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Differences and similarities between Monkeypox and Chickenpox in children during an outbreak*

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ABSTRACT

Introduction: Herein, we described cases of children under 16 years old suspected to be infected with Monkeypox virus (MKPV) and diagnosed with chickenpox in public hospitals of Marseille, south of France.
Material and methods: We conducted a retrospective study from March 23rd, 2022 to October 20th, 2022 in our institution of results of MKPV DNA and varicella-zoster virus (VZV) DNA detection by PCR performed on cutaneous lesions swabs collected from children <16 years old.
Results: None of the cutaneous swabs collected from 14 children were positive for MKPV DNA. In contrast, 30/168 (17 %) cutaneous swabs collected from children were positive for VZV DNA. Of these 30 VZV-positive children, 7 had been suspected of MKPV infection because of their atypical rash, due to the location of the lesions and the chronology of their appearance.
Discussion: As in our cohort, pediatric cases of the 2022 Monkeypox outbreak in non-endemic developed countries have been very rare. This variant of MKPV does not normally spread easily and requires very close physical contact between an infected person (skin lesions, bodily fluids or respiratory droplets) and another person to be transmitted. It will nevertheless be a question of remaining vigilant as not to ignore the possibility of close contact or sexual transmission of Monkeypox in a child, or the possibility of a new and more contagious variant.
Conclusion: It is difficult to differentiate Monkeypox infection from other infections associated with rashes, it is important to remember that viruses change as well as their forms of presentation.

1. Introduction

In May 2022, cases of Monkeypox were reported in non-endemic countries, mostly in Europe [1–3]. Such a large epidemic of Monkeypox only occurred previously in sub-Saharan Africa. The current outbreak was revealed to be caused by Monkeypox viruses (MKPV) of clade B.1, the ancestors of which are from Western Africa [4]. At the epidemic onset, clinically distinguishing between atypical rash among cases related to MKPV and among the ones related to Varicella-Zoster virus (VZV), agent of Chickenpox that was co-circulating [5], may have been complicated. Indeed, knowledge on the epidemiology and clinical presentation of Monkeypox was initially based on cases that occurred in Africa. Epidemiologically, Monkeypox was reported to be a zoonotic disease with relatively limited outbreaks of human-to-human transmission, and to be transmitted through interaction with animals, close proximity to diseased individuals, or through contacts with

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Table 1
Description of the clinical features of the 7 pediatric patients with VZV infection.

Patients	Sex	Age	Medical condition	Previous VZV infection	Previous VZV vaccination	Contact VZV	Contact MKP	Trip abroad in the previous month	State of birth	Sexual exposure in the previous month	Symptôms	Evolution	VZV tests	MKP tests
1	F	15 Y	None	None	None	Unknown	Unknown	Non	France	None	Fever, disseminated vesicles, all lesions appeared simultaneously	Favorable without treatment	Positive IgM for VZV in serology Positive PCR VZV in blood and on cutaneous swab	Negative serology, and PCR MPK in blood and on cutaneous swab
2	F	11 Y	None	None	None	Suspected in the family 7 days ago	Unknown	Non	Nigeria	None	Fever, disseminated vesicles, lesions of different ages, perineal and palmoplantar involvement	Favorable without treatment	Positive PCR VZV on cutaneous swab	Negative PCR MPK on cutaneous swab
3	M	2 Y	None	None	None	Unknown	Unknown	Non	France	None	Fever, disseminated vesicles, appearance, lesions of different ages, perineal and palmoplantar involvement, mucosal involvement	Favorable without treatment	Positive PCR VZV on cutaneous swab	Not tested
4	F	2 W	None	None	None	Suspected in the family 10 days ago	Unknown	Non	France	None	Fever, disseminated vesicles, lesions of different ages, perineal and palmoplantar involvement	Favorable after 5 days acyclovir, 250mg/m2/8 h	Positive PCR VZV on cutaneous swab	Not tested
5	F	8 W	None	None	None	Suspected in the family 10 days ago	Unknown	Non	France	None	Fever, disseminated vesicles, lesions of different ages, perineal and palmoplantar involvement	Favorable without treatment	Positive PCR VZV on cutaneous swab	Not tested
6	F	2 Y	Asthma	None	None	Suspected at child caregiver's home	Unknown	Non	France	None	Fever, disseminated vesicles, lesions of different ages, perineal and palmoplantar involvement, cervical nodes	Favorable without treatment	Positive PCR VZV on cutaneous swab	Not tested
7	M	6 Y	None	None	None	Suspected at school	Unknown	Non	France	None	Fever, disseminated vesicles, lesions of different ages	Favorable without treatment	Positive PCR VZV on cutaneous swab	Not tested

Fig. 1. Images of the 7 pediatric patients with VZV infection (1 = patient 1, 2 = patient 2, 3 = patient 3, 4 = patient 4, 5 = patient 5, 6 = patient 6, 7 = patient 7).

infectious fomites [6]. Clinically, the rash was reported to be often preceded by a fever, to reach the face (perioral area), and to extend to other parts of the body in particular the palmoplantar, and perineal regions [7]. Regarding Chickenpox, widely communicated knowledge put forward that its associated rash spared the palmoplantar and perineal regions [8]. The onset of the 2022 Monkeypox outbreak in Europe led to screening virologically for MKPV in clinically suspicious cases, including Chickenpox patients. Results largely contributed to evidence in our institution as in other centers [9] that MKPV during this outbreak was in fact mostly sexually transmitted and almost only diagnosed among men having sex with men, and that the clinical presentation of Monkeypox cases largely differed from previous knowledge [9]. As of April 27, 2023, 5002 cases have been confirmed in France, including 24 pediatric cases (12 biologically confirmed, none since early 2023) [10].

