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Short communication

Merkel cell polyomavirus infection occurs during early childhood and is transmitted between siblings☆

Claire Martel-Jantin[a,b,c,1], Vincent Pedergnana[d,e,1], Jérôme T.J. Nicol[f,g,1], Valérie Leblond[f,g], David-Alexandre Trégouët[h], Patricia Tortevoye[a,b], Sabine Plancoulaine[a,b,c,d,e], Pierre Coursaget[f,g], Antoine Touzé[f,g], Laurent Abel[d,e,i,1], Antoine Gessain[a,b,*,1]

[a] Institut Pasteur, Unité d'Epidémiologie et Physiopathologie des Virus Oncogènes, Département de Virologie, F-75015 Paris, France
[b] CNRS, UMR3569, F-75015 Paris, France
[c] Université Paris Diderot, Cellule Pasteur, Paris, France
[d] Laboratoire de Génétique Humaine des Maladies Infectieuses, branche Necker, Institut National de la Santé et de la Recherche Médicale, U980, 156 rue de Vaugirard, 75015 Paris, France
[e] Université Paris Descartes Sorbonne Paris Cité, Institut Imagine, Paris, France
[f] Université F Rabelais, Faculté de Pharmacie, F-37200 Tours, France
[g] INRA UMR 1282, Unité Infectiologie et Santé Publique, F-37200 Tours, France
[h] INSERM UMR S 937, Université Pierre et Marie Curie, 75013 Paris Cedex 13, France
[i] St. Giles Laboratory of Human Genetics of Infectious Diseases, Rockefeller Branch, The Rockefeller University, New York, NY, USA

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ABSTRACT

Merkel cell polyomavirus (MCPyV) is thought to be the etiological agent of Merkel cell carcinoma, but little is known about its distribution and modes of transmission. We conducted seroepidemiological surveys in more than 1000 individuals, from two populations from Cameroon. Overall MCPyV seroprevalence was high in both populations (>75% in adults). Data from the first population, comprising mainly children, indicated that MCPyV infections mostly occurred during early childhood, after the disappearance of specific maternal antibodies. Results from the second family-based population provided evidence for familial aggregation of MCPyV infection status. We observed significant sib–sib correlation (odds ratio = 3.42 [95% CI 1.27–9.19], $p = 0.014$), particularly for siblings close together in age, and a trend for mother–child correlation (OR = 2.71 [0.86–8.44], $p = 0.08$). Overall, our results suggest that MCPyV infection is acquired through close contact, possibly involving saliva and/or the skin, especially between young siblings and between mothers and their children.

1. Background

Merkel cell polyomavirus (MCPyV) has recently been identified as the probable etiological agent of Merkel cell carcinoma (MCC), an uncommon, but aggressive skin cancer of neuroendocrine origin [1–3]. Recent serological studies have indicated that this virus is responsible for a common human infection, at least in individuals of Caucasian origin. Indeed, a high specific seroprevalence of MCPyV, increasing rapidly with age since childhood and reaching 50–90% in adults, has been reported in blood donors and populations of patients living in European countries and the USA [4–8]. However, seroprevalence data are lacking for other populations, and the routes by which this virus is transmitted and acquired remain unknown.

2. Objectives

The goal of this work was to obtain new insight into the modes of distribution and acquisition of this human oncogenic polyomavirus from family-based epidemiological analyses in African populations.

3. Study design

This study was carried out on two populations from Cameroon, Central Africa, in which we had previously carried out

* Corresponding author at: Chef de l'Unité d'Epidémiologie et Physiopathologie des Virus Oncogènes, CNRS-URA3015, 28 Rue du Docteur Roux, 75724 Paris Cedex 15, France. Tel.: +33 1 45 68 89 37; fax: +33 1 40 61 34 65.
E-mail address: antoine.gessain@pasteur.fr (A. Gessain).

[1] These authors contributed equally to this work.

