COMUNICATION

Clinical and histopathological characterization and typing of the human papillomavirus in common warts of kidney transplant recipients

Caracterização clínica e histopatológica e tipagem do papilomavírus humano das verrugas vulgares nos receptores de transplante renal

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Abstract: The prevalence of skin lesions caused by the human papillomavirus (HPV) is high in kidney transplant patients. Twenty recipients of kidney transplants with a diagnosis of common warts were evaluated. HPV detection was performed by polymerase chain reaction (PCR) using the MY09/MY11 and RK91 primers. HPV typing was performed by restriction fragment length polymorphism analysis and direct sequencing. The presence of HPV was identified in 10 patients (50%) and the types identified were HPV-2, 27, 29, 34 and 57.
Keywords: Human papillomavirus infections; Kidney transplant; Warts

Resumo: Os pacientes receptores de transplante renal apresentam elevada prevalência de lesões cutâneas por HPV. Foram estudados 20 receptores de transplante renal com diagnóstico de verruga vulgar. A detecção do HPV foi realizada pela polimerização em cadeia (PCR) com os *primers* MY09/MY11 e RK91. A tipagem do HPV foi feita por meio da restrição enzimática e do sequenciamento automatizado. Identificamos a presença do HPV em 10 pacientes (50%) e os tipos identificados foram: HPV-2, 27, 29, 34 e 57.
Palavras-chave: Infecções por papilomavírus; Transplante de rim; Verrugas

Kidney transplant recipients have a 15-50% likelihood of developing common warts associated with the human papillomavirus (HPV) in the first year following the transplant and a 77-95% likelihood within five years. [1] With respect to the detection and typing of HPV in common warts, few publications are available of studies conducted in the Brazilian population, the only study having been carried out in an immunocompetent population infected by the human immunodeficiency virus (HIV) and in patients with epidermodysplasia verruciformis. [3] Therefore, the objective of the present study was to evaluate the clinical and histopathological characteristics of common warts in kidney transplant recipients and identify the types of HPV present in the lesions.

Twenty kidney transplant recipients with a clinical and histopathological diagnosis of common warts were evaluated and submitted to HPV detection (using polymerase chain reaction [PCR] with the MY09/11 and RK91 primers) and typing (using restriction fragment length polymorphism analysis [RFLP] and/or direct sequencing).

The mean age of the patients was 47.9 years. There was no difference in the incidence of the condi-

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Table 1: Distribution of kidney transplant recipients in accordance with the age and gender of the patient, time since transplantation, type of donor, time since developing warts, number of lesions and site of lesions

N.	Age (Years)	Sex	Tempo de transplante (meses)	Type of donor	Time since developing warts (months)	Number of lesions	Region of the body
1	36	M	52	living (nephew)	3	1	Right upper limb
2	33	F	92	living (husband)	24	1	Trunk
3	52	F	83	deceased	60	>20	Right and left upper limbs, right and left lower limbs, head.
4	67	F	93	deceased	120	2	Right upper limb, head
5	29	F	54	living (brother)	48	5	Right and left upper limbs, right lower limb
6	62	F	274	living (sister)	24	10	Right and left upper limbs, trunk
7	18	F	19	deceased	12	9	Right and left upper limbs
8	65	F	219	deceased	36	>20	Right and left upper limbs, right and left lower limbs, trunk
9	44	F	7	deceased	3	3	Right upper limb, head
10	53	M	44	deceased	5	1	Head
11	57	F	75	living (sister)	1	3	Right upper limbs
12	40	M	91	deceased	5	3	Right and left upper limbs, right lower limb
13	33	M	33	living (sister)	4	13	Right and left upper limbs
14	40	M	66	living (sister)	36	1	Left upper limb
15	67	M	13	deceased	12	2	Right and left lower limbs
16	58	M	79	living (sister)	12	>20	Right upper limb, right lower limb
17	55	M	9	living (sister)	4	4	Head, trunk
18	57	M	70	living (sister)	24	>20	Head, trunk, right and left upper limbs, right and left lower limbs
19	47	M	74	living (sister)	72	4	Left upper limb
20	45	M	90	living (sister)	3	>20	Right and left upper limbs

M = Male, F = Female

tion between the sexes (Table 1).

Eighty percent of the patients had more than one common wart, with 25% having more than 20 lesions, thus confirming the ease of infection and dissemination of HPV in kidney transplant recipients (Figure 1).

Figure 1: Clinical appearance of a common wart in a kidney transplant recipient

After six months of high-dose immunosuppressive therapy (induction phase), the dose of immunosuppressive drugs administered to the kidney transplant recipients was reduced in the so-called maintenance phase. In agreement with other reports in the literature,[4] it was in this phase that the highest frequency of common warts was found. The mean time since transplantation in patients in this study was 76.9 months.

Typical histopathological findings in common warts of immunocompetent individuals, such as hyperkeratosis, hypergranulosis and papillomatosis, were also found in the kidney transplant recipients. With respect to the histopathological signs of viral activity in these common warts, a high frequency of koilocytosis was found (85%) and, to a lesser extent, the presence of clumps of keratohyalin granules (70%). Parakeratosis was a less frequent finding