2. Objectives

Herein, we described cases of children under 16 years old suspected to be infected with MKPV and diagnosed with Chickenpox in public hospitals of Marseille, south of France.

3. Material and methods

We conducted a retrospective study from March 23rd' 2022 to October 20th' 2022 in our institution of results of MKPV DNA and VZV DNA detection by PCR performed as previously reported [9] on swabs collected on cutaneous lesions from children <16 years old.

4. Results

None of the cutaneous swabs collected from 14 children were positive for MKPV DNA. In contrast, 30/168 (17 %) cutaneous swabs

collected from children were positive for VZV DNA. Of these 30 VZV-positive children, 7 had been suspected of MKPV infection because of their atypical rash, considering the location of the lesions and the chronology of their appearance that cast doubt on a clinical diagnosis of Chickenpox. Their characteristics are described in Table 1 and the images of their skin lesions appear Fig. 1. Thus, vesicles were present on palmoplantar, oral and anoperineal locations, the rash occurred in a single wave in some of the patients which is usually described as more specific of Monkeypox and rare in Chickenpox in literature [7], some patients were adolescent which is an uncommon age of presentation in Chickenpox, in other patients' lesions were deeply embedded in the dermis and indurated, which is less common in Chickenpox than Monkeypox. However, no contacts with Monkeypox patients were reported while the Chickenpox outbreak was ongoing in France where VZV vaccination is not currently recommended in the general population. Virologically, skin lesions from all the 7 children suspected of Monkeypox were tested positive for VZV DNA, while those sampled for 2 of these children were tested negative for MKPV DNA.

In contrast, 159 of the 434 adults and adolescents ≥16 years old (36 %) were tested positive for MKPV DNA on cutaneous swab during the same period and 93/714 (13 %) adults and adolescents ≥16 years old were tested positive for VZV DNA on cutaneous swabs in our institution.

5. Discussion

As in our cohort, pediatric cases of the 2022 Monkeypox outbreak in non-endemic developed countries have been absent or very rare. A Dutch article reported the case of a <10 years old boy who had no identified contact with a Monkeypox-positive individual and presented with lesions that appeared in several outbreaks (a few sores which developed into a thick blister filled with liquid and evolved into lesions drying up, crusting over and falling off), but no oral or perineal lesions [11]. Also, a cohort of 16 children was described in Spain, and suspected modes of transmission were sexual contacts among those over 15 years of age, and contacts with infected people at home or other forms of contact (e.g., body piercings) for the youngest cases [12]. The only Monkeypox children cases identified in our region were secondary to intrafamilial transmission and diagnosed in our laboratory [13]. In France, as of April 27th, 2023, 5002 cases have been confirmed, including 24 pediatric cases (12 biologically confirmed, none since early 2023) [10].

At the onset of the 2022 Monkeypox outbreak, it was recommended to screen for any suspected case: children were historically the age group most affected and most at risk of developing a severe form, and at risk of rapid spread through direct-contact and droplets at school, therefore it was logical to test them [3]. Distinguishing clinically in case of atypical rash among cases related to Monkeypox and cases related to Chickenpox was difficult when the mode of transmission was unclear. Almost one year after the start of this epidemic, prevalence has been extremely low in children (0,5 % in France) [10], which can alter the positive predictive value of the diagnostic tests [14]. The outbreak was evidenced as almost only sexually transmitted and involving mostly men having sex with men. This variant of MKPV does not normally spread easily and requires very close physical contact between an infected person (skin lesions, bodily fluids or respiratory droplets) and another person to be transmitted. As a matter of fact, this 2022 outbreak in non-endemic countries was a new disease, and epidemiological and clinical "keys" that were proposed initially at the National scale as guidelines for Monkeypox diagnosis were strongly challenged. This highlights that previous knowledge has to be used with caution in case of emergence of infectious agents. This was also exemplified at the time of the SARS-CoV-2 emergence, as the epidemiological and clinical spectrum of this infection largely differed from what was known for other human coronaviruses. It will nevertheless be a question of remaining vigilant as not to ignore the possibility of close contact transmission or sexual transmission of Monkeypox in a child, or the possibility of a new and more contagious variant.

6. Conclusion

Based on the recent experience of the Monkeypox outbreak and how difficult it was to differentiate it from other infections associated with rashes (as Chickenpox), and even if it has been rare in children, it is important to remember that viruses change as well as their forms of presentation.

CRediT authorship contribution statement

E. Riche: Investigation, Software, Writing – original draft. **S. Aherfi:** Software, Validation. **P. Colson:** Resources, Writing – review & editing. **B. La-Scola:** Resources, Writing – review & editing. **S. Mallet:** Visualization. **P. Minodier:** Resources. **C. Zandotti:** Resources, Writing – review & editing. **L. Luciani:** Software, Validation. **A. Morand:** Conceptualization, Data curation, Methodology, Resources, Supervision, Writing – review & editing.

Declaration of competing interest

This study was registered under the General Data Protection Regulation number PADS23-57. It adhered to the tenets of the revised Declaration of Helsinki and followed the STROBE guidelines. All the authors have no conflict of interest.

This study has been presented as a poster at the congress of the French Pediatric Society, in June 2023.

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