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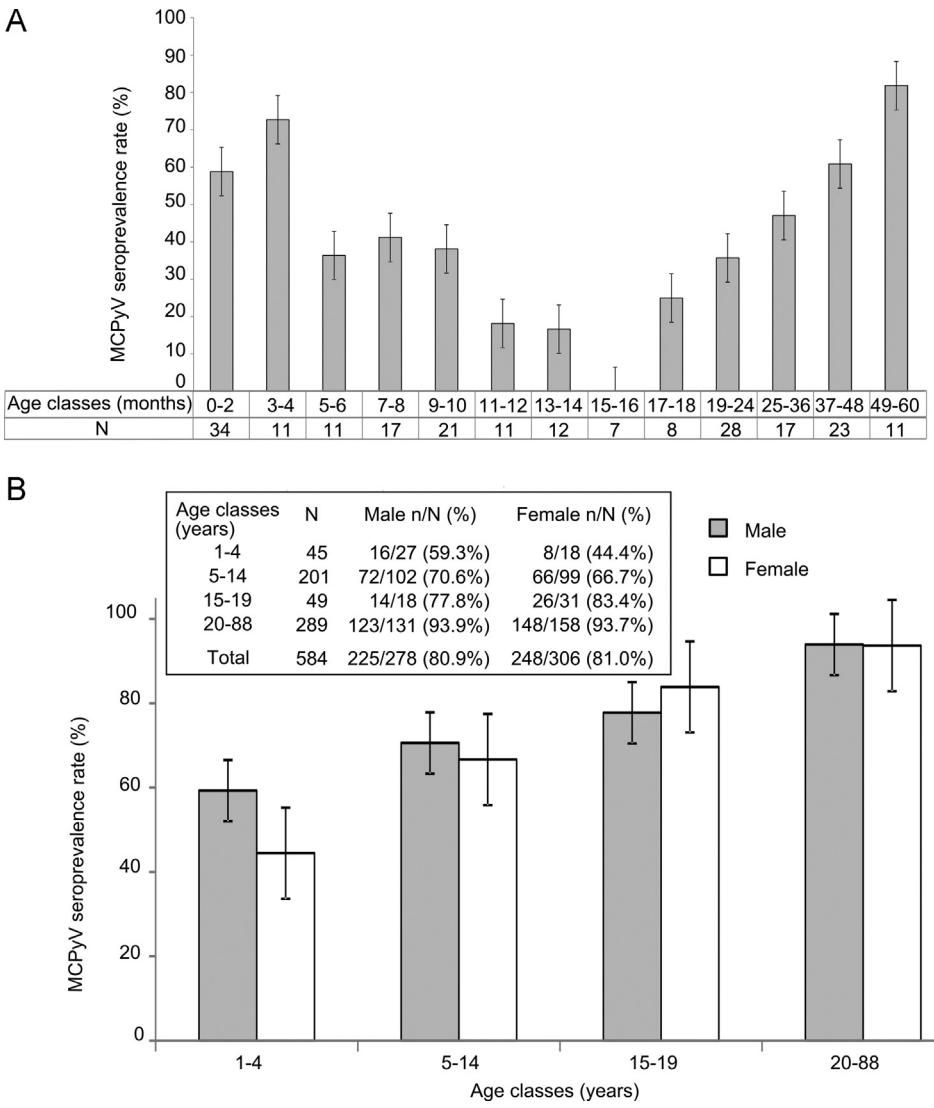

Fig. 1. Age-dependent Merkel virus seroprevalence in the two studied populations. (A) Age-dependent Merkel virus seroprevalence in 196 children aged 0–5 years from Yaoundé, Cameroon. Bars, 95% CI of the seroprevalence rates. N is the number of individuals per age class. (B) Age-dependent Merkel virus seroprevalence in 584 Bantou aged from 1 to 88 years from the village in the Ntem Valley, South Cameroon. Bars, 95% CI of the seroprevalence rates.

epidemiological studies searching for intrafamilial transmission of the human herpes virus 8 (HHV-8), the etiological agent of Kaposi sarcoma [9,10]. The first population, from Yaoundé, consisted mostly of children. The second consisted of villagers living in an isolated rural area of Southern Cameroon in which it was possible to establish familial relationships with full pedigrees. This survey was performed after authorization had been obtained from the local authorities and from the National Ethics Committee in Cameroon. In France, it was approved by the *Comité de Protection des Personnes* (N° 11-02-02). Each participant was provided with information about the study and informed consent was obtained from adults or from the parents of minors.

An ELISA detected specific antibodies against MCPyV. More specifically, anti-VP-1 antibodies were detected with MCPyV-like viral particles (VLPs) generated in insect cells, as previously described [7,11]. Briefly, microplates (Maxisorp, Nunc) were coated overnight at 4 °C with 100 ng/well of purified MCPyV VLPs. Plasma samples were tested at a 1:100 dilution and human IgG binding was detected by peroxidase-conjugated anti-human IgG (Southern Biotech, Clinisciences, Nanterre, France) diluted 1:20,000. A cut-off value for positive samples of 0.2 was used as previously determined [7,11].

4. Results

In the first population, which comprised 458 individuals (229 male and 229 female subjects), 68% of whom were children, the overall seroprevalence of antibodies directed against MCPYV VP-1 was 59%, with no significant difference ($p = 0.25$) between male (57%) and female (62%) subjects (Supplementary Figure 1). We further investigated the age at which the virus was acquired, by focusing on young children. Seroprevalence was quite high, at about 60–70%, from birth until the age of 4 months (Fig. 1A). Interestingly, this seroprevalence is very similar to that observed in women of child-bearing age (~70%). Seroprevalence then decreased with age, reaching 0% at 15–16 months of age, although there were only seven children in this age class. Seroprevalence then rapidly and steadily increased, beginning at 17 months of age, to reach about 60–80% in children aged 4–5 years. This pattern of seroprevalence in young children is consistent with the presence of maternal antibodies in very young children. These maternal antibodies then progressively disappear and infection is rapidly acquired in most children, beginning from the age of about 16 to 18 months.