MMJ

Malta Medical Journal, 33 (1): Pages (2021)
http://mmsjournals.org/index.php/mmj

CASE REPORT

Leprosy in Malta: not to be forgotten

Monique Cachia, Alicia Dimech, Alexandra Betts, Charles Mallia Azzopardi, Michael J Boffa

Leprosy is a granulomatous infection that was considered endemic in Malta up until being declared eradicated in 1999 thanks to the Malta Leprosy Eradication Programme. However, leprosy remains endemic in a number of low-to-middle income countries, and may be imported to non-endemic regions like Malta by migrants. We report a case of a man from the Philippines presenting with nodular lesions over the face, trunk and limbs and a hypoaesthetic patch over the arm. A skin biopsy supported the clinical suspicion of midline borderline/borderline lepromatous leprosy and triple therapy with clofazimine, dapsone and rifampicin was initiated. Despite having a wide clinical differential diagnosis, leprosy must always be kept in mind by clinicians, especially when treating nationals from endemic areas.

Monique Cachia* MD, MRCP(UK) (Derm)
Department of Dermatology
Mater Dei Hospital
Msida, Malta
monique.camilleri@gov.mt

Alicia Dimech MD, MRCEM, MRCP(UK), PgDip Derm (South Wales)
Department of Dermatology
Mater Dei Hospital
Msida, Malta

Alexandra Betts B.Ch.D., M. Phil, FRCPath
Department of Pathology
Mater Dei Hospital
Msida, Malta

Charles Mallia Azzopardi MD, FRCP(Lond.), DTM&H(Lond.)
Department of Medicine (Infectious Disease)
Mater Dei Hospital
Msida, Malta

Michael J Boffa MD, FRCP, Msc
Department of Dermatology
Mater Dei Hospital
Msida, Malta

*Corresponding author

Introduction

Leprosy is a chronic, progressive, granulomatous infection caused by *Mycobacterium leprae*. In Malta, this disease was once endemic but after the Leprosy Eradication Programme which started in 1972, no endemic cases have been reported since its termination in 1999.[1] However, in countries where the disease is still endemic the incidence remains relatively stable, possibly since many cases go unrecognised and therefore undiagnosed.[2] In view of its long incubation period, travelers from endemic countries may develop symptoms after migration. We present a case of a man from the Philippines residing in Malta, diagnosed with midline borderline/ borderline lepromatous leprosy.

Case Presentation

A 29-year-old man from the Philippines presented with a 4-year history of an enlarging erythematous patch over the outer aspect of the right arm (Figure 1) and a 6-month history of erythematous-to-brown nodular lesions over the face, trunk and limbs (Figures 2A and 2B). He reported numbness and reduced sweating over the right arm patch but all other lesions were asymptomatic. He was previously healthy, had moved to Malta from the Philippines 20 months previously and was residing with his partner who was asymptomatic. On examination there was a 12cm x 12cm annular erythematous patch with a hypopigmented centre on the right arm (Figure 1) The lesion had raised borders with palpable cord-like structures at one end and reduced sensation to cotton wool and pinprick. All other lesions appeared to have normal sensation. Incisional biopsies from the right arm, right cheek and left thigh showed granulomatous inflammation with sheets and nodules of foamy epithelioid histiocytes, lymphocytes and occasional plasma cells extending perineurally (Figures 3A and 3B). A Wade-Fite stain revealed moderate numbers of acid-fast bacilli within the cytoplasm of a minority of the histiocytes (Figure 3C). Based on the clinical and histological findings a diagnosis of tuberculoid/borderline tuberculoid leprosy recently downgrading to borderline lepromatous leprosy was made. Treatment with dapsone 100mg daily, rifampicin 600mg daily and clofazimine 50mg daily was started, for an expected duration of 24 months. A few weeks into treatment a widespread non-itchy, erythematous maculo-papular eruption, consistent with a Type 1 reversal reaction, appeared and was treated with one dose of intramuscular methylprednisolone acetate 80mg. Following improvement of these symptoms the patient decided to return to the Philippines. He was given written confirmation of his diagnosis and was strongly advised to seek medical attention and continue treatment on returning home.

