medical advice is common in Gozo which is more rural than its sister island, Malta.

Outcome of lesions

Therapy is indicated to minimize superinfection and scarring. Regimens constituting various physical therapies and chemotherapies have been used. Untreated lesions can last for 12 to 18 months prior to spontaneous resolution (Pace, 1982 & Hood, 1992).

Chemotherapies include pentavalent antimonials, rifampicin, dapsone, ketokonazole (Scott *et al*, 1992) and sometimes the antibiotic amphotericin B (Locksley R,1994).

In the Maltese Islands, cryotherapy is the treatment of choice for the vast majority of cutaneous leishmaniasis patients.

Immunity

There is evidence that spontaneous resolution of cutaneous leishmaniasis due to some *Leishmania* strains is associated with acquisition of protective immunity against the infecting strain (Pearson et al, 1990; Benenson, 1990). In many parts of the Middle East, infections are deliberately encouraged on the buttocks of babies in order to immunize them against further infections (thus avoiding disfiguring scars on the face).

Vaccine development

People have been successfully immunized in Israel and the Soviet Union with live L major promastigotes inoculated at inconspicuous sites on the body (Pearson *et al*, 1990). Although this approach has been successful, it has been discontinued because some of the resulting lesions heal slowly, others become secondarily infected, and even after healing, live parasites may persist at the site of inoculation. Efforts are now ongoing to identify specific leishmanial antigens that can elicit protective T cell responses in order to develop a defined vaccine (*ibid*).

1st Documented case of cutaneous leishmaniasis in Gozo.

Until 1981, cutaneous leishmaniases was unheard of in the Maltese population apart from the occasional case of post-Kala azar dermal leishmaniasis. Furthermore, cutaneous leishmaniases had never been reported in the numerous British Service Personnel stationed on the islands up until 1979 (Vella Briffa, 1985).

In 1981, Dr Simon Bor presented to the fellows of the St John's Hospital Dermatological Society a woman from Essex who had contracted primary cutaneous leishmaniasis during a holiday in Gozo. This prompted Dr D. Vella Briffa, consultant dermatologist at Boffa Hospital to investigate the problem of cutaneous leishmaniasis. Between February 1982 and February 1985 he diagnosed 13 cases of primary cutaneous leishmaniasis. All the patients resided in one relatively small coastal area of Gozo namely Qala, Nadur and Ghajnsielem, whereas the majority of visceral leishmaniases patients came from Malta (Vella Briffa, 1985).

1st Documented case of cutaneous leishmaniasis caused by L. donovani infantum

In March 1985, a 71-year-old English gentleman was referred to the Cambridge Military Hospital with several inflamed, granulomatous lesions on his face (Jolliffe *et al*, 1986). The lesions had first appeared in December 1984 following a holiday in Malta in September of that same year. In the 10 years

prior to his referral this patient had not visited any other leishmanial endemic area. A Montenegro skin test was positive and histological exam of tissue taken from the edge of one of the lesions revealed an intradermal granulomatous infitrate, with intracellular amastigotes identified in Giemsa stained sections. Culture of part of the biopsy specimen in biphasic Evans - modified Tobie's medium was successful and isoenzyme typing has shown the infecting organism to be *L. donovani infantum* London zymodeme 49 (Jolliffe *et al*, 1986).

Methods of control

In general control measures vary from area to area, depending on the habits of the vector phlebotomines and vertebrate hosts. Where their habits are known, applicable control measures may be carried out (Benenson, 1990). These include;

1. Systematic case detection and rapid treatment applies to all forms of leishmaniasis (both cutaneous and visceral) as one of the important preventive measures.

2. Avoid sandfly-infested areas, particularly after sundown, use protective clothing if exposure to sandflies is unavoidable as well as to install fine-mesh sandfly window nets.

3. Repellant skin lotion, should be applied to exposed skin and up to 3 inches covered by uniform.

4. Destroy animals implicated locally as reservoirs.

5. Eliminate rubbish heaps and other breeding places for sandflies.

6. Sandflies have a short flight range and are highly susceptible to control by periodic spraying of insecticides with residual action. Spraying should cover exterior and interior of doorways and other openings in dwellings.

