



Electron microscopy images of monkeypox virus infection in 24-year-old man

Markus Müller, Barbara Ingold-Heppner, Hartmut Stocker, Frank L Heppner, Carsten Dittmayer, Michael Laue

Lancet 2022; 400: 1618

Published Online

October 14, 2022

[https://doi.org/10.1016/S0140-6736\(22\)01969-9](https://doi.org/10.1016/S0140-6736(22)01969-9)

50140-6736(22)01969-9

Clinic for Infectious Diseases,

St Joseph Krankenhaus, Berlin,

Germany (M Müller MD,

H Stocker MD); Institute of

Pathology, DRK Kliniken Berlin,

Berlin, Germany

(B Ingold-Heppner MD);

Department of

Neuropathology, Charité -

Universitätsmedizin Berlin,

Berlin, Germany

(Prof F L Heppner MD,

C Dittmayer MD); Cluster of

Excellence, NeuroCure, Berlin,

Germany (Prof F L Heppner);

German Center for

Neurodegenerative Diseases

(DZNE), Berlin, Germany

(Prof F L Heppner); National

Consultant Laboratory for

Diagnostic Electron Microscopy

of Pathogens, Centre for

Biological Threats and Special

Pathogens (ZBS), Robert Koch

Institute, Berlin, Germany

(M Laue PhD)

Correspondence to:

Dr Michael Laue, National

Consultant Laboratory for

Diagnostic Electron Microscopy

of Pathogens, Centre for

Biological Threats and Special

Pathogens (ZBS), Robert Koch

Institute, Berlin 13353, Germany

LaueM@rki.de

Visit nanotomy.org for open

access pan-and-zoom view of the

entire large-scale EM data set.

Large-scale datasets are available

at <http://nanotomy.org/OA/Mueller2022Lancet/index.html>

See Online for appendix

A 24-year-old man presented to our clinic reporting severe anal pain and a pustular rash on his trunk, arms, penis, and fingers. The patient said the pain started 3 days after he had condomless penetrative and receptive anal intercourse with a man; he then developed a fever, chills, and inguinal lymphadenopathy. The skin lesions appeared approximately 8 days after the sexual activity: 2 days before he attended our clinic. The patient was previously fit and well with no medical history.

On examination, we found him to be in obvious distress because of the anal pain; his temperature was 37.1°C, heart rate was 98 beats per min, and blood pressure was 140/98 mm Hg. He had approximately 10 vesicular lesions, without surrounding erythema, containing yellow fluid, and measuring between 2 mm and 3 mm on his trunk, arms, penis, and fingers; his penis was oedematous.

Laboratory investigations showed a C-reactive protein concentration of 16 mg/L, which increased to approximately 7 times this concentration on day 2 of his hospital stay. Anorectoscopy showed ulcerating lesions adjacent to the pectinate line of the anal canal (appendix). Anorectal and oropharyngeal swabs tested positive for monkeypox virus by PCR.

Histopathological analysis of tissue samples taken from the anal lesions (appendix) showed prominent inflammation and regional disruption of the crypt epithelium, specifically loss of columnar cell shape. Notably, balloon-like expansion of epithelial cells and regular eosinophilic plasma inclusions, typical of poxvirus infections of the skin, were absent. Immunohistochemistry for cytomegalovirus and herpes simplex virus types 1 and 2, and nucleic acid

amplification tests for *Chlamydia trachomatis* and *Neisseria gonorrhoea* were negative.

Paraffin-embedded biopsy samples were processed for thin-section electron microscopy (EM) to investigate whether cells are infected by monkeypox virus and whether they propagate the virus. Ultrathin sections of the samples were analysed by transmission EM. One section was entirely digitalised at high resolution by EM—so-called large-scale scanning-transmission EM—to allow microscope-independent analysis by pan-and-zoom viewing at the computer screen. EM showed both mature and immature virus particles—indicating virus replication—organised in specific cytoplasmic areas of epithelial cells of colonic crypts and of interstitial cells (figure).

The patient was admitted to the infectious disease ward, because of anal pain, and prescribed a combination of morphine, metamizole, and gabapentin, which controlled his symptoms. He was allowed home, 8 days later, when his condition had improved. He had no antiviral treatment.

Contributors

MM and HS cared for the patient. BI-H and FLH did the diagnostic histopathological work. CD and ML did the electron microscopy imaging and analysis. All authors wrote the report and decided to submit the manuscript. Written consent to publication was obtained from the patient.

Declaration of interests

We declare no competing interests.

Acknowledgments

We would like to thank the Core Facility for Electron Microscopy of the Charité for support in acquisition of the large-scale electron microscope data.

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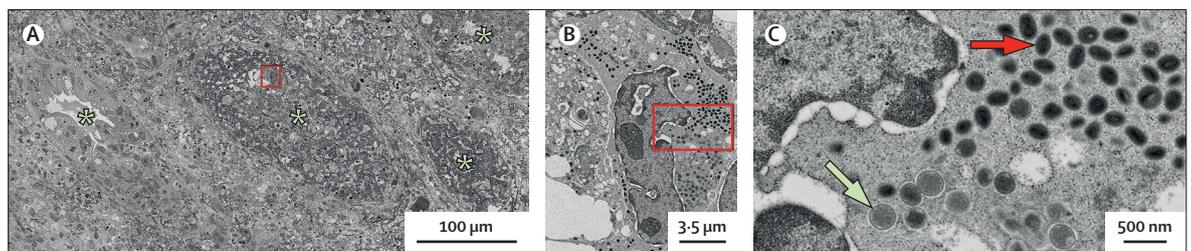


Figure: Monkeypox virus infection of the anorectal mucosa at the electron microscope

(A) Electron microscopy (EM) of colonic crypts shows (asterisks) varying degrees of epithelial damage correlating with the presence of viral particles. (B) EM shows greater magnification of area in box in image (A) with an infected enterocyte with many electron-dense poxvirus particles in the cytoplasm. (C) EM shows greater magnification of area of cytoplasm in box in image (B) with round and less dense immature viruses (green arrow) next to mature poxvirus particles; some with typical oval profile and dumbbell core (red arrow).