Figure 1 Well-demarcated anaesthetic patch with an erythematous border and central clearing/resolution over the outer aspect of right arm

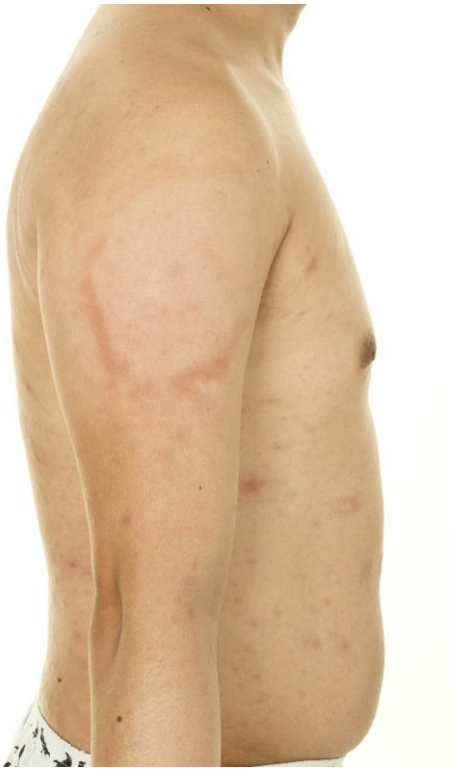


Figure 2A Multiple erythematous-to-brown nodular lesions over trunk (a) and lower limbs (b)

