# Hyperbaric oxygen therapy in the management of severe leg ulcers from prolidase deficiency

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## DESCRIPTION

A 31-year-old man presented to our attention showing infected ulcerative lesions with pseudoepitheliomatous hyperplasia of legs and feet, which rendered him unable to walk or to even stand. At the age of 8, he had been diagnosed with prolidase deficiency disorder, based on high levels of imidodipeptiduria and reduced enzymatic activity of erythrocytic prolidase.

At the time of hospitalisation, the patient presented diffuse lower limbs lymphedema, with sock-shaped ulcerative-hyperplastic areas, involving the medial and distal third of legs and feet. Such lesions were exudative and variably deep, showed irregular edges, increased tissue consistency and hyperplastic surrounding skin (figures 1 and 2). To confirm the diagnosis, genetic analysis and prolidase enzymatic activity assay were performed, showing homozygosis for the (c.1342G>A (p.Gly488Arg)) mutation, and a non-determinable prolidase activity in cutaneous fibroblasts. Multiple microbiological examinations from cutaneous swabs turned out to be constantly positive for *Pseudomonas aeruginosa*, occasionally positive for various bacteria and negative for mycetes. On the basis of this, the patient was put on intravenous meropenem, tobramycin and daptomycin, while topically applying in a trial-and-error fashion a series of products, such as povidone iodine 50% solution, 1/1000 potassium permanganate, gentamycin cream, iodoform gauze and a thin polyurethane membrane coated with a layer of an acrylic adhesive that contains 2% available iodine. None of these therapeutic options were successful in eradicating *P. aeruginosa*.

Given the poor therapeutic results, in an attempt to minimise ulcers extension and to decrease bacterial population, hyperbaric oxygen therapy (HBOT) was suggested and shortly after initiated; the patient's ECG and chest X-rays showed no contraindication. At the time of writing, the patient has had two cycles of HBOT. A cycle involves eight sessions of 60 min in duration, each split into three phases: compression at 15 metres/2.5 atmosphere absolute, prescribed time at pressure (three 20 min 100% oxygen stints) and decompression. After two

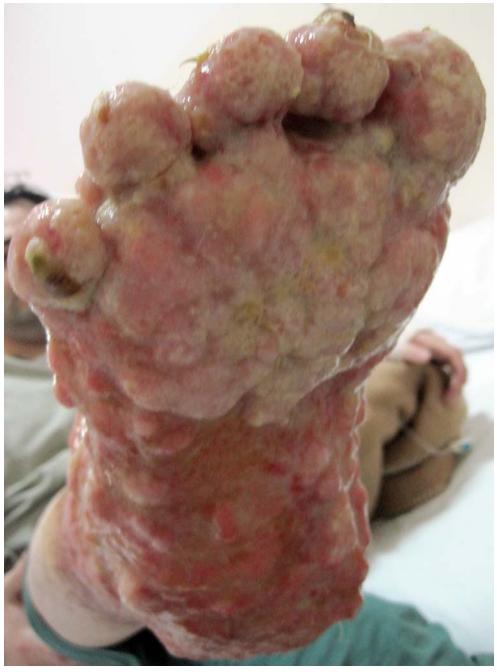

**Figure 2** Detail of the right foot.

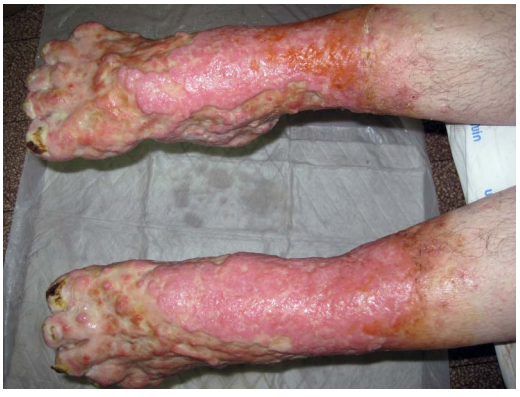

**Figure 1** Exudative sock-shaped ulcerative-hyperplastic areas involving the lower limbs.

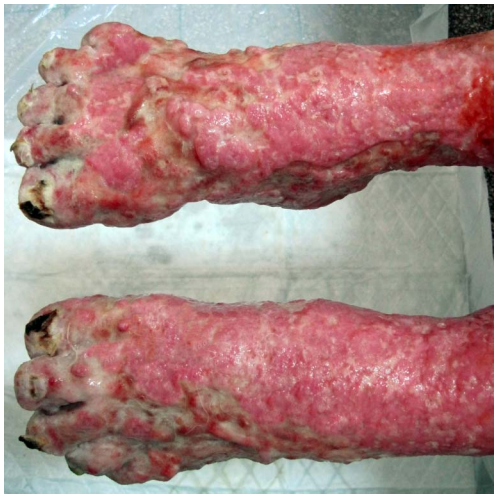

**Figure 3** After two cycles of HBOT. Notice the newly formed areas of granulation tissue and the decreased exudation.

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cycles of HBOT, a modest reduction in the extension of ulcerative-necrotic areas was obtained, with distinct new areas of granulation tissue, as well as a noticeable decrease in exudation and acrid odour (figure 3). Multiple control swabs were negative for *P. aeruginosa*. Moreover, our patient, previously unhopeful, manifested a clear improvement of his state of mind.

Prolidase deficiency is a rare autosomal-recessive disease, caused by mutations in the PEPD gene on chromosome 19 (19q12–q13.11), which presents with multisystem features, including chronic leg ulcers of variable severity.[1 2]

HBOT efficacy in chronic wounds is widely reported as is, to a lesser degree, its antibacterial capability.[3] The latter implies an improvement in polymorphonuclear function, bacterial clearance and antibiotic penetration, as well as a direct toxic effect on anaerobic bacteria.

To the best of our knowledge, this is the first reported case of prolidase deficiency-related leg ulcers managed with HBOT. In our case, HBOT was only marginally useful in reducing the extension of ulcerative lesions, but especially beneficial in eradicating *P. aeruginosa*, which was resistant to traditional therapies; this translated in an improvement of prognosis and quality of life.

On the basis of our observation, we suggest that HBOT should be considered as an effective option in the long-term management of leg ulcers associated with prolidase deficiency.

## Learning points

- Prolidase deficiency is a rare autosomal-recessive disease, caused by mutations in the PEPD gene, which presents with multisystem features, including chronic leg ulcers of variable severity.
- Hyperbaric oxygen therapy is useful in promoting wound healing of chronic wounds and also has antibacterial capability, through enhancement of polymorphonuclear function, bacterial clearance and antibiotic penetration, as well as through a direct toxic effect on anaerobic bacteria.
- On the basis of our our report, in cases of severe ulcerative lesions with multiresistant *P. aeruginosa* infection, hyperbaric oxygen therapy can be highly useful in eradicating the bacterium.

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**Contributors** MV is responsible for conception and final approval of the study, and involved in writing the manuscript. GG involved in drafting the manuscript and in final approval of it. DB is responsible for conception of the study and approved the manuscript. All authors agreed to be accountable for the article and to ensure that all questions regarding the accuracy or integrity of the article are investigated and resolved.

**Competing interests** None declared.

**Patient consent** Obtained.

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