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Letters to the Editor

Implementation of molecular techniques for diagnosis of mumps☆

Implementación de técnicas moleculares para el diagnóstico de parotiditis epidémica

Dear Editor,

It was with great interest that we read the work by Sanz et al.[1] on the serological diagnosis of mumps and the associated detection of elevated specific IgG titres. The authors reveal that 73.4% of patients with mumps (with no primary infection marker such as IgM) presented significantly elevated IgG titres and therefore conclude that new studies are needed which use other serological methods to clarify the diagnostic performance of IgG quantitation and to define the concept of "elevated titres". We would therefore like to illustrate our experience of the mumps epidemic that occurred in Valencia from January to November 2017, the incidence rate of which was 42.5 cases per 100,000 inhabitants (provisional data from the Public Health Directorate of the Valencian Community's Ministry of Health).

During this period, 140 saliva samples from suspected mumps cases were sent to our microbiology department (age range: 3–78 years; mean: 23.9; 80 males) for diagnosis through viral RNA detection with a Real-Time Polymerase Chain Reaction (RT-PCR) (BD MAX®, Beckton Dickinson, USA), following the protocol available on the Centers for Disease Control (CDC) website, available at: http://www.cdc.gov/mumps/lab/qa-lab-test-infect.html#realtime-pcr.

Eighty-eight cases were successfully confirmed, 50 of which were simultaneously subjected to the RT-PCR technique, qualitative serological IgM determination and quantitative determination of specific IgG by chemiluminescence (LIAISON®, Diasorin, Italy), with a measurement range of 5–300 arbitrary units (AU) and a positivity cut-off point of 11, according to the manufacturer. Only 16 cases tested positive for specific IgM antibodies, equating to 32% sensitivity. Of the 34 cases that presented no primary infection marker, 68.5% tested positive for elevated IgG antibodies (Ab) (>300 AU/ml). Likewise, of the 52 suspected cases that were not confirmed, since no viral RNA was detected in saliva, only 27 could undergo serological testing, with 25.9% presenting elevated IgG levels.

To analyse whether there is a link between the detection of viral RNA in saliva and the quantity of IgG Ab, Spearman's test was used, obtaining a correlation coefficient (rho = 0.573; $p < 0.05$). These results show that there is a direct and moderate relationship between both variables.

The results published by Sanz et al.,[1] as well as those detailed above, highlight the limited sensitivity of serology—24.7 and 32%, respectively—for the diagnosis of mumps in a largely vaccinated population. Similar findings were also published by Maillet et al., who obtained 45% sensitivity.[2] We found a moderate correlation between mumps cases confirmed by RT-PCR and elevated IgG levels. This phenomenon is similar to what may be observed in light of a secondary infection.[3] Following vaccination, the immune system produces antibodies to vaccine strains (Rubini and/or Jeryl Lynn). However, these antibodies are not protective and when the patient comes into contact with a circulating wild-type strain, it generates a rapid and intense antibody response against recognised antigens.

To improve the diagnostic results for mumps at our hospital, we decided to perform RT-PCR to confirm suspected mumps cases, as recommended by other authors,[4,5] and following the recommendations of the CDC's Manual for the surveillance of vaccine-preventable diseases.[6] As well as avoiding the diagnostic uncertainty generated by serology, the results considerably improved sensitivity, which reached 62.85% among the suspected cases versus 11.42% in the detection of IgM.

In our experience, the routine laboratory implementation of the RT-PCR technique on saliva samples is vital in order to provide a solid microbiological mumps diagnosis and relegates the usefulness of serology, which is far less sensitive, to an indicator of vaccination status.

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Reply to "Implementation of molecular techniques for diagnosis of mumps"☆

Respuesta a «Implementación de técnicas moleculares para el diagnóstico de parotiditis epidémica»

Dear Editor,

We were pleased to find that the results provided by Navalpotro Rodríguez et al.[1] coincide with our data which were published recently in the EIMC journal.[2] In their study, more than two-thirds of IgM-negative mumps cases—which obtained positive results with a Real-Time Polymerase Chain Reaction (RT-PCR)—showed elevated specific IgG levels (understood to be above the measurement limit of the chemiluminescence technique employed).[1] Unlike what happens with the other components of the MMR vaccine, in those that have international units of IgG (mIU/ml for measles and IU/ml for rubella), which enable the comparison of serological results from different studies,[3] in the case of mumps there is no standard serum that can be referred to in international units.[4] Moreover, the quantitation of IgG is expressed in terms of titres or arbitrary units relating to the techniques used.[1,2] Furthermore, the difficulties regarding the standardisation of quantitation methods for IgG in mumps[4] may hinder the comparison of data provided by different laboratories.[5] The fact that approximately a quarter of the cases which are negative with RT-PCR will also present a high degree of positivity, can perhaps be partly explained by the trend in the results obtained by laboratory tests for the diagnosis of mumps. RT-PCR techniques prove more sensitive in the early phases, following the onset of symptoms[6,7] but may come back negative as the infection advances. Thus, a negative RT-PCR result (in the late stages) does not definitively rule out infection. IgM detection improves from the second week, but lacks sensitivity in the vaccinated population.[6,7] Identifying elevated levels of specific IgG may increase this sensitivity. However, raised IgG levels may of course not prove too specific. The current Spanish vaccination schedule involves administering two doses of the MMR vaccine at 12 months and 3–4 years of age. Between 2007 and 2016, vaccination coverage in older children was sustained at 95% with the first dose and 90% with the second dose.[8] In our field, the levels of seroprevalence against mumps in young adults are approaching 90%.[9] However, despite this, mumps continues to appear in a cyclic presentation in Spain.[10] The emergence of periodic epidemic waves may lead to a "booster" effect in vaccinated individuals which prompts a raise in specific antibody levels after coming into contact with circulating wild-type viruses. We wholeheartedly agree with the authors that the implementation of RT-PCR on saliva samples is currently the best method for confirming mumps cases in our field. Serology may continue to be of interest in unvaccinated groups, in the conduct of epidemiological studies and in special circumstances where it was not possible to obtain samples in the early phases of the disease.

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