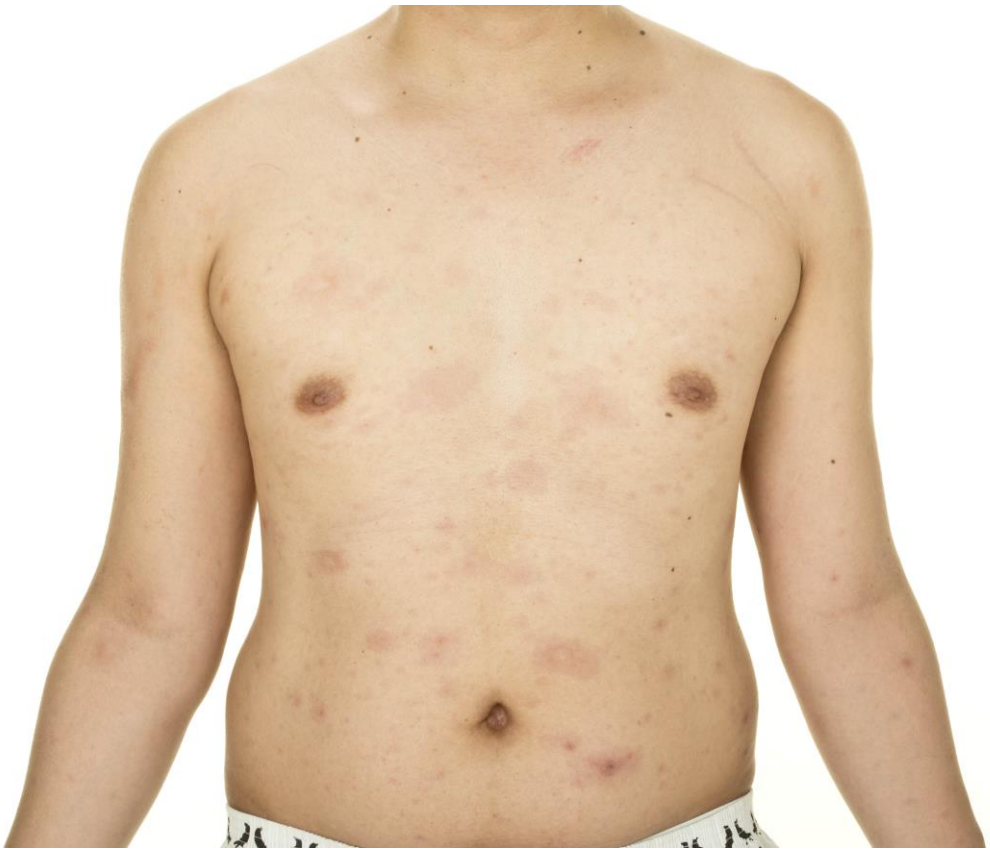


Figure 2A Multiple erythematous-to-brown nodular lesions lower limbs

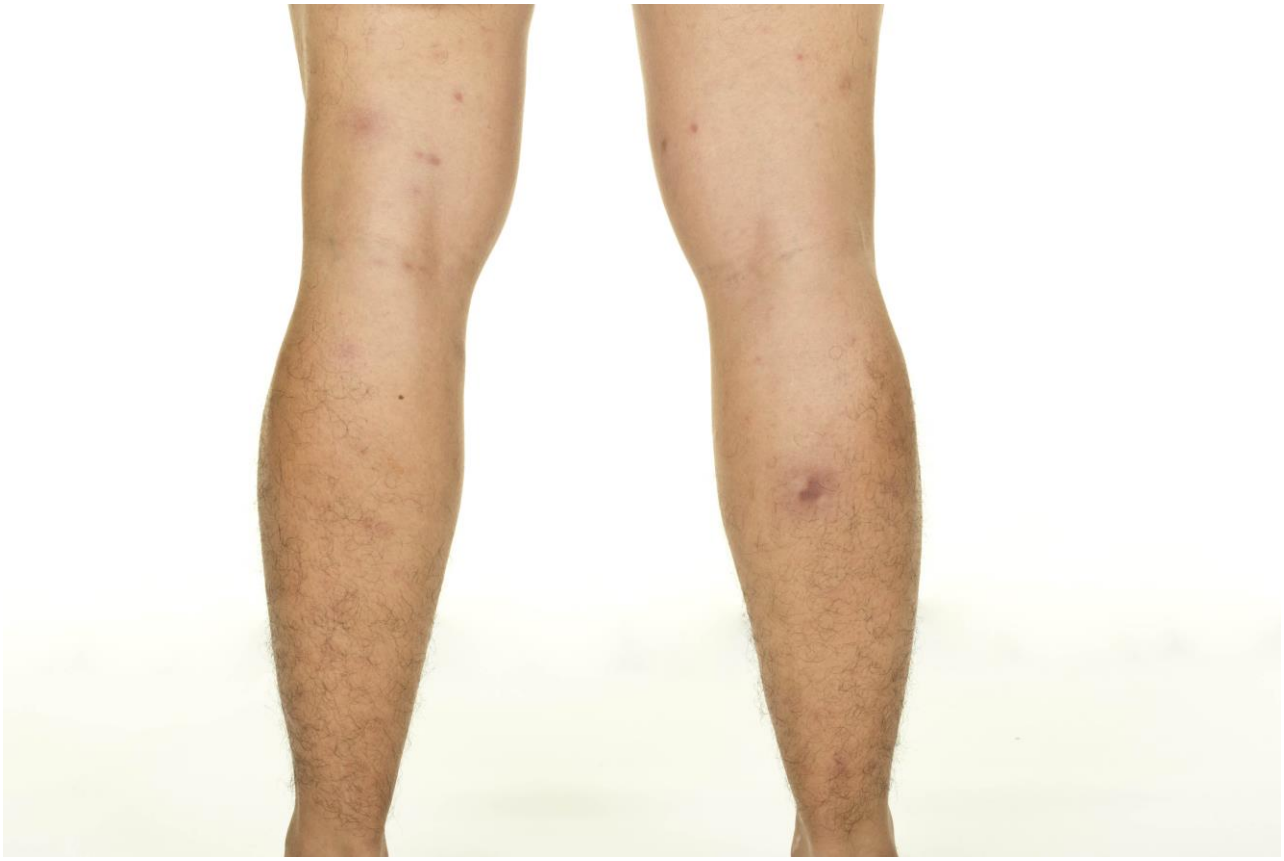


Figure 3A Low power view showing perineural granulomatous inflammation. H&E stain. Original magnification: x100

