One patient, two rare diseases: coexistence of epidermodysplasia verruciformis and Merkel cell carcinoma

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A 58-year-old woman with epidermodysplasia verruciformis (EV) diagnosed based on clinical manifestation and histological examination, was admitted to our clinic for a routine examination. Initial symptoms of EV were observed at the age of 17. The patient also reported a history of multiple basal and squamous cell carcinomas and Bowen disease. Physical examination revealed a typical EV lesion (FIGURE 1A and 1B) and an advanced basal cell carcinoma on the left auricle, which the patient had refused to treat (FIGURE 1C). Additionally, a firm, painless, immovable tumor on the left cheek was observed, accompanied by enlargement of cervical and submandibular lymph nodes on the left side (FIGURE 1D). According to the patient, the lesion appeared 3 months prior to the visit; it was painless and rapidly growing. Histological examination confirmed Merkel cell carcinoma (MCC), negative for leukocyte antigen (LCA–) and positive for nonspecific enolase (NSE+) and cytokeratin 20 (CK20+) (FIGURE 1E). On follow-up examination 3 weeks later, the tumor on the cheek increased significantly, with additional edema of the upper and lower eyelids on the left side (FIGURE 1F). The patient was referred to the Department of Maxillofacial Surgery; however, due to the size of the tumor and lymph node involvement, she was not eligible for surgery and received chemotherapy instead (no detailed medical data were available). The woman died as a result of multiple metastases a few months after the first manifestation of the disease.

Epidermodysplasia verruciformis is a very rare genodermatosis associated with the mutation of the *TMC6/EVER1* and *TMC8/EVER2* genes. It is characterized by an increased predisposition to infection with specific types of human papillomavirus, EV-HPV, while maintaining a proper response to bacterial and fungal infections. It manifests in childhood with skin lesions such as flat warts and tinea versicolor–like macules and patches located throughout the body. After the age of 30, most patients with EV develop skin cancers which arise mainly within previous erythematous lesions and are located primarily on body surfaces exposed to solar radiation. Most common types include squamous cell carcinoma and Bowen disease, whereas basal cell carcinoma develops less frequently. In patients with benign lesions, a large variety of EV-HPV infections have been identified, with EV-HPV-5 and EV-HPV-8 as the viruses most commonly associated with malignant neoplastic transformations in the skin.[1,2]

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FIGURE 1 A, B – pityriasis versicolor–like skin lesions in a patient with epidermodysplasia verruciformis





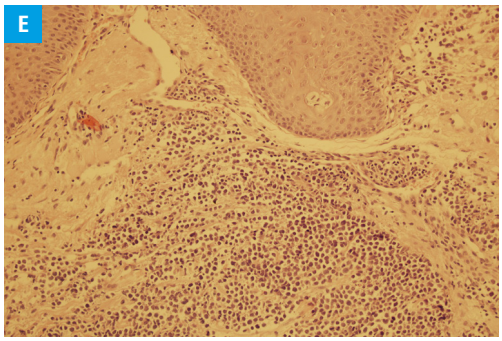




FIGURE 1
C – an ulcerated type of basal cell carcinoma; **D** – Merkel cell carcinoma on the left cheek; an ulcerated and infiltrated tumor; **E** – histological examination showing Merkel cell carcinoma cells (magnification × 10); **F** – Merkel cell carcinoma 3 weeks after identification: a significant expansion of the tumor

Merkel cell carcinoma is a very rare neuroendocrine cutaneous neoplasm originating from Merkel mechanoreceptors. The Surveillance of Rare Cancers in Europe (RARECARE) database reported the incidence rate of 0.13 per 100 000 between the years 1995 and 2002.[3] This malignancy is also associated with old age. The risk factors include: White ethnicity, exposure to ultraviolet light, infection with Merkel cell polyomavirus, history of hematological neoplasms as well as long-lasting iatrogenic immunosuppression. Lesions frequently present as firm, red to purple, nontender papules or nodules characterized by a rapid growth. Head and neck are involved in 48% of cases. Merkel cell carcinoma is a very aggressive, malignant tumor with a high mortality rate and a tendency to metastasize.[4] Avelumab, a human monoclonal antibody, is a novel therapeutic option with proven efficiency in patients with MCC metastasis.[5]

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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