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Traction bronchiectasis: is it as benign as we think?

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Recently, a group of experts from around the world defined bronchiectasis as a dilation of the airway lumen mainly produced by the destruction of the bronchial wall, secondary to the action of various proteolytic substances from local inflammation—usually neutrophilic inflammation,[1] although sometimes also eosinophilic inflammation,[2-4] and even with a systemic component[5,6]—and/or secondary bacterial products (usually as a chronic infection).[7-9] Furthermore, this radiological finding must be accompanied by symptoms related to it, especially productive cough (usually with a purulent component), with or without exacerbations.[10-12] Therefore, the definition of bronchiectasis must meet not only radiological criteria but also clinical criteria.[1,13] As a consequence, traction bronchiectasis (TBE) has been systematically excluded from diagnostic, prognostic, and therapeutic studies of bronchiectasis because it is not usually associated with a secondary clinical picture of airway inflammation or infection.[14]

It is true that TBE is usually due to dilation of the bronchial lumen caused by the destruction of the surrounding lung parenchyma. TBE is not usually accompanied by bronchial wall thickening related to excessive bronchial inflammation, and the probability of chronic infection with potentially pathogenic microorganisms is low. TBE is frequently observed in the context of advanced fibrotic processes secondary to interstitial diseases, after extensive infections or pulmonary emphysema, and, in general, after processes involving destruction of the lung parenchyma.[15]

In recent years, the presence of TBE has generated some particularly interesting questions about its ability to influence the prognosis of the underlying disease. Is TBE really as benign as we think? Could the presence of TBE influence the prognosis of patients, regardless of the usually associated interstitial pattern? Should the progression of TBE be monitored when it appears? Although the name bronchiectasis is still used for etymological reasons (*bronkos* = bronchus and *ectasis* = dilation), there is still no answer to these questions, since TBE has been systematically excluded, as mentioned above, from bronchiectasis studies of all types.

Recently, however, a study[16] involving 5,295 individuals with COPD (mean age = 59 years) seems to have indicated that the presence of TBE is not trivial at all and that TBE is capable of negatively impacting various important outcomes of COPD. In that study, Hata et al.[16] identified a subgroup of patients (n = 582) presenting interstitial abnormalities on CT scans. Those with associated TBE (n = 105) showed an adjusted linear correlation between greater radiological severity of TBE and poorer quality of life. Moreover, the patients with TBE presented an adjusted risk of death 3.8 times higher (95% CI: 2.6-5.6; $p < 0.001$) than did those without it.

These findings on the relationship between the presence of TBE and a poorer prognosis for the underlying disease are not new, having previously been described for various interstitial lung diseases such as idiopathic pulmonary fibrosis,[17] hypersensitivity pneumonitis,[18] and chronic eosinophilic pneumonia.[19] It is also a noteworthy fact that TBE has been shown to progress in most patients, resulting in a progressively worsening prognosis and greater severity of the underlying disease. The presence of TBE could therefore serve as a marker of the severity of interstitial diseases of any origin, which suggests—as it is already known—that early, intensified anti-inflammatory treatment during the inflammatory phase of the underlying disease is essential, before it progresses to an interstitial lesion and, consequently, to TBE. In fact, some authors have suggested the use of a TBE index[16,20] whose validity is distinguished by, among other things, excellent interobserver agreement for the diagnosis of TBE by chest CT (kappa index around 0.75). The TBE index classifies patients into four groups, according to the presence and type of TBE found in the interstitial process: type 1: no TBE; type 2: presence of bronchiolectasis; type 3: moderate TBE; and type 4: severe TBE. This classification system was used in the study by Hata et al,[16], as well as in another population-based study conducted in Iceland.[20] In the latter study, CT scanning was performed at baseline and 5 years after the inclusion of 3,167 participants in the study, 327 of whom had some type of interstitial alteration. The authors observed not only that TBE progressed in most individuals over time, but also that this progression was associated with an increased probability of death (hazard ratio = 1.68; 95% CI: 1.21-2.34; $p < 0.001$), adjusted for age, sex, BMI, and smoking habit after 11.5-14.0 years of follow-up.

All of these findings open up a timely topic of great relevance related to sequelae in the lung parenchyma of patients who have had SARS-CoV-2-related pneumonia. Various follow-up studies based on CT data have shown that a high proportion of such patients have suffered from chronic interstitial damage (especially after having severe pneumonia), often associated with TBE.[21,22] Will TBE even further worsen the prognosis or clinical severity in patients with interstitial alterations, in comparison with those without TBE? The answer to this question is still unknown, but it should certainly be a subject for research because an early aggressive treatment during

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the inflammatory phase of the disease would probably be the best option to prevent interstitial sequelae and the subsequent appearance of TBE. Moreover, it is also unknown whether, in addition to TBE, clinically active bronchiectasis might result in chronic infection with pathogenic microorganisms as a consequence of a vicious circle of excessive inflammation/infection over time. This situation cannot be ruled out since it is known that one of the most common etiologies of symptomatic bronchiectasis is after an infection, including viral infections.

In short, the supposed benignity attributed to TBE as part of an interstitial process within different underlying lung diseases (including both interstitial and non-interstitial disorders) does not seem to be confirmed in the literature. The presence of TBE could in fact worsen the prognosis and the clinical severity of the underlying disease responsible for it, over and above the prognosis resulting from the interstitial alteration itself. Another very important question remains to be clarified, which has already been generating a field of research of great interest: what will be the future impact of bronchiectasis associated with interstitial patterns in patients who have overcome COVID-19 pneumonia? There is still no answer to this question, but the data available so far indicate that a long-term follow-up period is required for such patients; if necessary, imaging techniques and even clinical monitoring should be used, including microbiological data, wherever possible.

CONFLICTS OF INTEREST

None declared.

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