Sequencing the evolution of vaccinia skin lesions in a laboratory worker: Insights from image analysis

Evolución de lesión dermatológica producida por Vaccinia en una trabajadora de laboratorio: secuencia de imágenes

A 43-year-old woman healthy laboratory worker, not previously vaccinated against smallpox presented to the emergency department with a 5-day history of a nodule in the second right finger (Fig. 1A). These symptoms appeared 6 days after she had been handling Western Reserve Vaccinia strains. She denied any laboratory accident while working, but she realized she had a broken glove which must have occurred while handling the centrifuge tube cap. Local symptoms worsened, and on day 7 she noticed a hemorrhagic bulla surrounded by erythematous and flogotic skin (Fig. 1B) so bacterial superinfection was diagnosed and amoxicillin/clavunate was prescribed. The patient improved slowly (Fig. 1C and D) to give way to a small lesion with crusting (Fig. 1E) which gradually disappeared over the next two months (Fig. 1F–H) until its completely resolution.

The patient refused the direct sampling from the lesion, so the PCR could not be performed. Since the lesion was highly characteristic of vaccinia, the virus exposure and the clinical progression was favorable, no further insistence was made, and only serology was performed on the obtained blood sample.

Serum was isolated from an analytical blood sample of the infected worker and used as the primary antibody in an indirect Western blot (WB) analysis to assess the possible presence of poxvirus protein antibodies. To confirm the presence of poxviral antibodies in the serum, a collection of monkey, hamster and human cell lines were infected with several poxviruses, and viral proteins were analyzed by WB using the collected serum (Fig. 1I). Viral antibodies presented in the serum were numerous and allowed the identification of different poxvirus strains (Fig. 1I). Specifically, human anti-vaccinia virus antibodies were primarily reactive against vaccinia virus (VACV) (WR and MVA) and monkeypox (MPOX) proteins with a molecular mass of approximately 75 (absent in MVA), 62 (absent in MPOX), 59 (absent in MVA), 35, 33, 25 (19 in MPOX) and 14 kDa. There was one prominent band with a molecular mass greater than 80 kDa in MPOX-infected cell lysates that were not present in WR- or MVA-infected cell lysates (Fig. 1I arrow) and others greater that 38 presents exclusively in MVA-infected sample (Fig. 1I, asterisk). In parallel, we performed an additional WB using a specific antibody against VACV viral protein (E3) validating our results of poxvirus infection (Fig. 1J).

VACV is used in the laboratory for a wide variety of purposes in the development of recombinant vaccines, immunotherapies, or oncolytic virotherapies.[1] However, it is potentially pathogenic in humans, and laboratory-acquired infections have been reported.[2] VACV is highly contagious through contact with lesion exudates,[3] and although it is less virulent than other poxviruses we cannot rule out its high pathogenicity in immunocompromised personnel, so it is necessary that laboratory workers would be fully vaccinated and use of safety precautions. As studies indicate robust VACV-specific immune responses in humans following vaccination, pre-exposure vaccination[4] with VACV may prevent laboratory workers. The Advisory Committee on Immunization Practices recommends routine vaccination with live smallpox vaccine for laboratory personnel who directly work with this virus or other orthopoxviruses that infect humans to avoid possible transmission.[5]