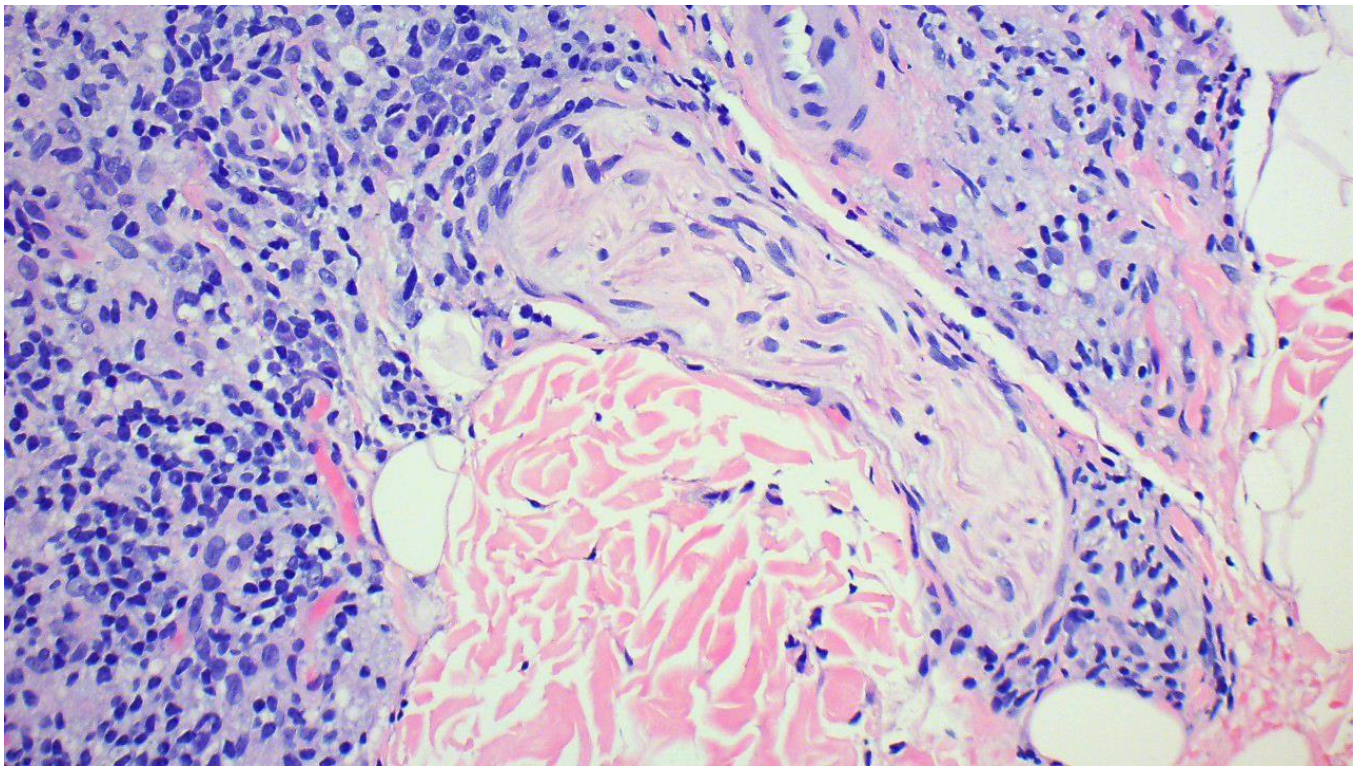


Figure 3B Medium power view showing non-necrotising granulomatous infiltrate composed of sheets of epithelioid histiocytes with abundant foamy cytoplasm and scattered lymphocytes. H&E stain. Original magnification: x200

