Considerations for Diagnosis in Potential Cases of Monkeypox

The World Health Organization (WHO) designated monkey pox a public health emergency of global significance on July 23, 2022 [1]. The emphasis is on methods to slow the spread of the disease as the number of cases is increasing exponentially in non-endemic areas. These initiatives comprise making a prompt diagnosis, quickly identifying close contacts, and taking immunization precautions. In order to help clinicians evaluate a suspected case of monkeypox, the main screening techniques and diagnostic procedures are addressed here briefly.

According to the Centers for Disease Control (CDC) case criteria, a patient is classified as having 'suspected monkeypox' if they meet any one epidemiological requirement and exhibit a distinctive rash without a plausible explanation [2,3]. The recognizable monkeypox rash develops centrifugally from macules to umbilicated vesiculopustules (**Box I**). Patients who present with fever and vesiculopustular exanthem may have painful lesions and frequent involvement of lymph nodes. This constitutes the so-called 'vesiculopustular phase'. The term "pseudo-vesiculopustules" is more aptly used to describe the stiff, challenging-to-deroof monkey pox vesiculopustules that lack fluid contents after deroofing [4].

In addition to the exanthem, monkeypox can result in an enanthem, which can be difficult to treat. The oropharyngeal mucosa is involved, which causes pharyngitis and tongue ulcers. At times, the sole presenting characteristic of the disease may be anogenital mucosal involvement. Rectal discomfort, diarrhea, proctitis, tenesmus, or isolated genital ulcers are common first signs in patients [5,6]. Differential diagnoses include clinical conditions which manifest with similar-looking rashes viz., varicella zoster, measles, rubella, scabies, bacterial skin infections, syphilis, and drug-rash [7,8].

Box I Mucocutaneous Manifestations of Monkeypox

Exanthem

- Onset of rash on face, palms, soles or anogenital area
- Evolution from painful macules to papules to vesiculopustules
- Umbilicated vesiculopustules progressing to crusted lesions healing with scar formation
- Interval of 2 weeks between prodrome and scabe Often <20 evolving lesions in different stages of evolution

Enanthem

- Ano-genital ulcers
- Nasal or ocular lesions
- Oral or tonsillar lesions

It is also important to understand how monkeypox specimen collection differs from those of other morphologically comparable vesiculopustular eruptions. Swabs can be taken from intact vesiculopustules and scabs/crusts in the case of monkeypox [2]. In contrast, herpetic exanthems require thorough base swabbing before specimens are taken from deroofed fluidfilled vesiculopustules. To confirm the diagnosis, non-variola orthopoxvirus DNA and monkeypox virus DNA isolation tests using polymerase chain reaction (PCR) are conducted sequentially. Testing must be done in Biosafety Level 2 facilities by personnel who have received their vaccinations.

A skin biopsy is not necessary for diagnosis because the results are often not specific. Other tests such as immunohistochemical staining, anti-orthopoxvirus IgM antibodies, atomic force microscopy and viral cultures are useful [2]. In ambiguous cases and atypical findings, clinicians must take into account further testing in addition to sampling cutaneous, oral mucosal and rectal mucosal areas to rule out sexually transmitted diseases, which may be seen concurrently or may mimic monkeypox.

An understanding of the clinical characteristics and diagnostic procedures, and being aware of monkeypox imitators will prepare professionals to quickly and correctly arrive at a diagnosis.

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