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Short Communication

The first case of monkeypox virus infection detected in Taiwan: awareness and preparation



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ABSTRACT

Objectives: Monkeypox has recently been detected outside African countries. This study aimed to report and analyze the first case of monkeypox virus infection in Taiwan.

Methods: The global epidemiological information was collected from the World Health Organization (WHO) and US Centers for Disease Control and Prevention (CDC). The data from the first confirmed Taiwanese monkeypox case was obtained from Taiwan Centers for Disease Control. Monkeypox diagnosis and prevention strategies were obtained from WHO guidelines on monkeypox. Phylogenetic tree analysis and sequence alignment and comparison were used to identify the phylogeny and single nucleotide polymorphism (SNP) characterization.

Results: Epidemiological data indicated that since 2013, monkeypox has caused outbreaks outside African countries through contact with infected animals and international travels. Recently, two confirmed monkeypox cases were reported in Singapore and South Korea. On June 24, 2022, Taiwan CDC reported the first confirmed case of monkeypox virus infection in a 20-year-old man who returned from Germany, from January to June 2022. This is the third confirmed case of an imported monkeypox infection in Asia. Phylogenetic analysis demonstrated that this imported monkeypox virus belonged to the West African clade and is clustered with the 2022 European outbreak monkeypox isolates. Full-length sequence analysis indicates that this virus contains 51 SNPs, and has five variant SNPs compared with the recent outbreak strains.

Conclusion: This study suggests that active surveillance, enhancing border control, and the development of vaccines and antiviral drugs are urgently required to prevent and control the burden of monkeypox disease.

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On June 24, 2022, the Taiwan Centers for Disease Control (Taiwan CDC) reported the first case of monkeypox virus infection de-

tected in Taiwan, making this the third confirmed monkeypox infection in humans reported in Asian countries (Taiwan CDC, 2022). The other cases of monkeypox human infection were reported in Singapore and South Korea in June 2022 (Figure 1A). A case of imported monkeypox infection was detected in Singapore in May 2021 (Figure 1A). Although at present, there are only a few monkeypox cases in Asia, this re-emerging zoonotic disease poses a potential threat to not only Asia but also globally.

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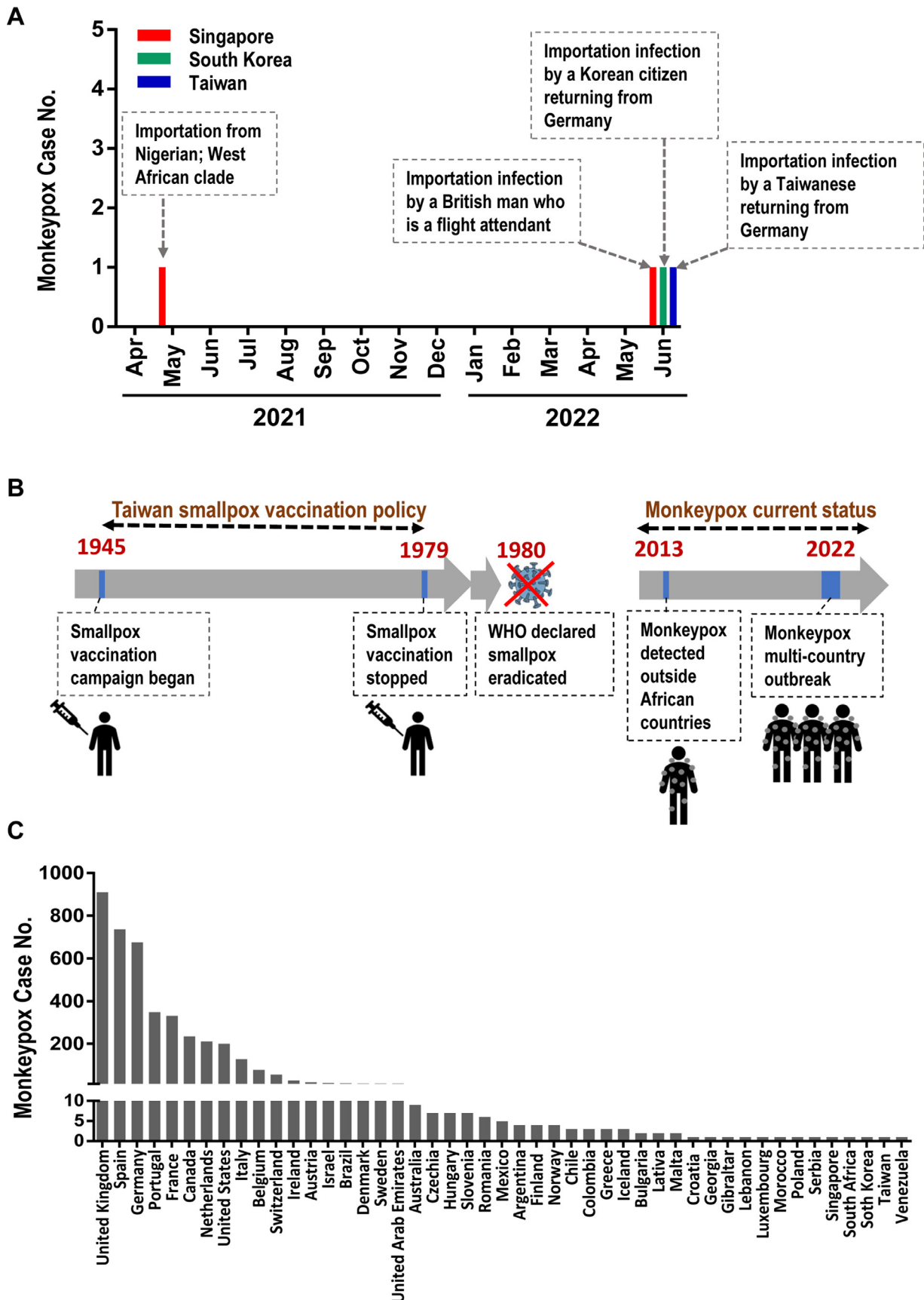