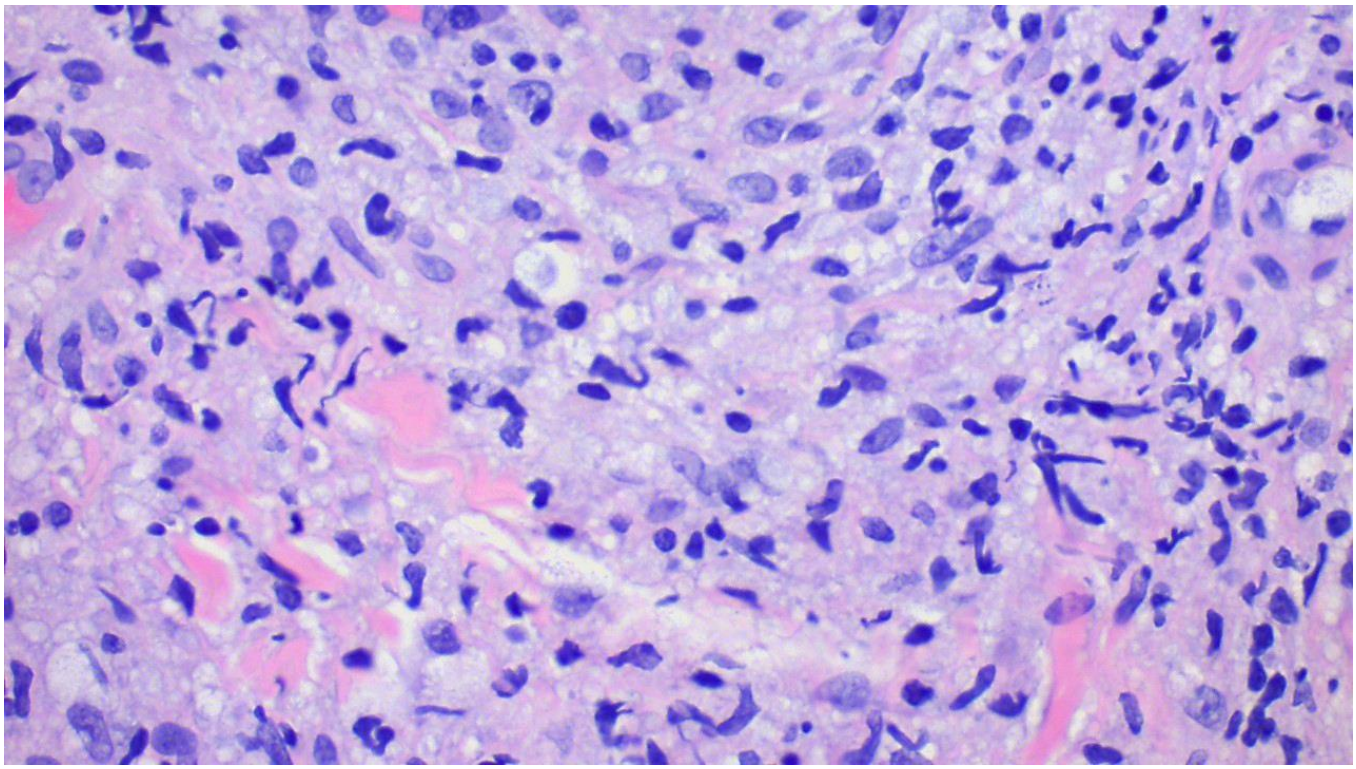
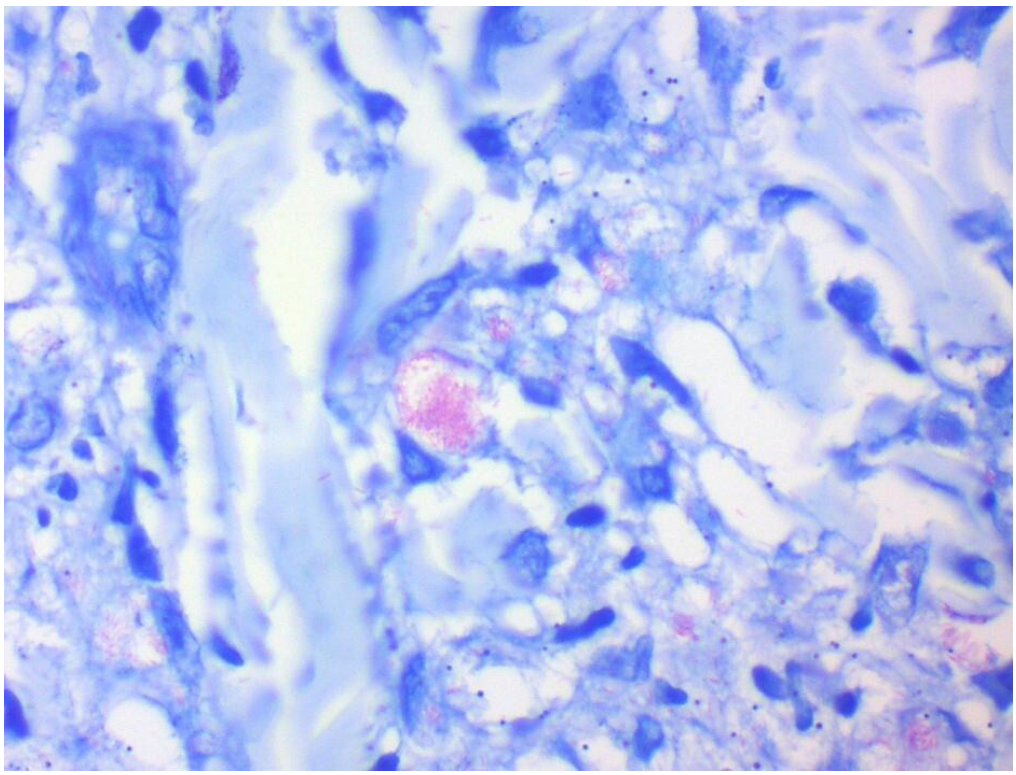


