Early signs that patient's own bone-marrow stem cells could treat multi-drug resistant tuberculosis

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Findings of a preliminary study published in *The Lancet Respiratory Medicine* suggest that a patient's own bone-marrow stromal (stem) cells could be used to treat multidrug-resistant and extensively-drug tuberculosis.

"Conventional treatment for MDR-TB uses a combination of TB drugs (antibiotics) which are harmful (toxic) to patients. Our new approach, using the patients' own bone-marrow stromal cells is safe and could help overcome the body's excessive inflammatory response, repair and regenerate inflammation-induced damage to lung tissue, and lead to improved cure rates", explains Professor Markus Maeurer from Karolinska University Hospital in Stockholm, Sweden who led the research.

WHO estimates that in Eastern Europe, Asia, and South Africa 450 000 people have MDR-TB, and around half of these will fail to respond to existing treatments.

TB bacteria trigger an inflammatory response in immune cells and surrounding lung tissue that can cause immune dysfunction and tissue damage. Bone-marrow mesenchymal stromal cells (MSCs) are known to migrate to areas of lung injury and inflammation and repair damaged tissue. They also modify the body's immune response and could boost the clearance of TB bacteria.

In this phase 1 safety study, 30 patients with MDR or XDR TB aged 21 years old receiving standard TB antibiotic treatment were also given an infusion of around 10 million of their own stromal cells. The cells were obtained from the patient's own bone marrow, then cultured into large numbers in the laboratory before being re-transfused into the same patient.

MSC infusion was generally safe and well tolerated. During the 6 months follow-up, no serious adverse events were recorded. The most common grade 1 or 2 adverse events were high cholesterol levels (14 of 30 patients), nausea (11 patients), and lymphopenia or diarrhoea (10 patients).

Further analyses showed 16 patients treated with MSCs were deemed cured at 18 months compared with only 5 of 30 TB patients with similar disease not treated with MSCs.

According to Professor Maeurer longer follow up with more patients is needed to establish the safety and efficacy of MSC therapy. "The procedures for obtaining stromal cells from the patient's own bone marrow are relatively simple, and if successful in phase 2 trials, will provide a viable adjunctive therapy for patients with MDR-TB not responding to conventional drug treatment or those with severe lung damage", he concludes.

Co-author Professor Alimuddin Zumla from University College London, UK adds, "The results of this novel and exciting study show that the current challenges and difficulties of treating MDR-TB are not insurmountable, and they bring a unique opportunity with a fresh solution to treat hundreds of thousands of people who die unnecessarily of drug-resistant TB. Further evaluation in phase 2 trials is now urgently required to ascertain efficacy and further safety in different geographical regions such as South Africa where MDR-TB and XDR-TB

are rife."

Writing in a linked Comment, Professor Robert J Wilkinson from Imperial College London, UK discusses the "long history" of adjunctive immunotherapy against TB, concluding that, "This field is…complex with an underlying problem being a relatively poor understanding of what constitutes protective and pathological immunity in human tuberculosis or even whether these are precisely separable. Nevertheless, the potential to investigate an increasing range of more specific biological therapies or the repurposing of existing anti-inflammatory agents continues to attract interest. Whether relatively complex and expensive MSC therapy will join this list remains to be determined."

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