and, via leaky lymphatics, disseminate throughout the body. Depending on local, environmental factors, such as lymphatic drainage, other organs can show symptomatic disease. It is probably more than coincidence that WD and lepromatous leprosy both show lymphangiectasia. T. whipplei and Mycobacteria leprae have much in common: they belong to the Actinobacteria class; ostensibly show tropism for macrophages; neither disease is associated with increased susceptibility to other pathogens; and the level of activation of macrophages (the DTH response) predicts the disease course and clinical manifestations, ranging from focal inflammatory disorders with few detectable organisms (high activation) to widespread, multiorgan infiltrates with abundant organisms (no activation). While an intrinsic defect in macrophage or lymphocyte function cannot be excluded as the underlying cause of WD, the consequences of systemic antigenaemia and lymphatic failure readily explain the absence of specific immunity and life-long susceptibility to T. whipplei.

Transparency declarations
None to declare.

References

Figure 1. Lymphangiectasia is a marker of lymphostasis and is a common finding in WD. Illustrated herein are numerous dilated lymphatic vessels in duodenal WD (arrow points to one of many PAS+ macrophages in the lamina propria, top panel). D2-40 (podoplanin) expression of the lining endothelial cells confirms their lymphatic nature (bottom panel).
Similarly, in our study on OPAT for BJIs, we found that teicoplanin was the most common antibiotic choice for MRSA infections and the clinical results were satisfactory. Teicoplanin can be given once daily or three times a week, and is effective and safe with a low adverse-event rate that makes it a first choice for OPAT. However, the growing body of evidence indicating that glycopeptide MIC has an impact on patient outcome can be a limitation for these drugs. In addition, glycopeptides showed worse activity against stationary-phase and non-dividing S. aureus cells, which are common in device-related infections, such as prosthetic joint infections. Thus, new drugs may be a good alternative. Linezolid is very active against MRSA, and is available as parenteral and oral (100% bioavailability) formulations, making it possible to switch from an intravenous to oral route in the outpatient setting. It may cause reversible anaemia or thrombocytopenia, reversible optic neuropathy and irreversible peripheral neuropathy after months of treatment. At the present time, its administration is not recommended for >28 days; however, there are anecdotal reports of longer use under careful observation, without adverse effects. Only limited data on linezolid combination therapy with rifampicin are available, but drug interaction between linezolid and rifampicin is probably not relevant, because the rifampicin level, which is certainly the more crucial one, remains unchanged. Daptomycin has excellent efficacy against stationary-phase staphylococci and it is being used in clinical practice to treat patients with BJIs caused by Gram-positive pathogens, including MRSA. The once-daily administration makes it attractive for OPAT. Recently, a new delivery method has been approved for once-daily daptomycin injection, allowing its administration as a 2 min intravenous injection rather than as a 30 min infusion, which is more attractive for patients in the outpatient setting. Although the ideal dose of daptomycin has not been well established, dosages ≥6 mg/kg are desirable. Because of its high bone penetration and broad antibacterial spectrum, tigecycline might be an option for the treatment of BJIs that are due to resistant bacteria, including MRSA, although there are few data in this setting and these are limited to experimental models or to patients with diabetic foot infections. Future prospects in OPAT include the use of more recently launched drugs, such as telavancin and ceftaroline, although, currently, there are only data on experimental models. Among these, the once-daily administration of telavancin makes it attractive for OPAT.

In conclusion, MRSA infections have a higher risk of treatment failure than methicillin-susceptible S. aureus infections. Where high glycopeptide MICs are reported, new antibiotics may be an alternative option.

Transparency declarations
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