Figure 3C High Power view showing occasional clusters of acid-fast bacilli. Wade-Fite stain. Original magnification: x400



Discussion

Leprosy is a chronic and still-feared infectious disease. Early diagnosis and treatment are essential to help prevent the physical disability and psychological sequalae associated with this disfiguring disease.[3]

The clinical manifestations are varied and can include hypopigmented, erythematous or scaly macules, patches, plaques and nodules. These features depend on the host's cellular immune response to the causative organism and predominantly affect the skin and peripheral nerves. Because of its varied clinical presentation leprosy can mimic several skin conditions including granuloma annulare, tinea corporis, annular psoriasis, lupus erythematosus, cutaneous leishmaniasis and mycosis fungoides. Diagnosis of leprosy may be particularly challenging in pigmented skin and a key distinguishing feature of lesions is impaired sensation.[4]

There are two main classifications of leprosy (Tables 1 and 2).[5-6] The Ridley-Jopling classification categorises leprosy in five groups, based on cutaneous, neurological, histopathological and immunological features.[5] The World Health Organisation (WHO) classification is simpler and is based on the number of skin lesions and bacilli on skin smear.[7]

Table 1 Ridley-Jopling classification.[4,6]

Observation / Test	Ridley-Jopling classification				
	Type of leprosy				
	TT	**BT**	**BB**	**BL**	**LL**
No. of lesions	Single usually	Single or few	Numerous (+)	Numerous (++)	Numerous (+++)
Size of lesions	Variable	Variable	Variable	Variable	Small
Surface of lesions	Very dry, sometimes scaly	Dry	Slightly shiny	Shiny	Shiny
Sensation in lesions (not face)	Absent	Moderately or markedly diminished	Slightly or moderately diminished	Slightly diminished	Not affected or minimally affected
Hair growth in lesions	Absent	Markedly diminished	Moderately diminished	Slightly diminished	Not affected
AFB in lesions	Nil	Nil or scanty	Moderate numbers	Numerous (+)	Numerous with globi (++)
AFB in nasal scraping or in blows	Nil	Nil	Nil	Usually nil	Numerous with globi (++)
Lepromin test	Strongly positive (+++)	Weakly positive (+/++)	Negative	Negative	Negative

AFB: Acid fast bacilli, TT: polar tuberculoid, BT: Borderline tuberculoid, BB: Mid-borderline, BL: Borderline lepromatous, LL: Polar lepromatous

Table 2 WHO Classification.[5]

WHO Classification	
Paucibacillary Leprosy	**Multibacillary Leprosy**
5 or fewer skin lesions without detectable bacilli on skin smear	6 or more skin lesions and may have detectable bacilli on skin smear

Our patient had a single long-standing hypoaesthetic lesion on his right arm suggestive of tuberculoid/borderline tuberculoid leprosy. The new infiltrated lesions on the face, trunk and limbs were in keeping with progression to borderline lepromatous disease, supported by the presence of numerous acid-fast bacilli within the cytoplasm of the histiocytes on histology.

Current recommended treatment of tuberculoid leprosy is dapsone (100mg daily) and rifampicin (600mg daily) for 12 months whilst for patients with leprosy at the lepromatous end of the spectrum dapsone (100mg daily), rifampicin (600mg daily) and clofazimine (50mg daily) for 24 months is recommended.[4] Accordingly, our patient was treated with the latter regimen.

Possible immunologic reactions in leprosy patients include type 1, reversal reaction (RR) and type 2, erythema nodosum leprosum (ENL) and can affect up to half of patients during or after completion of treatment.[4] RR, as seen in this case, manifests as oedema and erythema of existing skin lesions in association with fever, ulceration and nerve involvement. ENL typically presents with acute tender red skin nodules, fever and sometimes multiorgan involvement including neuritis, uveitis, arthritis, orchitis and hepatosplenomegaly. [4]

In 1972, Malta became the first country worldwide to institute a leprosy eradication programme with a multidrug therapy regime. This consisted of 2 tablets of rifampicin 300mg and 2 tablets of isoprodian taken 6 days a week for at least 5 months, depending on the clinical and bacteriological status of the patient. Each isoprodian tablet consisted of 75mg isoniazid, 75mg prothionamide and 50mg dapsone.[1, 8] Prior to this, standard leprosy treatment involved lifelong dapsone monotherapy. In the 5-year period 1967-1971 prior to initiation of this programme the mean annual incidence of new cases of Leprosy was 2.7 cases per 100,000 per year.[9] In the programme all known leprosy patients (irrespective of their bacteriological status) and new patients subsequently diagnosed were treated and subsequently monitored closely for possible relapse.

The success of this programme led to its methodology being implemented by the WHO in the mid-1980s in an attempt to eradicate the disease on a global scale and multidrug therapy has since then become accepted worldwide as the standard treatment for leprosy. The global prevalence of the disease has since diminished drastically from 5.4 million to a few hundred thousand.[10]

Presently the overwhelming majority of leprosy cases are in the developing countries of Southeast Asia, South America, Africa, Western Pacific and the Eastern Mediterranean.[10] According to the WHO global leprosy update (2019), South-East Asia region (SEAR) has contributed to 71% of the new leprosy cases worldwide.[11] Migration, however, can result in patients with leprosy presenting anywhere. In the past few years Malta has seen an increasing influx of migrants and workers from countries where leprosy is endemic. For example the number of migrants residing in Malta, originating from SEAR countries such as the Philippines and India has increased by fourfold and ninefold respectively between 2014 and 2018.[12]

