Acta Otorrinolaringol Esp. 2013;64(6):396–402

Acta Otorrinolaringológica Española

www.elsevier.es/otorrino

ORIGINAL ARTICLE

Primary Cutaneous Neuroendocrine Carcinoma, Merkel Cell Carcinoma. Case Series 1991–2012☆

Ramón Campillo,[a] Elisa Gil-Carcedo,[b,*] David Alonso,[a] Luis A. Vallejo,[b] Juan M. Oñate,[c] Luis M. Gil-Carcedo[b]

[a] *Servicio de Cirugía Plástica, Hospital Universitario Río Hortega, Universidad de Valladolid, Valladolid, Spain*
[b] *Servicio de Otorrinolaringología, Hospital Universitario Río Hortega, Universidad de Valladolid, Valladolid, Spain*
[c] *Servicio de Anatomía Patológica, Hospital Universitario Río Hortega, Universidad de Valladolid, Valladolid, Spain*

Received 12 March 2013; accepted 24 June 2013

KEYWORDS
Carcinoma;
Old age;
Skin;
Neuroendocrine;
Immunohistochemistry;
Surgery;
Radiochemotherapy

Abstract
Introduction and objectives: Merkel cell carcinoma was first described by Toker in 1972. It is an uncommon, primary neuroendocrine skin carcinoma which appears in the dermoepidermic area, grows fast, is very aggressive and has a poor prognosis. The aim of this work is to highlight the importance of this tumour, which develops mainly in the skin of the head and neck area, and whose prevalence has increased in recent years.
Material and method: We gathered data on 16 patients suffering cutaneous neuroendocrine carcinoma treated at our hospital between September 12, 1991 and July 13, 2012. We indicated the age and gender of patients. We described the area where the tumour was located, indicating the size in millimetres, according to the major axis of the lesion.
Results: Most of the patients studied were over 70 years old, except for one who was 55. The highest frequency of cases appeared among patients aged over 80 years. In the cases studied, when the tumour appeared in the head and neck region (10/16), its location could be nasal-lateronasal, cheek-malar, upper eyelid, frontal or mandibular. The major axis of the lesion ranged between 7 and 35 mm. Unlike with epidermoid or basocellular carcinomas, recurrence and ganglionar metastases were common. Immunohistochemical (CK20) tests are essential for a correct diagnosis. Treatment is usually surgical and occasionally followed by radiotherapy and chemotherapy.
Conclusion: This carcinoma is not a very common skin tumour. It appears in old age, in the head and neck region in 50% of cases and often leads to exitus.

☆ Please cite this article as: Campillo R, Gil-Carcedo E, Alonso D, Vallejo LA, Oñate JM, Gil-Carcedo LM. Carcinoma neuroendocrino primario de la piel, carcinoma de células de Merkel. Casuística 1991-2012. Acta Otorrinolaringol Esp. 2013;64:396–402.

* Corresponding author.
E-mail address: e.gilcarcedo@gmail.com (E. Gil-Carcedo).

2173-5735/$ - see front matter

PALABRAS CLAVE
Carcinoma;
Anciano;
Piel;
Neuroendocrino;
Inmunohistoquímica;
Cirugía;
Radioquimioterapia

Carcinoma neuroendocrino primario de la piel, carcinoma de células de Merkel. Casuística 1991-2012

