Enfermedades Infecciosas y Microbiología Clínica 40 (2022) 150–154

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Scientific letter

Modifying SARS-CoV-2 vaccine schedule in Spain: When numbers matter

Modificación del calendario de vacunación contra el SARS-CoV-2 en España: cuando los números importan

After a year, SARS-CoV-2 has taken the world by storm, affecting up to 81 million and killing more than 1.8 million people world wide.[1] Treatments have proven to be of little or of no efficacy, and there are progressively increasing number of patients with late sequelae.[2] At this point, with a vaccine already in place, there is a ray of hope for slowing the advance of this disease.

Spain has been particularly hit by COVID-19, with nearly 2 million of infected as for 2 January 2021.[1] Since 29 December 2020, the vaccine against SARS-CoV-2 Cominarty® (Pfizer-BioNTech) has been implemented in our country following a strategy that prioritizes population groups to be vaccinated, including the protection of the most vulnerable people.[3] To achieve a 95% efficacy the first dose should be followed by a second 21 days later.[4]

But with more than 50,000 deaths in Spain behind us, and in the context of a high and increasing incidence of COVID19 in the last weeks, it might be placed a high priority on promoting rapid, high levels of vaccine uptake. This can be more easily and quickly achieved if the current scheme is modified, as already recommended in other countries, as UK.[5] While the trial data shows that the vaccine conferred immunity to 52% of the participants three weeks after the first dose and just before the second dose,[4] experts of the Joint Committee on Vaccination and Immunization states that each dose only begins to take effect after several days. Therefore, they interpreted data from the period immediately after the second dose as indicative of efficacy of the first, increasing significantly this 52% protection measured.[5] Food and Drug Administration also pointed that efficacy against severe COVID-19 occurring after the first dose was 88.9% (95% CI 20.1, 99.7).[6]

The basic reproduction number (R0) of SARS-CoV-2 infection have been estimated to range 2 to 6. With an estimated R_0 of 3, the herd immunity threshold is about 67%.[7] Two ways to reach this desirable percentage group immunity are natural immunization after infection and mass vaccination of the population.

In Spain, the large longitudinal sero-epidemiological population-based study ENE-COVID estimated that the global prevalence (percentage of population with IgG antibodies against SARSCoV-2 since the beginning of the study in April, to November 2020) is 9.9% (IC95%: 9.4–10.4).[8] Nevertheless, this information must be taken with caution: not every infected person develops antibodies, and these antibodies can disappear over time. But these do not necessarily mean an absence of immune memory, since cellular immunity seems to play an important role on protection.[9]

More than 47 million people live currently in Spain. With the aforementioned reported vaccine efficacy of 95%, to achieve 67% of the immune population at least 33 million citizens would have to be vaccinated, which means 66 million doses of vaccine.

Pfizer has committed to deliver to Spain 350,000 doses every week. That means we would need 95 weeks (1.8 years!) to reach the herd immunity in our country, which is definitely unacceptable. This excessively long-time frame could be improved by increasing the number of doses supplied to Spain by the laboratory (assuming that there is enough production capacity) and/or authorizing the administration in Spain of vaccines from other laboratories apart from Pfizer-BioNTech (as Moderna, AstraZeneca, J&J, Sanofi and Curevac), together with accelerating the negotiation process for their acquisition.

In the meantime, one possible strategy might be to administer a single dose of vaccine to as many eligible individuals as possible, delaying the second dose. This will have the greatest impact on reducing mortality, severe disease and hospitalizations, protecting our overloaded National Health System. But the real fact is that the protection from a single dose of Pfizer-BioNTech's vaccine has not been definitively tested because the study was not designed to assess the efficacy of a single-dose regimen. This raises questions about if it is less effective to receive the second dose a few months later than recommended schedule or how long the protection from a single dose will last.

The dilemma of whether to vaccinate fewer people with the best protection possible or provide twice the number of people with a single shot, covering more of the population but with slightly weaker protection should be weighted soon. Now, more than ever, numbers matter.

