

## Four cancers related to HPV 16 infection in a 34-year-old woman

### *Cztery ogniska raka związanego z infekcją HPV 16 u 34-letniej kobiety*

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**Słowa kluczowe:** leczenie chirurgiczne, radioterapia, rak płaskonabłonkowy, wirus brodawczaka ludzkiego.

#### Abstract

Human papilloma viruses are widespread among people. Two hundred subtypes of these viruses have been described. Most of the infections are not clinically relevant. Long-term infection by some high sub-type of human papilloma virus, however, can lead to pre-invasive and invasive cancers of urogenital organs, head and neck region, and skin. The paper presents the case of 34-year-old woman in whom four cancers associated with infection with human papilloma virus subtype 16 were diagnosed. The patient was treated with surgery and radiotherapy for cancers of the vulva, the perianal area, fingers, and cervix. This paper describes the course and outcome of the treatment.

#### Streszczenie

Wirusy brodawczaka ludzkiego są rozpowszechnione wśród ludzi. Opisano ok. 200 podtypów tych wirusów. Większość infekcji wirusem brodawczaka ludzkiego nie ma klinicznego znaczenia, jednak przy długotrwałej infekcji podtypem wysokiego ryzyka wirus ten może powodować raka przedinwazyjnego i inwazyjnego układu moczowo-płciowego, regionu głowy i szyi oraz skóry. W pracy przedstawiono przypadek 34-letniej kobiety, u której zdiagnozowano cztery ogniska raka związanego z infekcją wirusem brodawczaka ludzkiego podtypu 16. Pacjentka była poddana leczeniu skojarzonemu – chirurgii i radioterapii, z powodu raka sromu, skóry okolicy okołoodbytowej, palców i szyjki macicy. W artykule opisano przeprowadzone leczenie i jego wyniki.

#### Introduction

Human papillomaviruses are widespread among people. Papillomaviruses are human pathogenic viruses. Specific types can cause cervical cancers and their high-grade precursor lesions. Human papilloma virus can induce also a great variety of neoplastic lesions of mucosa epithelia and skin. The long lasting infection by some subtypes (subtype 16, 18) can lead to pre-invasive and invasive cancers of urogenital organs, head and neck region, and skin. These tumours account for 5.2% of the whole worldwide cancer burden [1–3].

This paper presents the case of the patient with four cancers caused by human papilloma virus (HPV

subtype 16). Multifocal infection: fingers, anus area, vulva, and vagina could be caused by a mechanical transmission of the virus because of clinical symptoms (itching). The patient was diagnosed and successfully treated.

#### Case report

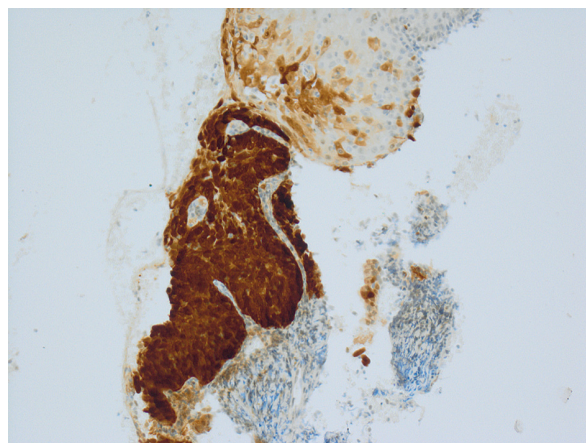
A 34-year-old woman was admitted in December 2009 to Holycross Cancer Centre (HCC) in Kielce with changes in vulva and skin around the anus. In addition, the patient complained of pain in the fingers of both hands, caused by periungual ulcers, which were observed for several years. Before being admit-

ted to HCC, based on biopsy, squamous cell cancer of the fingers was recognised, and for this reason she was treated with a photodynamic therapy without good effect. In the clinical examination at admission, tumour of the vulva, around the anus on the skin ulcers, lumps and discoloration were observed. Based on specimens from the vulva and anal area, vulvar intraepithelial neoplasia (VIN) 3 and anal intraepithelial neoplasia (AIN) 3 were diagnosed. The patient was qualified to vulvectomy and regional lymph node dissection. The procedure was carried out in March 2010. The histopathological diagnosis was squamous cell carcinoma G2, and pathological diagnosis was established at pT2 N0 M0 (primary tumour size of 90 mm). The patient was referred to receive adjuvant pelvic radiation therapy to the vulva, regional lymph nodes, and the area of the anus. A total dose of 60 Gy fractionated conventionally was delivered. She completed radiotherapy on 2<sup>nd</sup> October 2010. During the first and subsequent control visits at HCC there was no recurrence in the area in the vulva, and complete regression of changes in the anal area were observed. In 2011 (August–November) radical irradiation to the distal phalanges of the fingers with a dose of 60 Gy in 30 fractions was carried out with total regression of tumours. On the 2<sup>nd</sup> April 2012, the patient was operated by total hysterectomy because of pre-invasive cancer of the cervix. Histopathological diagnosis confirmed pre-invasive cancer. The Department of Pathology in Holycross Cancer Centre performed the immunohistochemical examination and confirmed infection of HPV 16 in histopathological material from the vulva, anus, cervix, and fingers (Figure 1). The most recent clinical review of the patient in November 2016 showed no signs of the tumour in the pelvis and fingers. The function of the fingers was assessed as good and unaltered.

## Discussion

Human papillomaviruses are widespread among people. Two hundred subtypes of these viruses have been described. They move mainly by sexual contact and by skin contact. Some of these viruses cause infections in the genitourinary region both in men and women. Most of the infections are not clinically relevant. However, some high-risk subtypes of long-term infection, often lasting years, may lead to carcinogenesis and the formation of malignant tumours of the anogenital area, the lower gastrointestinal tract, the region of the head and neck, and skin. High-risk subtypes are: 5, 8, 16, and 18 [1, 2].