Resumen
Introducción y objetivos: El llamado clásicamente carcinoma de células de Merkel fue descrito por Toker en 1972, se trata de un carcinoma neuroendocrino primario de la piel. Aparece en la unión dermoepidérmica, es poco frecuente, de crecimiento rápido, agresivo y de mal pronóstico. El objetivo de este trabajo es dar a conocer este carcinoma que se implanta preferentemente en la piel de la cabeza y del cuello, y que aumenta su prevalencia en los últimos años.
Material y método: Recogemos 16 pacientes afectados por el carcinoma neuroendocrino primario de la piel, tratados en nuestro centro entre 12/09/91 y 13/07/12. Se precisa la edad y el sexo. Se describe la zona de implantación del tumor. Su tamaño lo expresamos en milímetros según el eje mayor de la lesión.
Resultados: Nuestros pacientes son mayores de 70 años, excepto la última incluida que contaba 55, la mayor frecuencia es en mayores de 80. Los casos recogidos, cuando asientan en la piel de cabeza y cuello (10/16) tienen localización: nasal-lateronasal, mejilla-malar, párpado superior, frontal, mandibular. El eje mayor de la lesión oscila entre 7 y 35 mm. A diferencia de lo que ocurre en los carcinomas espinocelulares o basocelulares son frecuentes las recurrencias y las metástasis. Para el diagnóstico es imprescindible la inmunohistoquímica con citoqueratina 20. El tratamiento es quirúrgico, ocasionalmente seguido de radioterapia y quimioterapia.
Conclusión: Se trata de un carcinoma poco frecuente de la piel, aparece en la edad avanzada, asienta en cabeza y cuello en más del 50% de los casos y conduce con frecuencia al exitus.

Introduction

Merkel cell carcinoma was first described by Toker in 1972 when reporting 5 cases of elderly patients with solid tumours apparently derived from the dermis and hypodermis. When viewed under an optical microscope, their fundamental histo-architectural feature was seen to be the trabecular or string formation of cells with scant cytoplasm, for which reason it was referred to as cutaneous trabecular carcinoma. Toker initially assumed this tumour to be derived from undifferentiated eccrine gland cells.[1]

When later studied under electron microscopy using immunohistochemistry techniques, the presence of electrodense granules was detected, along with a positive response to neuroendocrine and epithelial staining, characteristics shared by Merkel cells, so it began to be referred to as a Merkel cell tumour.

In 1875, Sigmud Merkel detected clear oval cells on the dermoepidermal junction and these elements (which have since borne his name) are arranged to form an extensive axis at the level of the base layer, in close relation with melanocytes and nerve cells.

Although the exact origin and function of Merkel cells is still under investigation, they are thought to have characteristics of both epithelial and neuro-endocrine origin, and to arise from cells with the function of responding to mechanical pressure (mechanoreceptors). The most widely accepted hypothesis at the present time is that they originate on a common pluripotential precursor that gives rise to neuroendocrine and epithelial cells.[2–7]

This carcinoma has received a number of names in the articles published in the literature: Toker's tumour, cutaneous neoplasma of Merkel cells, cutaneous apudoma, neuroendocrine carcinoma of the skin, primitive carcinoma of small skin cells, primary undifferentiated carcinoma of the skin, cutaneous carcinoma of murky cells, primitive cutaneous carcinoma of small cells with endocrine differentiation and malignant trichodiscoma.[2] We believe that the denomination best identifying its characteristics is that used in the title of this paper: primary cutaneous neuroendocrine carcinoma (PCNC).

This is a fast-growing carcinoma of the skin that appears on the dermo-epidermal junction. It is an infrequent, aggressive tumour with a poor prognosis and low survival rate, characterized by its relatively early tendency to invade lymph nodes and blood vessels, and by a high percentage of loco-regional recurrence in the year after surgical removal.

In a large percentage of PCNC cases, the existence of a mutation has been found, using molecular biology techniques, in the short arm of chromosome 10, which would bring about the inactivation of PTEN (a tumour suppressor gene).[8]

In 27% of cases, this malignant tumour is associated with the concomitant existence of other cutaneous neoplasias, such as Bowen's carcinoma, basal cell carcinoma or epidermoid carcinoma. PCNC may appear together with lymphocytic leukaemia, B cell lymphoma or myeloma; and also in patients with immunological alterations, those subjected to organ transplants, or under prolonged treatment with immunosuppressant drugs.[7–10]

PCNC habitually presents in Caucasian adults over 65 years of age, although cases have been reported in young patients carrying congenital ectodermal dysplasia syndrome. The advanced age of onset is related to the physiological reduction in both humoral and cellular immune function in elderly patients.[11,12]