References

1. Ministerio de Sanidad. Situación actual COVID. Available from: https://www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/situacionActual.htm [cited 02.01.21].
2. Centers for disease control and Prevention. Late Sequelae of COVID-19. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/late-sequelae.html [cited 02.01.21].
3. Ministerio de Sanidad. Estrategia de vacunación covid-19 en España. Available from: https://www.mscbs.gob.es/gabinetePrensa/notaPrensa/pdf/24.112411201444317769.pdf [cited 02.01.21].
4. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med. 2020;383:2603–15, http://dx.doi.org/10.1056/NEJMoa2034577. Epub 2020 Dec 10.
5. Joint Committee on Vaccination and Immunization: advice on priority groups for COVID-19 vaccination; 2020. Available from: www.gov.uk/government/publications/priority-groups-for-coronavirus-covid-19-vaccination-advice-from-the-jcvi-30-december-2020/joint-committee-on-vaccination-and-immunisation-advice-on-priority-groups-for-covid-19-vaccination-30-december-2020 [cited 02.01.21].
6. Food and Drug Administration Briefing Document. Vaccines and related biological products advisory committee meeting December; 2020. Available from: https://www.fda.gov/media/144245/download [cited 02.01.21].
7. Randolph HE, Barreiro LB. Herd immunity: understanding COVID-19. Immunity. 2020;52:737–41, http://dx.doi.org/10.1016/j.immuni.2020.04.012.
8. Ministerio de Sanidad. Estudio ene-covid: cuarta ronda estudio nacional de sero-epidemiología de la infección por sars-cov-2 en España; 2020. Available from: https://www.mscbs.gob.es/gabinetePrensa/notaPrensa/pdf/15.121512201633481113.pdf [cited 02.01.21].
9. Cox RJ, Brokstad KA. Not just antibodies: B cells and T cells mediate immunity to COVID-19. Nat Rev Immunol. 2020;20:581–2, http://dx.doi.org/10.1038/s41577-020-00436-4.

Enfermedades Infecciosas y Microbiología Clínica 40 (2022) 150–154

Marta Díaz-Menéndez[a,*], Eduardo Malmierca[b]

[a] *La Paz – Carlos III University Hospital-IdiPAZ, National Referral Unit for Imported Tropical Diseases, Tropical & Travel medicine Unit, Infectious Diseases Department, Madrid, Spain*
[b] *Infanta Sofía University Hospital, Infectious Diseases Department, Universidad Europea de Madrid, Madrid, Spain*

* Corresponding author.
E-mail address: marta.diazmenendez@salud.madrid.org
(M. Díaz-Menéndez).

https://doi.org/10.1016/j.eimc.2021.01.009

Erythema nodosum: An uncommon manifestation of Rickettsiosis

Eritema nodoso: una manifestación infrecuente en las rickettsiosis

Erythema nodosum (EN) is a well defined cutaneous syndrome that can be primary or secondary to systemic and autoimmune diseases, inflammatory bowel disease, pregnancy, neoplastic diseases, drugs or infections.[1] Between infectious agents, Streptococci and *Mycobacterium tuberculosis* are the most common causes in developed and developing countries, respectively. Many other microorganisms have been involved in EN, but *Rickettsia* spp. have only been related in very few case reports.[2,3]

A 30-year-old woman without any previous diseases, had a property vaccinated dog and lived in a rural area. In mid-autumn she began suffering fevers of up to 38 °C, headache, stiff neck and vomiting, so she went to the Emergency Department of our hospital. Upon arrival, blood pressure was 110/78 mmHg, heart rate 124 beats per minute and oxygen saturation by pulse-oximetry was 100%. At physical exploration, neurological examination was normal; she had a black, scabby and painless skin lesion on her scalp, as well as multiple red, indurated and painful lesions on palpation in both lower limbs, suggestive of EN. A blood test was performed: CRP of 270 mg/L, procalcitonin of 1.41 ng/mL, neutrophilia of 8710/μL with lymphopenia of 770/μl and discrete prolongation of prothrombin time (15.5 s). CSF analysis was normal, and CSF, blood and urine cultures were all negative. Chest x-rays and abdominal ultrasound were normal too. The patient was admitted to the Infectious Diseases Unit. A skin biopsy from one of the lesions in the lower limbs was taken (Fig. 1).

