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Emerging viral diseases center

Division of Infectious Diseases

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Monkeypox summary

Epidemiology:

Zoonosis, Endemic in Central and West Africa (mainly Nigeria/DRC) where cases are regularly confirmed and/or epidemics, usually limited, contact with the natural environment is a risk factor

Outside of Africa:

- 2021: one imported case in the US (Texas) from Nigeria, UK: 3 members of the same family (returning from Nigeria).
-2019: imported case in the UK, 1 imported case in Singapour
-2018: imported cases in the UK from Nigeria, with 1 secondary case of nosocomial transmission; Israel: 1 imported case
- 2003, USA – an epidemic of 53 cases caused by the importation of rodents

Currently (since May 7, 2022): unusual number of cases and geographical distribution of cases acquired outside Africa, in Europe, North America and Australia

- First confirmed case in the UK: 7 May 2022: traveler who returned from Nigeria;
- Since then multiplication of the number of confirmed cases in the UK, no link with the imported case.
- New cases confirmed on May 18 in Portugal and 1 in the USA (traveler returning from Canada), without epidemiological link together
- Since May 19: confirmed cases in North America: Canada, USA, Europe: UK, Portugal, Spain, Italy, Sweden, France, Belgium, Germany), Australia
- Most confirmed cases have been reported to be young men. In some countries, most declared to be close to the gay, bisexual, MSM community.

Virology:

- Orthopoxvirus (MPXV), subfamily: chordopoxvirinae; genus: orthopoxvirus; species: Monkeypox virus. Close to smallpox virus, ds DNA virus
- First isolated in 1958 from sick monkeys sent from Singapore to Denmark.
- First identified in humans (children) in 1970 in the DRC.
- 2 different phylogenetic clades: Clade 1 (the former Central African (Congo Bassin clade)) and clade 2 (the former West Africa (the one from West Africa being less severe)).
- The virus involved in the current 2022 outbreak derives from clade 2, and already accumulated around 50 mutations, suggesting of a circulating in the human population since several years (lineage B.1).

Transmission:

- Reservoir: rodents (monkeys and humans are accidental hosts)
- Animal to Human: contact with blood or infected fluid
- Human to Human transmission:
    - Human-to-human transmission is generally low
    - Mostly direct contact with a lesion (infected biological fluid)
    - Epidemiological data of the current outbreak do not support a large aerosol/droplet transmission
    - Possible contagiousness before the development of skin lesions (oropharynx)
    - Depends on the strain: attack rate: range from 3 to 50% depending on the epidemic.
    - Vertical mother to child transmission (pregnancy)
    - Fomites

Incubation:

-Less than 14 days (5-12; mean 8 days, max 21 days), but shorter if there was a high risk exposure (ex: an open wound)

Physiopathology:

-Entry via respiratory or intradermal routes: initial intradermal or naso/oropharyngeal replication then spread to the local lymph nodes.
-Viremia and hematogenous dissemination to all organs; viremia correlates with the appearance of the first signs of illness.

Clinical presentation:

Usual mild course of disease, spontaneously resolving, low mortality rate for the West Africa MPX clade; complications may arise.

Classic "textbook" presentation
-Starts with fever and flu-like illness: chills, lymphadenopathy (submandibular, cervical, inguinal), headache, and myalgia.
-Fever precedes the rash by approximately 2 days.
-Maculopapular rash followed by papules, vesicles and pustules: beginning on the face, the mouth, the torso, then expands to the hands, palms and soles are affected
Lesions of 0.5-1 cm (oral lesions may be large, may cause difficulty eating); followed by an umbilication/central depression, then a swollen and painful crust and desquamation in 2-3 weeks.

Currently:
- up to 30% of the patients present with isolated genital and/or perianal lesions, without prodroms.
-Possible differences in presentation depending upon the strain

Complications: secondary bacterial skin and ENT (Ears, Nose, Throat) infections (retropharyngeal abscess), nausea and vomiting with dehydration, pneumonia (secondary bacterial infections), encephalitis. Rarely, corneal lesions causing blindness. Sequelae: skin lesions (pitting scarring).
-Abortion, foetal deaths during pregnancy
-The mortality is variable according to socio-economic context, and possibly the strain: it is low outside Africa, but up to 10% during epidemics in Africa.

Lab: hepatitis, leukocytosis, thrombocytopenia, hypoalbuminuria.

Case Definition:

- Suspected case: Fever followed by vesico-pustular rash

  Or Fever or Vesiculo-pustular rash + epidemiological link

- Probable case: Suspected case with epidemiological link with a probable or confirmed case

- Confirmed case: laboratory confirmed case (PCR positive)

Differential Diagnosis:

-Varicella (chickenpox) and smallpox (eradicated), or another parapox (vaccine)
-Anything that causes skin lesions (e.g. syphilis)

Diagnostics:

-PCR: gold standard

- cutaneous lesion swabs of exsudate, crusts or biopsy: gold standard (to be stored in Viral Transport Media, VTM), ideally from 2 different lesions
- Throat swab: (in VTM) (especially before the appearance of lesions)
- Rectal swab: (in VTM) , stools, urine: to be discussed on a case by case basis
- Viremia of short duration (plasma)

-To be sent to Centre national de Référence des Infections Virales Emergentes (CRIVE)

- Poxvirus PCR
- https://www.hug.ch/laboratoire-virologie/formulaires-informations
- Category B UN 3373 for suspicions and confirmations

-Serology : IgM/IgG ELISA 5-8 days after the rash (not routinely used), IgM
-Microscopy, Culture: not routinely used for diagnostic

Mandatory declaration of the disease to the cantonal doctor within 24 hours in case of a positive result, by the treating physician
https://www.bag.admin.ch/bag/fr/home/krankheiten/infektionskrankheiten-bekaempfen/meldesysteme-infektionskrankheiten/meldepflichtige-ik/meldeformulare.html#-1790465635.
Additionally, compulsory declaration of a positive result by the laboratory (to the cantonal doctor and FOPH), also within 24 hours.

Treatment:

- Most often symptomatic (mild course of disease)
- Cidofovir (DNA polymerase inhibitor) was shown to be effective in animal models, also brincidofovir (licensed in the USA against smallpox)
- Tecovirimat (VP37 assembly protein inhibitor) approved in the USA against smallpox, dose: 600 mg 2x/day PO for 14 days 30 minutes after a meal, no dose adjustment in the event of renal and hepatic insufficiency.
-Passive immunization: Immune globulin vaccinia (6000 UI/kg to 24 000 UI/kg)

Prevention:

-Immunization:

- Prior immunization against smallpox (stopped in Switzerland in 1972) results in a 5x lower risk a symptomatic infection, but only 75% protection against infection (Rimoin, PNAS, 2010). Probably decreased efficacy with time since last vaccination.
- Modified Vaccinia Ankara vaccine (MVA) live attenuated non-replicating vaccine: Imvamune or Imvanex and approved in the US against smallpox and monkeypox (also suitable for children and pregnant women), also usable and recommended for post exposure prophylaxis only in the event of a high risk (and not in people already previously vaccinated against smallpox)
- Immune globulin vaccinia

- Infection prenvention control:
  - airborne and contact measures (until the crusts fall off)
  - https://vigigerme.hug.ch/fiche-vigigerme/orthopoxivirus

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Geneva Center for Emerging Viral Diseases