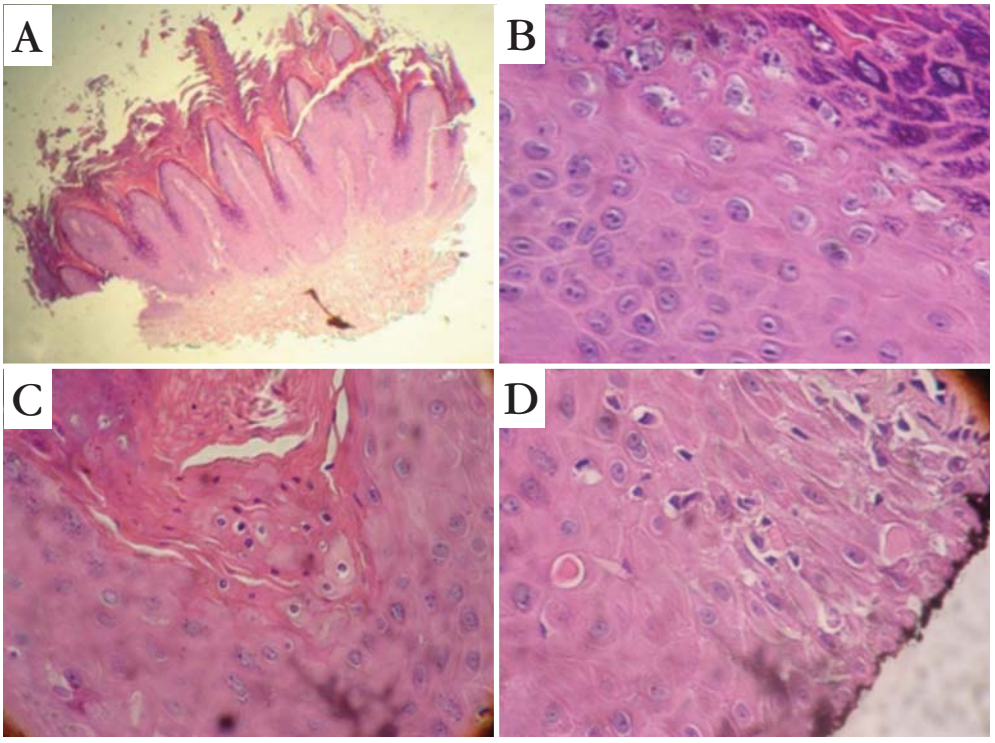

Figure 2: Histopathology of a common wart in a kidney transplant recipient. **A** Hyperkeratosis, hypergranulosis and papillomatosis (hematoxylin-eosin staining, magnification 40x). **B** Koilocytosis and clumps of keratohyalin granules (hematoxylin-eosin staining, magnification 400x). **C** Hyperparakeratosis (hematoxylin-eosin staining, magnification 400x). **D** Hyalin bodies/dyskeratotic cells in the epidermis (hematoxylin-eosin staining, magnification 400x)

(20%). This may represent a histological characteristic of old warts and, indirectly, the chronicity of this process in kidney transplant recipients, and is in agreement with the long duration of the condition, as reported by the patients. Analyzing the presence of vacuolization of the keratinocytes, which also characterizes viral infection, this was found principally in the upper layers of the epidermis, in agreement with lesions described in the literature (Figure 2). [5]

The HPV types described in the international literature as being the most frequently found in common warts of immunocompetent individuals are HPV-

Table 2: PCR results with MY09/MY11 and RK91 primers, RFLP analysis and sequencing

Patient	PCR MY09 MY11 Primers	RFLP analysis	PCR RK91 Primer	Sequencing
1	Negative	N/A	Negative	N/A
2	Positive	HPV-34	Negative	N/A
3	Negative	N/A	Negative	N/A
4	Negative	N/A	Positive	HPV-29 - 99%
5	Positive	HPV-27	Positive	NI
6	Negative	N/A	Negative	N/A
7	Positive	HPV-34	Positive	NI
8	Negative	N/A	Negative	N/A
9	Positive	HPV-2a	Negative	N/A
10	Positive	NI	Negative	N/A
11	Negative	N/A	Positive	HPV-2a - 99%
12	Negative	N/A	Positive	HPV-57 - 99%
13	Negative	N/A	Negative	N/A
14	Negative	N/A	Negative	N/A
15	Negative	N/A	Positive	HPV-57c - 99%
16	Negative	N/A	Negative	N/A
17	Negative	N/A	Negative	N/A
18	Negative	N/A	Negative	N/A
19	Negative	N/A	Positive	NI
20	Negative	N/A	Negative	N/A

HPV = human papillomavirus; N/A = not applicable; NI = not identified;
PCR = polymerase chain reaction; RFLP = restricted fragment length polymorphism.

2, HPV-27 and HPV-57. [6] In the present study, the presence of HPV was detected in 10 patients (50%). HPV-2, HPV-34 and HPV-57 were detected in two samples each and HPV-27 and HPV-29 in one sample each (Table 2). In two patients, the HPV types were not identified despite their positivity for the MY09/MY11 and RK91 primers. HPV-2, HPV-27, HPV-29 and HPV-57 have already been described in common warts of kidney transplant recipients. [7-9] One interesting finding was that HPV-34, an alpha-papillomavirus commonly described in mucosal infections, was identified in two of the patients in the present study. On the other hand, HPV-2, HPV-27, HPV-29 and HPV-57 have been detected all over the skin. The MY09/11 and RK91 primers failed to detect any of the types described in epidermodysplasia verruciformis in the patients in the present study. [10]

Depending on the HPV type, skin infection may be associated with an increase in the incidence of carcinomas, particularly squamous cell carcinoma. In kidney transplant recipients, the proliferation of keratotic lesions in exposed areas often results in diagnostic confusion between common warts, actinic keratoses and seborrheic keratoses as well as squamous cell carcinoma. The presence of multiple, polymorphic and atypical skin lesions was also found in the population of the present study, principally in exposed areas subject to micro-traumatisms and sun exposure such as the upper and lower limbs.

The low detection rate of HPV in the lesions of patients in this study may be explained by the presence of unusual HPV types not commonly found in common warts. In this case, repeating PCR using other primers may increase the likelihood of HPV detection.❑

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