On the day after admission, the patient referred blurred vision. An Ophthalmologist found mild vitritis, retinal vasculitis, patchy retinitis and severe papillitis in her right eye, as well as mild patchy vasculitis in the posterior pole of her left eye.

ANA, antiDNA and ENA antibodies were all negative. Serologies for *Coxiella burnetii*, HIV, VEB and CMV were negative but *Rickettsia* spp's serology was positive IgM and negative IgG (Chemiluminiscent immunoassay or CLIA; *Rickettsia conorii* Virclia, Vircell®: Moroccan strain ATCC VR-141). At that moment, doxycycline 100 mg every 12 h was initiated for 7 days, along with corticosteroids to treat the ocular disease. The patient became afebrile 36 h after starting doxycycline. She improved quickly and could be discharged home. New serologies were made against *Rickettsia* spp in successive weeks: positive IgM and negative IgG persisted 2 weeks later; 3 months later, serology was still IgM positive by CLIA but undetermined IgM (1/40; *Rickettsia conorii* IFA IgM, Vircell®: Moroccan strain ATCC VR-141) and positive total antibodies by immunofluorescence assay (IFA).

The dermatological manifestations of rickettsiosis can be diverse. An eschar with epidermal necrosis at the site of inoculation is characteristic (tache noire). In addition, this infection can cause generalized vasculitis with involvement of the intima and media with vascular and perivascular infiltration of polymorphonuclear cells, lymphocytes and histiocytes. Other findings rarely seen are

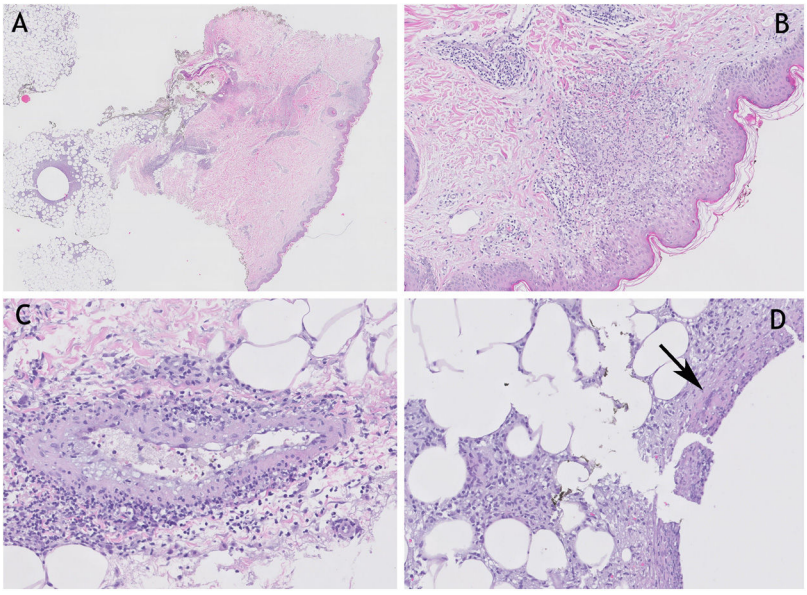

Fig. 1. (A) (H&E 20×) cutaneous punch in which superficial, deep dermis and adipose panniculus are appreciated. (B) (H&E 200×) detail of lichenoid dermatitis with vacuolar degeneration of basal epidermal layer, and underlying granulomatous reaction. (C) (H&E 200×) medium-sized vessel with vacuoleated endothelium and enveloping lymphocytic inflammatory infiltrate. (D) (H&E 400×) lobular and septal panniculitis with presence of giant multinucleated cell (arrow). H&E: hematoxylin and eosin.