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

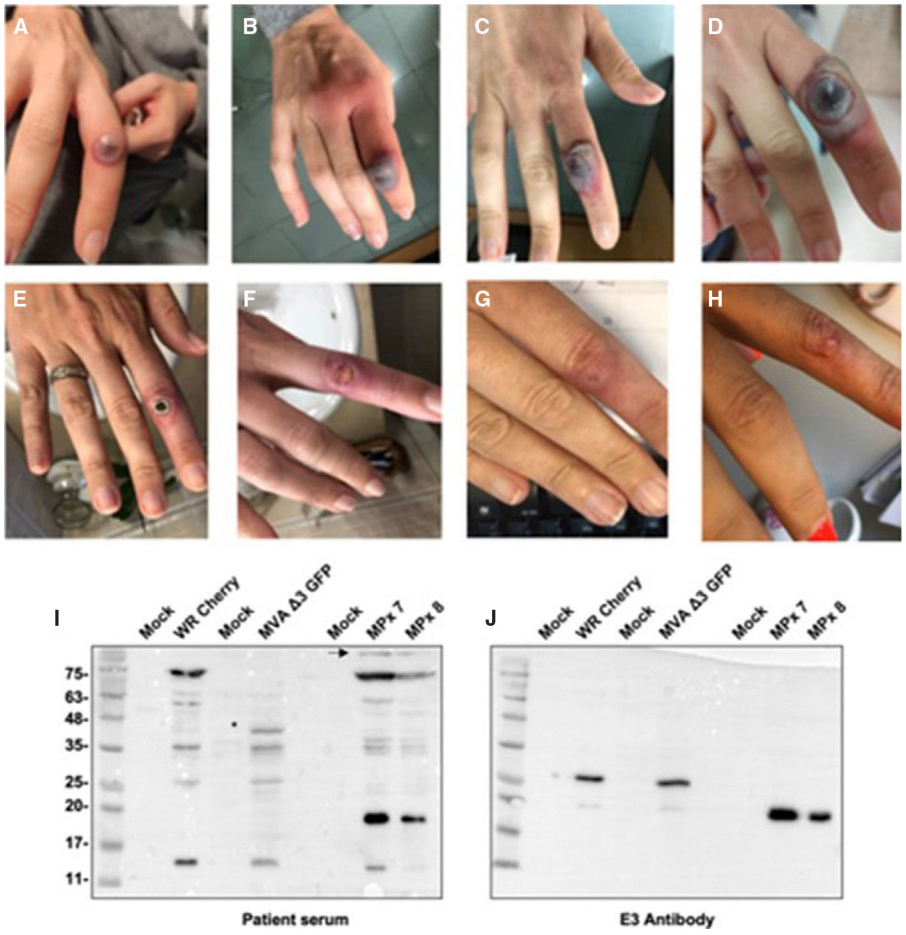

Fig. 1. Progression of local reaction on the second right finger after accidental inoculation with vaccinia virus (A: day 5, B: day 6, C: day 11, D: day 14, E: day 38, F: day 49, G: day 65 and H: day 120). WB analysis of proteins expressed in cell lines infected with poxvirus. Lysates from BSC40, DEF-1 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.

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]

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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Conflict of interest

The authors have declared no conflicts of interest.

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Use of isavuconazole in cryptococcal meningitis in a cirrhotic patient

Uso de isavuconazol en la meningitis criptocócica de un paciente cirrótico

Cryptococcal meningoencephalitis (CM) is a serious disease that causes 181,100 deaths worldwide each year.[1] The main causative species are *Cryptococcus neoformans* and *Cryptococcus gattii*. It is frequently associated with HIV infection in a situation of advanced immunosuppression or with other types of immunodeficiencies (solid organ transplant, cancers and patients undergoing chemotherapy or on immunosuppressive drugs). However, up to 20% of cases occur in immunocompetent patients, with the prevalent varieties being *C. neoformans grubii* and *C. gattii*.[2] We present an autochthonous case of CM due to *C. gattii* resistant to fluconazole with a favourable response to isavuconazole.

The subject is a 59-year-old man with a history of poly-drug addiction, ischaemic stroke with right hemiparesis and Child-Pugh B cirrhosis due to C virus with sustained viral response. He went to the Emergency Care Service with a three-week history of unsteadiness in gait, sensation of spinning objects and fever. Examination revealed upward gaze, fundus without papillary oedema, and no alterations in the rest of the physical and neurological examination.

Head CT was without findings and lumbar puncture (LP) showed cloudy cerebrospinal fluid (CSF) with normal pressure and biochemistry suggestive of bacterial meningitis (glucose 8 mg/dl, total proteins 383.7 mg/dl, leucocytes 8297 cells, 92% polymorphonuclear); yeasts compatible with *Cryptococcus* spp. were found in the Gram and India ink staining (Fig. 1), confirming the detection of

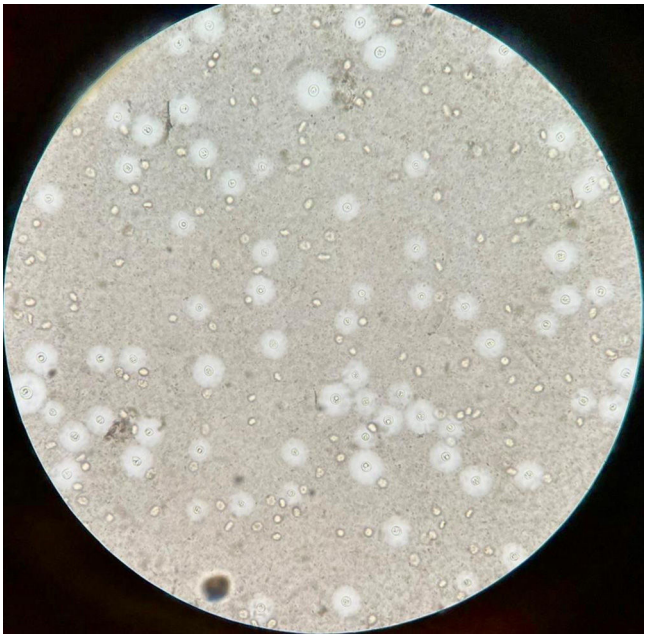

Fig. 1. Direct study of the patient's CSF using India ink technique in which yeast-like structures with a capsule are observed, some of them large (halo or clear-transparent halo, with a central element) on the dark background.

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