Multifocal infection: fingers, anus area, vulva, and vagina, can be caused by mechanical transmission of the virus because of clinical symptoms (itching). Some subtypes can also be detected in pre-invasive changes cervical intraepithelial neoplasia (CIN), AIN, or VIN [4].



**Figure 1.** Positive IHC for protein P 16 characteristic for HPV 16

Currently there is no targeted drug therapy for HPV infection. The body itself fights with it using immunological mechanisms. The treatment of benign lesions caused by HPV uses surgery, laser therapy, or cryotherapy. Treatment is more aggressive in the case of malignant tumours, and in many cases it is combined (surgery, radiotherapy, and chemotherapy). In the case of vulvar and cervical cancers, treatment of patients is determined by the stage [5]. For patients with a diagnosis of invasive cancer of the anal canal and the skin around the anus, chemo-radiotherapy is the standard [5]. This treatment modality is, however, not recommended in patients with pre-invasive cancer. In our patient's case the consensus decision was to combine perianal region irradiation with post-vulvectomy radiotherapy. The treatment resulted in complete regression of the lesions without evidence of damage to the sphincter function.

Multifocal squamous cell carcinoma of the skin of the fingers constituted a simultaneous therapeutic problem for this patient. Previous conservative treatment was not effective. The patient did not accept the amputation of phalanges. Cancer involved several fingers of both hands: left – fingers II and IV, right – five fingers. The literature describes tumours in fingers, with the thumb being the most frequent location – 44% of all cases [6]. Changes typically involve the distal phalanx. The disease is most common in men aged 50–69 years, and the vast majority concerns right hand [7]. The symptoms of this disease are soreness, changes in the shape of the nail, pain, swelling, itching, redness, and purulent discharge, depending on the stage [8]. In the case of bone involvement, amputation is the method of choice. Local microsurgery can be an alternative to amputation. The use of tissue transplants is sometimes necessary to cover the tissue loss. Radiation therapy may be effective in such patients. Grootenboers presented the history of 12 patients with subungual squamous cell carcinoma



**Figure 2.** Left hand of the patient 5 years after radiotherapy

treated with irradiation. The mean follow-up time was 62 months. Complete regression was achieved in 11 patients, in one patient with a recurrence, but the amputation of the phalanx was effective. The functional effect was good in 10 patients [9]. Yarpalvi *et al.* described the case of a patient irradiated with 60 Gy due to cancer of the nail with an observation period free of recurrence of 17 months [10]. Rosen described three patients treated with radiotherapy of the fingers. After the 4-year follow-up there was no local recurrence. Functional outcome was also good. The total dose of radiation was 55–62.5 Gy in 22–25 fractions [11]. The technique and radiation doses used in our patient were consistent with the literature data. Functional outcome was also good (Figure 2).

## Conclusions

Chronic infection with human papillomavirus can cause multifocal invasive or non-invasive cancers. The use of treatment: surgery and radiotherapy in a 34-year-old patient with four foci of cancer in the anogenital and skin areas was effective. Five years after the treatment to the pelvis and fingers of both hands the patient is alive, without evidence of recurrence or spread of cancer. There were no complications of radiation therapy and surgery.

## Conflict of interest

The authors declare no conflict of interest.

## References

- zur Hausen H. Papilloma viruses and cancer: from basic studies to clinical application. *Nat Rev Cancer* 2002; 2: 342-50.
- Parkin DM, Bray F. The burden HPV-related cancers. *Vaccine* 2006; 24 (Suppl. 3): 11-25.
- Parkin DM. The global health burden of infection-associated cancers in the year 2002. *Int J Cancer* 2006; 118: 3030-44.

- Stanley MA, Winder DM, Steling JC, Goon PK. HPV infection, anal intraepithelial neoplasia (AIN) and anal cancer: current issues. *BMC Cancer* 2012; 12: 398.
- Zalecenia postępowania diagnostyczno-terapeutycznego w nowotworach złośliwych. Krzakowski M, Dziadziuszko R, Fijuth J, Herman K, Jarosz J, Jarzab M, Jassem J, Kawecki A, Kornafel J, Kowalski DM, Krzemieniecki K, Litwiniuk M, Mazurkiewicz T, Mądry R, Misiak M, Nawrocki S, Polkowski W, Potemski P, Rubach M, Rutkowski P, Stelmach A Wysocki PJ (eds). *Via Medica*, Gdańsk 2011.
- Bui-Mansfeld L, Pulcini JP, Rose S. Subungual squamous cell carcinoma of the finger. *AJR* 2005; 185: 174-5.
- Attiyeh FF, Shah J, Booher RJ, Knapper WH. Subungual squamous cell carcinoma. *JAMA* 1979; 241: 262-3.
- Lumpkin LR 3<sup>rd</sup>, Rosen T, Tschen JA. Subungual squamous cell carcinoma. *J Am Acad Dermatol* 1984; 11: 735-8.
- Grootenboers D, Poortmans P, Haas R. Radiotherapy preserves fingers in the management of subungual cell carcinoma, obviating the need for amputation. *Radiation Oncol* 2007; 85: 473-5.
- Yarpalvi R, Mhadevia PS, Gorla GR, Beitler JJ. Radiation therapy for the salvage of unresectable squamous cell carcinoma. *Dermatol Surg* 2003; 29: 294-6.
- Rosen L, Powell K, Katz S, Wu HT, Durci M. Subungual squamous cell carcinoma: radiation therapy as an alternative to amputation and review of the literature. *Am J Clin Dermatol* 2010; 11: 285-8.

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