7. Educate the public concerning modes of transmission and methods of controlling sandflies.

Cases of Leishmaniasis should be reported to the Disease Surveillance Branch of the Department of Public Health where they are registered and referred to the Medical Officers of Public Health (MOH) for investigation. The Medical Officer of Public Health contacts the patient and with the aid of a structured questionnaire attempts to identify the source of infection, determine the local transmission cycle and interrupt it.

Notification of cases by doctors, apart from being a legal obligation under the Medical and Kindred Professions Ordinance (Chapter 31) and Prevention of Diseases Ordinance (Chapter 36), is the key to useful preventive action in the interests of the whole community.

Conclusion

There is clear association between the prevalences of the infection in dogs and man (Marty et al, 1992). The Maltese Islands being relatively small islands, effective control of leishmaniasis should be possible by the early diagnosis and treatment of infection in local dogs, the only known reservoir hosts (Fenech, 1997). The introduction of legislation to have compulsory dog registration in Malta is long awaited. Once this is introduced it will be possible to screen most if not all dogs and thus help in the eradication of this disease in the Maltese Islands.

REFERENCES

1. Amato Gauci AJ (1990) 'The control of Leishmaniasis in the Maltese Islands' MFPHM Dissertation, Malta.

2. Benenson AS (1990) 'Leishmaniasis' In: Control of Communicable diseases in man APHA pg. 206-8

3. Breasson A (1995) Disease sheet: Leishmaniasis-Data sheet. WHO.
WHO homepage; bresson @ hei.unige.ch

4. Cap 31 & Cap 36 of the Laws of Malta

5. DH File 256/84 'Leishmaniasis in Gozo'

6. Disease Suruveillance Branch (1998) Dept of Public Health, Malta

7. Hood AF (1992) 'Dermal Plaques on the Face of a child' Archives of Dermatology Vol 128(A), 680

8. Fenech FF (1997) 'Leishmaniasis in Malta and the Mediterranean Basin' Annals of Tropical Medicine & Parasitology Vol. 91, No.7, 747-753

9. Gradoni L, Gramiccia M, Leger N, Person B, Madulo-Leblond G, Killick-Kendrick R, Killick-Kendrick M, Walton BC (1991) 'Isoenzyme characterization of Leishmania from man, dog and sandflies in the Maltese islands' Transactions of the Royal Society of Tropical Medicine & Hygiene 85, 217-219

10. Infectious Disease Register (1997) Dept of Health Information, Malta

11. Jolliffe DS, Evans DA, Bryceson ADM (1986) 'Cutaneous Leishmaniasis' Brittish J of Dermatology 114, 745-749

12. Leger N, Marchais R, Madulo-Leblond G, Person B, 13. 13. Kristensen A, FErte H, Killick-Kendrick RR & Killick-Kendrick M (1991) 'Les phlebotomes impliques dans la transmission des leishmanioses dans l'ile de Gozo (Malte)' Annals de Parasitologie Humaine et Camparee 66, 33-41

14. Locksley RM (1994) 'Leishmaniasis' In: Harrison's Principles of Internal Medicine. International edition Mc Graw-Hill Inc Vol 11, 896-9

15. Mancianti F, Gramiccia M, Gradoni L, Pieri S (1988) 'Studies on canine Leishmaniasis control 1 Evolution of infection of different clinical forms of canine Leishmaniasis following antimonial treatment' Transactions of the Royal Society of Tropical Medicine and Hygiene 82, 566-567

16. Pace JL (1982) 'Cutaneous Leishmaniasis' Archives of Dermatology Vol 118, 880

17. Pearson, Navin, Sousa, Evans (1990) 'Leishmaniasis' In: Kass H, Platt R (eds) Current Therapy in Infectious Disease-3, Decker Inc Toronto

18. Vella Briffa D (1985) 'Cutaneous Leishmaniasis in the Maltese islands' Brittish Journal of Dermatology, 113, 370-371