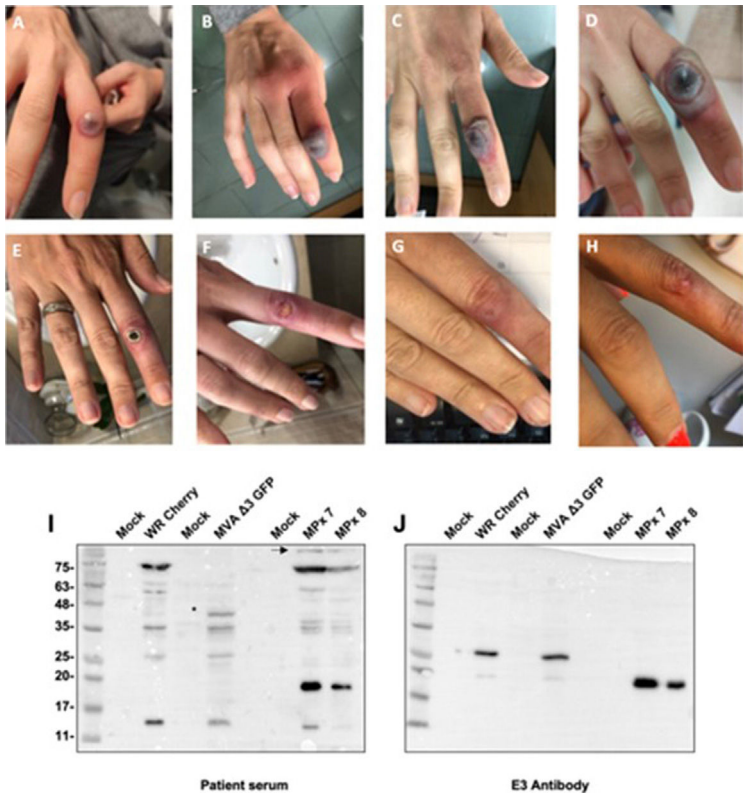

Fig. 1. Progression of local reaction on the second right finger after accidental inoculation with vaccinia virus (A: day 5, B: day 6, C: day 11, D: day 14, E: day 38, F: day 49, G: day 65 and H: day 120). WB analysis of proteins expressed in cell lines infected with poxvirus. Lysates from BSC40, DEF-1 or HTerT cells infected at an MOI of 10 with WR, MVA or MpX were transferred to nitrocellulose and used for Western blot analysis using the human serum collected from the infected laboratory worker as the primary antibody. An arrow indicates the protein detected exclusively in MPX infected cell lysates and an asterisk for in MVA-infected lysates.

This kind of vaccinia lesions have good prognosis although resolution is slow and a scar can persist. Treatment is usually symptomatic and the main aim is avoid complications as bacterial superinfections.

Authors' contributions

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Uso de isavuconazol en la meningitis criptocócica de un paciente cirrótico

Use of isavuconazole in cryptococcal meningitis in a cirrhotic patient

La meningoencefalitis criptocócica (MC) es una enfermedad grave que ocasiona 181.100 muertes anuales en el mundo[1]. Las principales especies causantes son *Cryptococcus neoformans* y *Cryptococcus gattii*. Frecuentemente se asocia a infección por el VIH en situación de inmunodepresión avanzada o a otro tipo de inmunodeficiencias (trasplante de órgano sólido, neoplasias y pacientes en quimioterapia o con fármacos inmunosupresores); sin embargo, hasta el 20% de los casos ocurren en pacientes inmunocompetentes donde predominan las variedades *C. neoformans grubii* y *C. gattii*[2]. Presentamos un caso autóctono de MC por *C. gattii* resistente a fluconazol con respuesta favorable a isavuconazol.

Varón de 59 años con antecedente de politoxicomanía, ictus isquémico con hemiparesia derecha y cirrosis Child-Pugh B por virus C con respuesta viral sostenida. Acudió al servicio de Urgencias por inestabilidad en la marcha, sensación de giro de objetos y fiebre de 3 semanas de evolución. En la exploración destacó supraversión de la mirada, con fondo de ojo sin edema papilar, no presentando alteraciones en el resto de la exploración física y neurológica.

Se realizó una TC craneal sin hallazgos y una punción lumbar (PL) con líquido cefalorraquídeo (LCR) turbio con presión normal y bioquímica sugestiva de meningitis bacteriana (glucosa 8 mg/dl, proteínas totales 383,7 mg/dl, leucocitos 8.297 células, 92% polimorfonucleares); en la tinción de Gram y en la tinta china se observaron levaduras compatibles con *Cryptococcus* spp. (fig. 1), confirmándose la detección de ADN para *C. gattii/ neoformans* mediante una técnica molecular basada en ácidos nucleicos de PCR múltiple (Biomérieux, FilmArray™). En el cultivo se identificó *C. gattii*. Los hemocultivos fueron negativos y el título basal del antígeno criptocócico en LCR (látex) fue > 1/10.000.

La resonancia magnética craneal mostró criptococomas cerebelosos. Se determinaron subclases de inmunoglobulinas, complemento, poblaciones linfocitarias, serología VIH y se descartaron neoplasias ocultas. En la TC se detectó esplenomegalia sin signos de hipertensión portal.

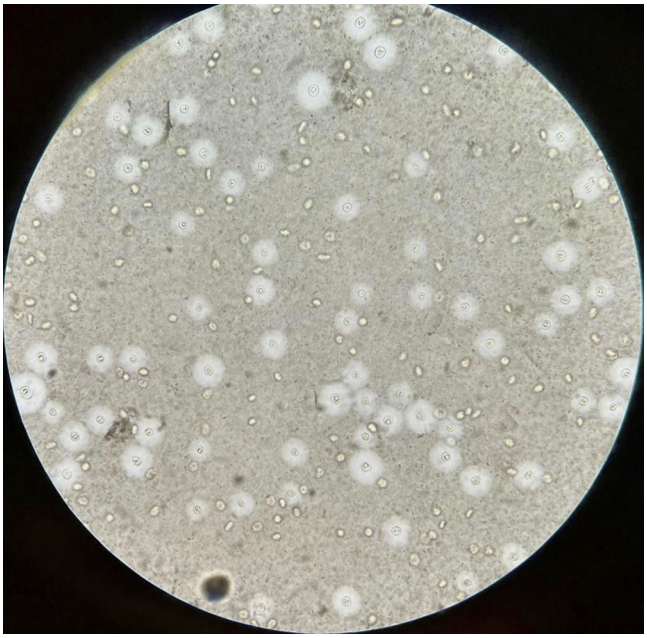

Figura 1. Estudio directo del LCR del paciente mediante técnica de tinta china en la que se observan estructuras levaduriformes con cápsula, algunas de ellas de gran tamaño (halo o aureola clara-transparente, con elemento central) sobre el fondo oscuro.