Sugar coating bronchiectasis

Michael Loebinger

Bronchiectasis is a condition characterised by damage and dilatation of airways. Clinically, this manifests with productive cough and recurrent infective exacerbations. The importance of bronchiectasis is increasingly becoming recognised with data demonstrating an increased prevalence and significant associated morbidity, mortality and healthcare burden.1 2 This has stimulated a surge in interest from academics and industry alike, with the start of several multicentre clinical trials. These have however been limited in part by the heterogeneity of bronchiectasis, with multiple different causes and significant variability in disease progression.3 The development of bronchiectasis severity scoring systems4 has helped to stratify patients into prognostic groups; however, the underlying basis for much of this heterogeneity has not been determined.

In Thorax, Taylor et al5 investigate one possible genetic predisposition to a worse bronchiectasis phenotype. They used the well-published, prospective cohort from the BLESS trial, which assessed the impact of long-term erythrocyte-generosity has not been determined. The underlying basis for much of this heterogeneity has not been determined. The development of bronchiectasis severity scoring systems has helped to stratify patients into prognostic groups; however, the underlying basis for much of this heterogeneity has not been determined.

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to an inconsistent effect or relate to the different underlying chronic pathologies, for example, COPD severity may be less driven by infection and changes in the microbial community, and changes in CF due to FUT2 status may be masked by the differing epithelial and mucus environment in these patients. However, viral infections have similarly been implicated as having a role in some exacerbations in these other chronic respiratory conditions.20

In any event, the data presented in this issue are from a small number of patients based on a single centre study with no external validation cohort. Furthermore, the inclusion criteria for patients in the original study selected a generally severe population, limiting the ability to demonstrate differences in severity of disease between the secretor types. Consequently, while these data are interesting, significant caution is required and the study would need to be repeated in different, independent bronchiectasis populations including a wider range of severities and potentially different bronchiectasis aetologies.

There are few other studies that have looked at potential gene associations in bronchiectasis, with mannose binding lectin21 and matrix metalloproteinase gene variants22 implicated in modifying bronchiectasis severity and conflicting reports on the association of Killer cell Immunoglobulin-like Receptors (KIR) and Human Leukocyte Antigen (HLA)-C type with susceptibility to bronchiectasis.23 24 Bronchiectasis is also included in the UK 100 000 genome project where the whole genome sequencing approach may provide new genetic associations. This study is interesting and well performed and if it is a consistent and repeated finding in further studies, together with more evidence relating to the underlying mechanisms, then it may have implications for clinical management of patients with bronchiectasis. It does give some insight into the factors relating to pathogenesis and heterogeneity in bronchiectasis and may potentially help explain the differences in susceptibility to certain microbes. This in turn may provide the opportunity for more targeted monitoring strategies, particularly with regard to microbial status and may also lead to lower thresholds for therapies in certain patient groups. The potential alterations to the microbial community driven by these genetic changes may also provide different responses to present therapeutic options in bronchiectasis, in particular the use of long-term antibiotics. This study did not provide data on whether there was any difference in the response of the secretor and non-secretor groups to the long-term macrolide; however, numbers in these subgroups would have been low and not adequately powered to look at this.

There is much still to learn about bronchiectasis and the underlying heterogeneity, but understanding this further will be key to adequately designing and stratifying clinical trials and subsequently being able to better manage and assess patients appropriately. Recent studies have started to try and address this with phenotyping of patients by different methods such as by microbiome,25 molecular microbiology,26 27 severity scoring systems or clinical phenotype.28 The goal of these methods, which is shared by this study, is to try and move closer to a precision medicine approach within bronchiectasis.

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REFERENCES