Figure 1. The number of confirmed monkeypox cases and their distribution. The monkeypox cases reported in Singapore, South Korea, and Taiwan. (B) The timeline of smallpox vaccination policy in Taiwan and the current monkeypox outbreaks. (C) The global monkeypox-confirmed cases and their reported countries. The data were collected as of June 24, 2022.

Monkeypox is a rare infectious disease caused by animals or humans infected with the monkeypox virus. Monkeypox virus belongs to the genus *Orthopoxvirus* of the *Poxviridae* family. Vertebrates and arthropods have been reported to serve as natural hosts for this virus (Durski et al., 2018). Monkeypox was first discovered in 1958 when two outbreaks occurred in monkeys that were kept for research and began presenting a pox-like disease (Ligon, 2004). However, the disease was first confirmed in humans in 1970, when a child was suspected of having smallpox in the Democratic Republic of Congo. In 2003, the first monkeypox outbreak outside of Africa was reported in the United States of America (Durski et al., 2018; Ligon, 2004). Furthermore, monkeypox was reported to be transmitted by travelers, causing human-to-human transmission. There are two distinct genetic clades of the monkeypox virus, including the Central African (Congo Basin) clade and the West African clade. The Central African clade has historically caused more severe disease and was thought to be more transmissible. The mortality rate for the Central African clade was approximately 10.6%, whereas the mortality rate for the West African clade was approximately 3.6% (Bunge et al., 2022).

Taiwan is an island country beside mainland China with a few indigenous transmissible diseases. Taiwan CDC has indicated that many infectious diseases are caused from imported infections. Taiwan is a monkeypox nonendemic country and had no monkeypox cases reported until recently (Taiwan CDC, 2022). On 16 June 2022, a 20-year-old man studying in Germany, from January to June 2022, returned to Taiwan (Figure 1). After 4 days, he developed symptoms that included fever, sore throat, muscle pain, lymph node swelling in the groin, and a skin rash. Over the next 2 days, he sought medical attention, and his case was reported to the Taiwan CDC as a suspected case of monkeypox. On June 24, Taiwan CDC confirmed that this was a case of monkeypox virus infection (Taiwan CDC, 2022). According to the report from Taiwan CDC and Tainan City Public Health Bureau, this patient showed atypical skin lesions compared with the patients infected with European monkeypox (Tainan City Public Health Bureau, 2022). All the close contacts were quarantined for further observation and diagnosis. Taiwan CDC suggested the close contacts to undergo health monitoring or quarantine for 21 days after contact (Taiwan CDC, 2022). Smallpox vaccination is believed to exert cross-protectivity against monkeypox virus infection owing to the high nucleotide identity (96.3%) in the central region between these two viruses (Kumar et al., 2022). The smallpox vaccination campaign began in Taiwan in 1945 (Figure 1B). The last domestic case of smallpox reported in Taiwan occurred in 1955, and the routine smallpox vaccination was terminated in 1979 (Taiwan CDC, 2022), indicating that most people who were born before 1979 still contain anti-smallpox antibodies (Figure 1B). The younger age group (<45 years) may be required to receive the smallpox vaccine for cross-protection against monkeypox. Recently, monkeypox caused worldwide outbreaks outside endemic regions (Figure 1C). According to phylogenetic analyses reported by European CDC, the monkeypox viruses that caused the recent outbreak belong to a distinct cluster within the West African clade (European CDC, 2022). Similarly, our phylogenetic tree analysis indicated that the phylogeny of the detected Taiwanese monkeypox virus belongs to the West African clade and forms a unique cluster with the 2022 European monkeypox outbreak isolates, including the UK and Germany isolates (with a bootstrap value of 100) (Supplementary Figure S1).