Whereas the Malta Leprosy Eradication Project was formally concluded in December 1999 and Public Health Department records show no new cases of leprosy diagnosed in the indigenous Maltese population from the year 2000, new cases have been diagnosed in migrants in 2008, 2011 and 2019 (the current case).[13-14]

Thus, physicians must be aware of the increasing possibility of encountering leprosy, and the potential for leprosy to mimic a number of conditions. Moreover, although infectivity of leprosy is considered to be low, it is higher in patients at the lepromatous end of the spectrum and thus it is important that patients are diagnosed and treated as soon as possible.

Conclusion

This case highlights the importance for clinicians in Malta to maintain an index of suspicion for non-endemic diseases such as leprosy, particularly given the recent rise in immigration and ever changing population dynamics.

Acknowledgements

The authors thank Drs James Degaetano, George Depasquale, Paul Gatt and Tanya Mellilo for their helpful input in this case.

Clinical photographs (Figures 1 and 2) courtesy of Dr Brian Cassar, Medical Illustration Unit, Mater Dei Hospital.

References

1. Depasquale G. The Leprosy Eradication Programme of Malta. Lepr. Rev. 1975;46:215-217
2. Ramam M. The Continuing Relevance of Leprosy. JAMA Dermatol 2019;155:1107-1108
3. Sarode G, Sarode S, Anand R, Patil S, Jafer M, Baeshen H et al. Epidemiological aspects of Leprosy. Dis Mon. 2019;6(7)
4. Human Resources and Services Administration [Internet]. NHDP Guide to the Management of Hansen's Disease. National Hansen's Disease Programs. Available from: https://www.hrsa.gov/sites/default/files/hrsa/hansens-disease/pdfs/hd-guide-management.pdf [Accessed 2020 Feb 21]
5. Ridley DS, Jopling WH. Classification of leprosy according to immunity. A five-group system. Int J Lepr Other Myocbact. Dis. 1966;34:255-273
6. Mathur MC, Chimire RB, Shrestha P, Kedia SK. Clinicohistopathological correlation in leprosy. Kathmandu Univ Med J (KUMJ) 2011;9:248-251
7. World Health Organisation. WHO Expert Committee on Leprosy. World Health Organ Tech Rep Ser. 1988;768;1-51
8. Depasquale G. The Malta experience. Isoprodian-rifampicin combination treatment for Leprosy. Lepr Rev.1986;57 Suppl 3:29-37

9. Savona-Ventura C. Leprosy Archives The Maltese Islands. The Grand Priory of the Maltese Islands, The Military and Hospitaller Order of Saint Lazarus of Jerusalem, 2006 Available from: https://www.um.edu.mt/library/oar/bitstream/123456789/24377/1/leprosy.pdf

10. World Health Organisation. Global leprosy update, 2015: time for action, accountability and inclusion. Weekly epidemiological record 2016;91:405-420

11. World Health Organisation. Global leprosy update, 2018: moving towards a leprosy-free world. Weekly epidemiological record. 2019; 94; 389-412

12. National Statistics Office. Eurostat database. All valid permits by reason, length of validity and citizenship on 31 December of each year. [updated 2020 Jan 31] Available from: https://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=migr_resvalid&lang=en [Accessed 2020 Feb 21]

13. Freerksen E, Rosenfeld M, Depasquale G, Bonnici E, Gatt P. The Malta Project--a country freed itself of leprosy. A 27-year progress study (1972-1999) of the first successful eradication of leprosy. Chemotherapy. 2001; 47:309-331

14. Infectious Disease Prevention and Control Unit. (MT). Annual notifiable infectious diseases reports 2000-2019. MT. 2000-2019. Available from: https://deputyprimeministercms.gov.mt/en/health-promotion/idpcu/Pages/annualtables.aspx