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Idiopathic bronchiectasis. What are we talking about?

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The origin of bronchiectasis is marked by a necessary underlying pathophysiological condition: the existence of inflammation in the bronchial wall. In most patients, this consists of mixed inflammation with a predominance of neutrophils, although there is also an increase in the number of eosinophils and mononuclear cells in some individuals.[1,2] This inflammation has many origins, although in most cases it is caused by a bronchial infection by pathogenic microorganisms (usually bacteria and mycobacteria)[3,4] or by the bronchial wall's inflammatory reaction to the underlying disease (either intra or extrapulmonary) responsible for bronchiectasis[1] or in an exacerbation period.[5] Sometimes, however, the origin of this inflammation is unknown. Be that as it may, pro-inflammatory products (especially proteases and elastases) derived from both the immune cells themselves (especially neutrophils) and pathogenic microorganisms are the ultimate causes of the airway damage and typical images of lumen dilation with thickening of the bronchial wall observable on CT.[1,2] It is important to consider that the diagnosis of bronchiectasis requires this inflammatory pathophysiological substrate to be accompanied by a clinical impact on the patient, usually in the form of chronic cough with expectoration, sometimes with a purulent component, and exacerbations of an infectious profile.[5,6]

One of the peculiarities of bronchiectasis is its great clinical heterogeneity, mainly determined by dozens of possible etiologies, both local and systemic. All national and international guidelines on bronchiectasis recommend an exhaustive etiological study, particularly to diagnose potentially treatable etiologies. However, despite the performance of multiple tests, some of the causes of bronchiectasis are still not being identified reliably, giving rise to what has come to be called "idiopathic bronchiectasis."[1]

There is no precise definition of idiopathic bronchiectasis. Although from a theoretical point of view it would refer to the lack of any specific etiology, in most cases it is due to ignorance of the existing cause or an incomplete etiological analysis. The percentage of idiopathic bronchiectasis varies enormously in the different registries in the world. Thus, in the recently published data from the European Bronchiectasis registry,[7] comprising almost 17,000 patients from 28 countries, the overall percentage of idiopathic bronchiectasis was 38.1%, the overall percentage of idiopathic bronchiectasis was 38.1%, similar to those observed in the South Korean and the Australian registries (41% and 32.5%, respectively).[8,9] However, when the various European countries that have contributed with data to the European registry[7] are analyzed separately, the percentages vary enormously, from almost 60% in Poland to less than 10% in Croatia, Slovenia, Bulgaria, and North Macedonia. Broadly speaking, the percentage of idiopathic bronchiectasis was higher in Southern Europe (36.3%) and in the UK (44.5%) than in Northwest Europe (28.8%) and Central-East Europe (26.4%).[7]

Paradoxically, some countries with fewer health care resources, such as India[10] and some Latin American countries,[11] present substantially lower percentages of idiopathic bronchiectasis (22.4% and 26%, respectively). Finally, a third pattern can be seen in China, with very high relative percentage of idiopathic bronchiectasis (66% in Shangong and 46% in Guantzu).[12,13]

What could be the causes of this enormous heterogeneity in the percentages of idiopathic bronchiectasis? The explanation may be multifactorial. On the one hand, as it has already been remarked, there is no clear definition of idiopathic bronchiectasis, or, in other words, there is no agreement on the necessary etiological tests to perform before considering bronchiectasis as idiopathic due to the substantial variations in the definition used by different countries. On the other hand, it is possible that there are factors capable of causing bronchiectasis which are not generally subject to etiological tests, such as gastroesophageal reflux and long-standing mild immunodeficiencies (e.g., the quantitative or functional deficit of IgG subclasses).

One interesting conundrum is why countries such as India[10] or some areas in South America,[11] with no specific bronchiectasis guidelines, present a significantly lower percentage of idiopathic bronchiectasis than other countries with greater health care resources. This can probably be explained by the fact that idiopathic bronchiectasis is measured as a percentage, and that, in these countries, post-infectious (including post-tuberculosis) bronchiectasis clearly predominates. Something similar can be deduced from the data of the European registry,[7] in which those countries with less than 10% of idiopathic bronchiectasis are the ones that present a higher percentage of post-infectious bronchiectasis. However, it is important to reflect that post-infectious bronchiectasis (especially when attributable to childhood infections) is usually diagnosed via a process of elimination, which can lead to an underestimate of the percentage of idiopathic forms. Perhaps this problem is less noticeable in post-tuberculosis bronchiectasis, since its usual characteristics (previous pulmonary tuberculosis and bronchiectasis at the site of the pulmonary infiltrate, predominantly in the upper lobes, together with cavernous areas) tend to give rise to fewer diagnostic errors. This circumstance could explain the low rate of idiopathic bronchiectasis found in countries

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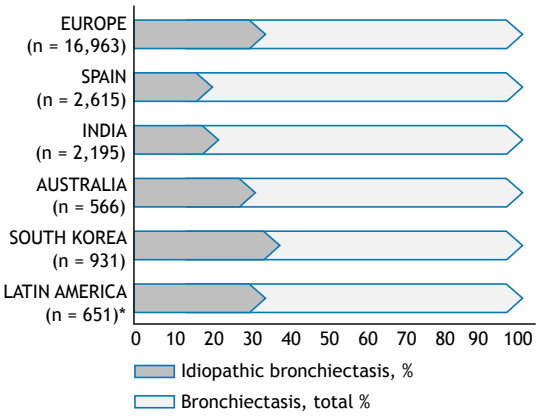

Figure 1. Relative percentages of idiopathic bronchiectasis. Based on published national and international registries and large bronchiectasis databases. *Five series included: three from Brazil (n = 474; range of idiopathic bronchiectasis: 25.3-44.7%), one from Argentina (n = 108; 34.2% of idiopathic bronchiectasis), and one from Chile (n = 69; 59% of idiopathic bronchiectasis).

such as India[10] and various Latin American[11] and European countries.[7]

As regards the evolution over time of the percentage of idiopathic bronchiectasis, there are hardly any data in the literature. Only in Spain can a significant reduction in the percentage of this type of bronchiectasis be observed from the beginning of the 21st century to the present day (from 24.2% to 18.2%), maybe because Spain has bronchiectasis regulations dating back more than 15 years, including a more recent one (from 2018) with clear algorithms for performing diagnostic tests to avoid the term "idiopathic" as much as possible. Spain has also been collecting data from patient registries for 20 years. However, in view of the increase in post-infectious bronchiectasis, from 30% in the first Spanish registry (2002-2011) to 40% in the second one (2015-2019) ,[14,15] it cannot be ruled out that some idiopathic bronchiectasis has wrongly been attributed to post-infectious bronchiectasis.

In short, it is important to recognize that the term "idiopathic bronchiectasis" does not mean, in most cases, bronchiectasis with no etiology, but rather an etiology of unknown origin—in most cases derived from the lack of performance of tests needed to rule out known causes. It is absolutely essential, in this respect, to at least rule out potentially treatable causes, as well as to reach an international consensus that clearly defines general and specific tests to be performed before bronchiectasis can be considered idiopathic.

AUTHOR CONTRIBUTIONS

The authors equally contributed to this work.

CONFLICTS OF INTEREST

None declared.

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