To prevent the expansion of monkeypox outbreak and dissemination, several measures are required to contain the viral transmission, including the potential use of the smallpox vaccine for post-exposure prophylaxis of close contacts, the establishment of rapid

diagnostic assays with high sensitivity and specificity, as well as active surveillance and monitoring system. As for the treatment, most monkeypox symptoms often resolve on their own without further treatment. However, if the patients show severe symptoms, vaccinia immune globulin may be recommended for these cases. At present, there is no treatment approved specifically for monkeypox virus infections. However, antiviral drugs developed for use in patients with smallpox have proven to be beneficial against monkeypox; Tecovirimat (commercialized as TPOXX) has been approved for the treatment of monkeypox as of January 2022 (US CDC, 2022a). Polymerase chain reaction is currently the preferred laboratory diagnosis tool in clinical diagnosis because of its high accuracy and sensitivity. The serology and antigen detection methods are not recommended owing to their major cross-reactivity. The optimal diagnostic samples for monkeypox testing include skin lesions, fluid from vesicles and pustules, and dry crusts.

As mentioned earlier, monkeypox virus is predominantly endemic in West and Central African countries with rare appearances reported outside these regions. Most of these rare cases are associated with importation of infection from endemic countries (Bunge et al., 2022; WHO, 2022). However, recently, several monkeypox outbreaks have been reported outside the endemic countries and have gradually caused worldwide outbreaks with unknown epidemiological links to West or Central Africa (European CDC, 2022; US CDC, 2022a). The reasons for a surge in confirmed cases of monkeypox are still not fully understood. The most probable cause is transmission via imported cases who have traveled to those monkeypox endemic countries. A recent study indicated that one possibly could not completely rule out the hypothesis of a prolonged period of cryptic dissemination among humans or animals in a nonendemic country (Isidro et al., 2022). However, silent human-to-human transmission seems unlikely, as affected individuals develop disease characteristics such as visible localized or generalized skin lesions (Adler et al., 2022; Kumar et al., 2022). Furthermore, a large number of these monkeypox virus infections have occurred in bisexuals and men who have sex with men, suggesting the possibility of sexual transmission (Kumar et al., 2022; US CDC, 2022b). This suggestion cannot be dismissed, even if it does not support the already known epidemiology of the disease. This may include new knowledge and previously unknown facts.

Notably, recent studies reported that the 2022 monkeypox outbreak-associated isolates deviate by a mean of 50 SNPs from the related 2018–2019 viruses, which is around six- to 12-folds more than one would expect, considering previous estimates of the substitution rate for Orthopoxviruses (1–2 substitutions per site per year) (Firth et al., 2010; Isidro et al., 2022). Such a divergent branch might represent a recent evolutionary jump. Reports from sequence analysis indicated that there were mutations in three amino acids (D209N, P722S, M1741I) present in the immunogenic surface of the glycoprotein B21R (MPXV-UK_P2-182) (Isidro et al., 2022), and this region contains important antibody targets as well as several key immunodominant epitopes (Hammarlund et al., 2005). Furthermore, these mutation signatures detected in recent monkeypox isolates might suggest the potential action of apolipoprotein B mRNA-editing catalytic polypeptide-like 3 (APOBEC3) enzymes in the viral genome editing (Pecori et al., 2022). Similar observations were found in this first imported case of monkeypox virus infection in Taiwan (Figure 2). This first detected monkeypox virus in Taiwan contains 51 SNPs (26 nonsynonymous, 21 synonymous and four intergenic), with five variant SNPs compared with other recent isolates (Figure 2). However, the impact of these SNPs of currently circulating monkeypox viruses in

