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Editorial

Tuberculosis Outbreaks: Beyond the Tuberculin Skin Test☆

Brotes de tuberculosis: más allá de la prueba de la tuberculina

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Essential elements in the proper control of tuberculosis include an early diagnosis, the correct treatment of patients, a contact study for the detection of new cases, and the treatment of carriers at risk of developing the disease.[1]

Epidemic outbreaks of tuberculosis have been and continue to be common in our setting. Factors facilitating outbreaks of disease include tight-knit communities, delay in diagnosis of the index cases, the susceptibility of the affected population and the "fitness" of the strain (how efficiently it spreads).

In 2005, Sarrat Torres et al.[2] described a tuberculosis outbreak in a kindergarten in Zaragoza, in which 11 of the 94 children studied were infected (11.7%). Of these, 10 were diagnosed with active disease, confirmed microbiologically from gastric aspirate samples in 9. The disease was all the more easily transmitted because of the pulmonary and laryngeal infection sites, the significant delay in diagnosing the index case (the teaching assistant), and the close contact between the young children.[2]

In another school outbreak in a primary school in Madrid, the contagion rate, including patients and carriers, was 94%.[3] After identification of the initial 3 pediatric cases, the real index case turned out to be the teacher, who was diagnosed with bacilliferous cavitating pulmonary tuberculosis. In this outbreak, all infected contacts provided gastric aspirate sampling as part of a full diagnostic evaluation before starting treatment for latent tuberculous infection. This lead to the diagnosis of 7 new cases, 2 of which were asymptomatic with normal chest X-rays. In another school microepidemic, induced sputum samples were found to give a good yield, with isolation of *Mycobacterium tuberculosis* in 3 of the 7 pupils who were diagnosed with the disease.[4]

In Catalonia, 27 tuberculosis outbreaks were described between 1998 and 2002. A total of 70% of these had occurred among family groups, while figures among the immigrant population remained low.[5] In subsequent years (2003–2004), a study performed in the city of Barcelona used molecular epidemiological techniques to investigate tuberculosis transmission patterns in Spanish-born and foreign-born populations. This study revealed that almost 40% of strains occurred in 65 clusters, of which approximately 55% involved Spanish-born subjects only, 11% foreign-born subjects only, while 34% were a mixed population sharing the strain. It should be pointed out that most foreign-born patients included in the mixed clusters were from South America, leading the authors to surmise that cultural similarities may act as a significant factor in encouraging contact, hence bi-directional transmission of tuberculosis among communities.[6]

In this edition of Archivos de Bronconeumología, Hernán García et al. describe an outbreak of isoniazid-resistant tuberculosis in an immigrant community in Valladolid.[7] After notification of a case of tuberculosis in a Bolivian-born patient, an active search was conducted among cohabitants and contacts, and 5 new cases were detected. Genotyping and antibiotic resistance profiling of the sputum samples revealed isoniazid-resistant *M. tuberculosis* in all patients. Transmission among communities was not addressed in this outbreak, since all secondary cases were born in Spain or were descendants of the Bolivian family, who had been living in Spain for over 10 years, and who had not recently traveled to their country of origin. As the authors rightly point out, it is difficult to determine if the disease in the index case was a reactivation of imported tuberculosis or if it was a recent infection. This can only be determined by using molecular epidemiological techniques and/or studies of the lineage of other similar strains in a research setting.[6]

By conducting a comprehensive study of samples from contacts, new cases can be definitively diagnosed, sensitivity to antituberculous drugs can be determined, and molecular coincidences corroborating the epidemiological suspicions can be identified. In London, in 2000, the use of molecular epidemiological techniques (IS6110-restriction fragment length polymorphism [RFLP]) helped to retrospectively determine the extent of a highly transmissible tuberculosis outbreak with single isoniazid resistance – the first case had appeared 5 years previously.[8]

Commercial molecular techniques that have been validated in recent years (GenoType® MDRTBplus-Hain, GeneXpert®-TB-Cepheid) facilitate the detection of genetic mechanisms determining isoniazid and/or rifampicin resistance, not only from cultivated strains but also from direct samples.[9] Early diagnosis of possible resistances makes them very useful tools for speeding up contact studies, avoiding delays and inappropriate treatment regimens for tuberculous disease and infection. The World Health Organization has declared the GeneXpert®-TB technique as the gold standard

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for the diagnosis of tuberculosis in countries with a high burden of resistant disease and poor laboratory support infrastructures.[10] In Spain, the use of these techniques is recommended in positive cultures or directly on samples with strongly positive sputum smear results, if resistance seems likely: immigrant population, previous treatments, therapeutic failure, or contact with resistant patients.[1] Nevertheless, no clinical–analytical protocol has been established for the use of these molecular techniques in direct samples, and each hospital still adopts their own criteria. Since most laboratories in Spain have the technical capacity to perform these tests, and since most new cases are from immigrant populations in areas of high resistance rates, one possibility would be to routinely perform molecular resistance studies directly on clinical samples, particularly in bacilliferous cases.

The study of Hernán García et al.[7] is an example of how the use of new laboratory techniques and close coordination between the microbiologist, the clinician, and the public health system are the cornerstones of good management of tuberculosis outbreaks in the community, particularly when resistant strains are suspected.

References

1. González-Martín J, García-García JM, Anibarro L, Vidal R, Esteban J, Blanquer R, et al. Documento de consenso sobre diagnóstico, tratamiento y prevención de la tuberculosis. Arch Bronconeumol. 2010;46:255–74.
2. Sarrat Torres R, Macipe Costa R, de Juan Martín F, Lezcano Carreras MA, Bouthelier Moreno M, Marín Bravo MA, et al. Brote epidémico de tuberculosis en una guardería de Zaragoza. An Pediatr (Barc). 2006;65:219–24.
3. Tagarro A, Jiménez S, Sánchez A, Arroyo A, Aracil J, Cañete A. Brote de tuberculosis en un colegio de primaria: descripción y consideraciones sobre el valor del jugo gástrico en el manejo de microepidemias. Enferm Infecc Microbiol Clin. 2011;29:90–5.
4. Bran CM, Cayla JA, Domínguez A, Camps N, Godoy P, Orcau A, et al. Estudio de los brotes de tuberculosis que han generado informes epidemiológicos en Cataluña (1998–2002). Arch Bronconeumol. 2006;42:260–6.
5. Antón MP, Carrasco JAG, Lois GL, Villeneuve IM, Beckouche ML, García E. Brote de tuberculosis en una escuela. An Pediatr (Barc). 2007;67:18–21.
6. Borrell S, Español M, Orcau A, Tudo G, March F, Cayla JA, et al. Tuberculosis transmission patterns among Spanish-born and foreign-born populations in the city of Barcelona. Clin Microbiol Infect. 2010;16:568–74.
7. Hernán García C, Moreno Cea L, Fernández Espinilla V, Ruiz Lopez del Prado G, Fernández Arribas S, Andrés García I, et al. Brote de tuberculosis resistente a isoniacida en una comunidad de inmigrantes en España. Arch Bronconeumol. 2016;52:289–92.
8. Ruddy MC, Davies AP, Yates MD, Yates S, Balasegaram S, Drabu Y, et al. Outbreak of isoniazid resistant tuberculosis in north London. Thorax. 2004;59:279–85.
9. Caminero Luna JA. Update on the diagnosis and treatment of pulmonary tuberculosis. Rev Clin Esp. 2015, http://dx.doi.org/10.1016/j.rce.2015.09.005. pii:S0014-2565(15)00230-1.
10. WHO. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert® MTB/RIF system policy statement. World Health Organization; 2011. p. 1–35.