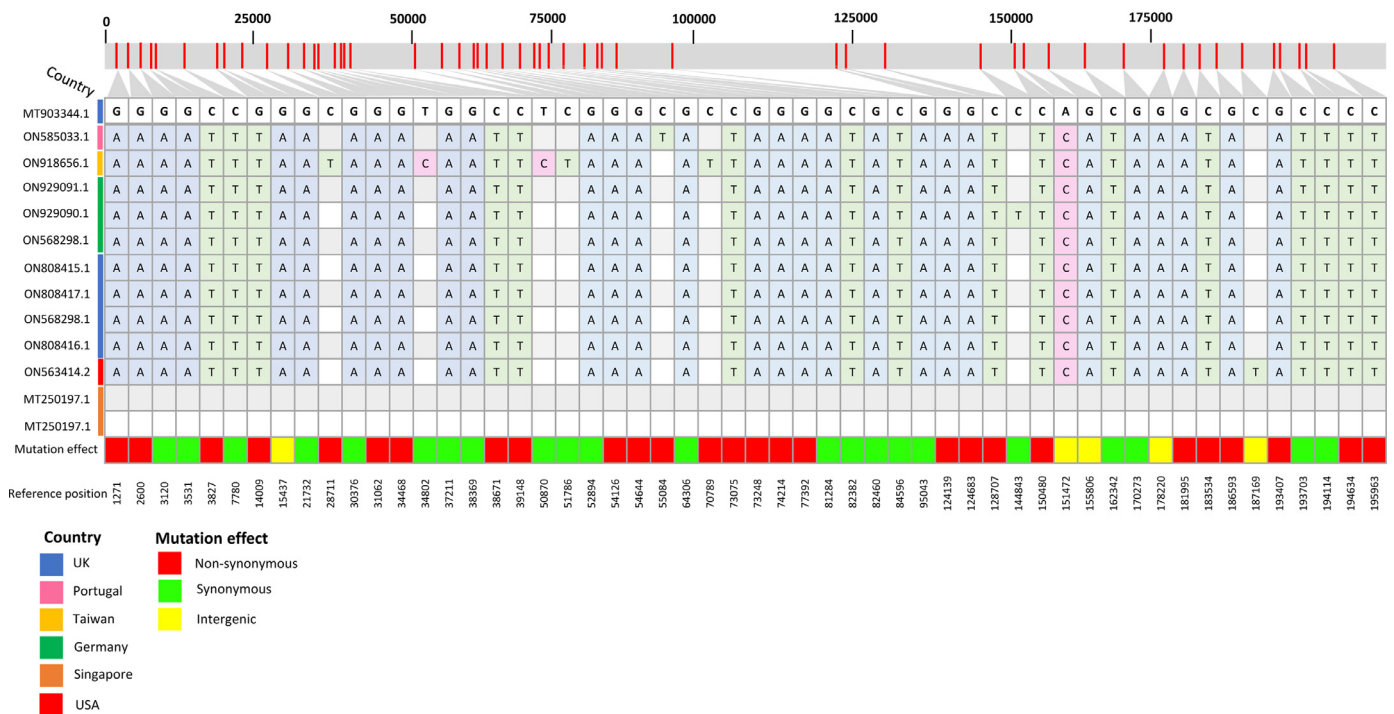


Figure 2. SNP characterization among 2022 monkeypox outbreak variants. Light-colored mutations represent the SNPs separating the MPXV 2022 outbreak cluster from MPXV_UK_P2 (MT903344.1) reference sequence. Dark-colored mutations represent the genetic diversity within the outbreak cluster. The first monkeypox virus detected in Taiwan (ON918656.1) was used to compare with other recent isolates in different countries. MPXV, monkeypox virus.

altering the viral characteristics or virulence as well as facilitating monkeypox dissemination outside the endemic countries requires further and deeper investigations.

To date, there have been more than 800 monkeypox cases globally and continue to increase daily across more than two dozen previously nonendemic countries. At present, this is the first confirmed case of monkeypox virus in Taiwan; however, whether monkeypox virus will lead to an outbreak in Taiwan still remains unknown. We suggest that, in the current state, active surveillance and detection, enhancing border control and development of vaccine and antiviral drugs are urgently required to prepare for any future monkeypox outbreaks.

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Ethical approval statement

Ethics approval was not required for this study.

Author contributions

ZSY, CYL, ANU, and WHW assisted in manuscript preparation. PLL, YHC, MLY, and SFW discussed the concept and designed the manuscript. WA, SPT, and SFW made critical revisions to the manuscript and made suggestions. All authors read and approved the final manuscript.

Declaration of Competing Interest

The authors have no competing interests to declare.

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