

Merkel cell carcinoma: need for information and awareness. A case series of 47 patients from an Italian website

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ABSTRACT

Merkel cell carcinoma (MCC) is a rare and aggressive neuroendocrine tumor of the skin. The clinical experience with this tumor is generally limited. A sample of 47 cases of our series was collected from the website www.neuroendocrini.it. The data on these patients offer some insight into the difficulty of managing MCC as a result of inappropriate therapeutic approaches and neglect of existing recommendations, which may lead to poor survival associated with a very low quality of life. We have observed that networks can be useful for information sharing so that the needs of the patient can be met.

Introduction

Merkel cell carcinoma (MCC) is a rare and aggressive tumor of the skin characterized by frequent local relapses, progression of disease, poor quality of life, and short survival¹. MCC was first described by Toker² in 1972 as a trabecular carcinoma of the skin, and later as a neuroendocrine carcinoma of the skin, placing it therefore in the large family of APUDomas³⁻¹⁰.

Our observation of a large number of cases of MCC, the majority as a request for a second opinion following local relapse or progression of disease¹¹, has induced us to review the expertise and level of information concerning MCC, also with the support of a personal website network.

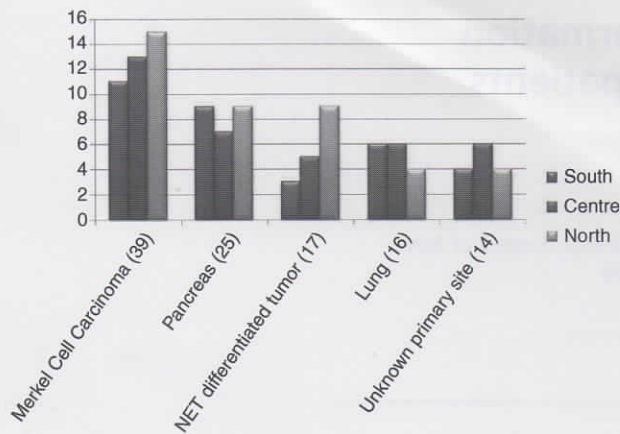
Materials and methods

We have considered a total of 74 patients collected between January 1990 and June 30, 2013 by the Rare Hormonal Tumors Group at Cremona Hospital. Of these cases, 39 were collected from the website www.neuroendocrini.it from its inception in November 2002 up to June 30, 2012¹² (Figure 1), and 8 were collected up to June 30, 2013, amounting to a total of 47 patients only from the website (63.51%). These patients had access to the website to obtain information about the biological characteristics and management of their tumor, in particular for the presence of local or distant relapse after a short time following tumor excision. Thirty patients were men (63.8%) and 17 were women (36.1%). The mean age was 69.6 years with a range of 32 to 89 years for both sexes. Patients older than 70 years were 26 (55.3%). Lombardy was the most represented region with 8 requests for information by patients, followed by Lazio, Campania and Piemonte (Figure 2). Of the 47 patients, 29 (61.70%) had local recurrence secondary to the lack of surgical radicalization and/or the lack of radiotherapy after surgery; 11 patients (23.40%) had advanced disease; in 5 patients (10.63%) staging of MCC was inappropriate, and in the remaining 2 patients (4.25%) the proper management of MCC needed to be confirmed.

Key words: Merkel cell carcinoma, rare tumors, website network, health information, expertise.

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	Merkel Cell Carcinoma	Pancreas	NET differentiated tumor	Lung	Unknown primary site
North	33%	18%	15%	19%	15%
Centre	12%	13%	6%	31%	38%
South	34%	27%	9%	18%	12%
Total	35%	23%	15%	14%	13%

Figure 1 - Tumor types and sites of disease stratified by geographic area.

North: Piemonte, Lombardy, Veneto, Trentino Alto Adige, Friuli Venezia Giulia, Liguria, Valle d'Aosta.

Center: Emilia Romagna, Tuscany, Umbria, Marche, Lazio.

South: Campania, Abruzzo, Molise, Basilicata, Calabria, Puglia, Sicily, Sardinia.

Modified from www.neuroendocrini.it/storia.php

Results

In more than 10 years of activity (to date over 100,000 visitors and over 2500 emails received), the website

www.neuroendocrini.it has collected a large series of MCC cases, giving us the opportunity to learn about the needs of patients. Patients use the website to communicate with experts and share their apprehension, thus becoming less invisible and alone with their disease. For us, tracing a map of patients' needs has made it possible to ascertain the different cultural and technological resources across the regions of our country¹².

The large number of requests for information mainly in case of local relapse or metastatic disease (85%) suggests that MCC patients might need more expertise and help, also given the advancing age of the population, higher rates of sun exposure, and increasing number of immunocompromised individuals¹. A smaller proportion of patients (4.25%) expressed the need for confirmation about the diagnostic and therapeutic management of MCC.

Discussion

MCC is a highly aggressive cancer of the skin. In the US, its incidence tripled between 1986 and 2001, and MCC has become the second most common cause of nonmelanoma skin cancer deaths¹³. When feasible, surgery is the mainstay of treatment. A favorable outcome depends mainly on early and wide excision, and on sequential radiotherapy to avoid local relapse and/or progressive disease¹¹. The role of chemotherapy should be revisited, including the use of novel molecules¹⁴.

There are several open issues to consider. The large number of patients observed in our series suggests that

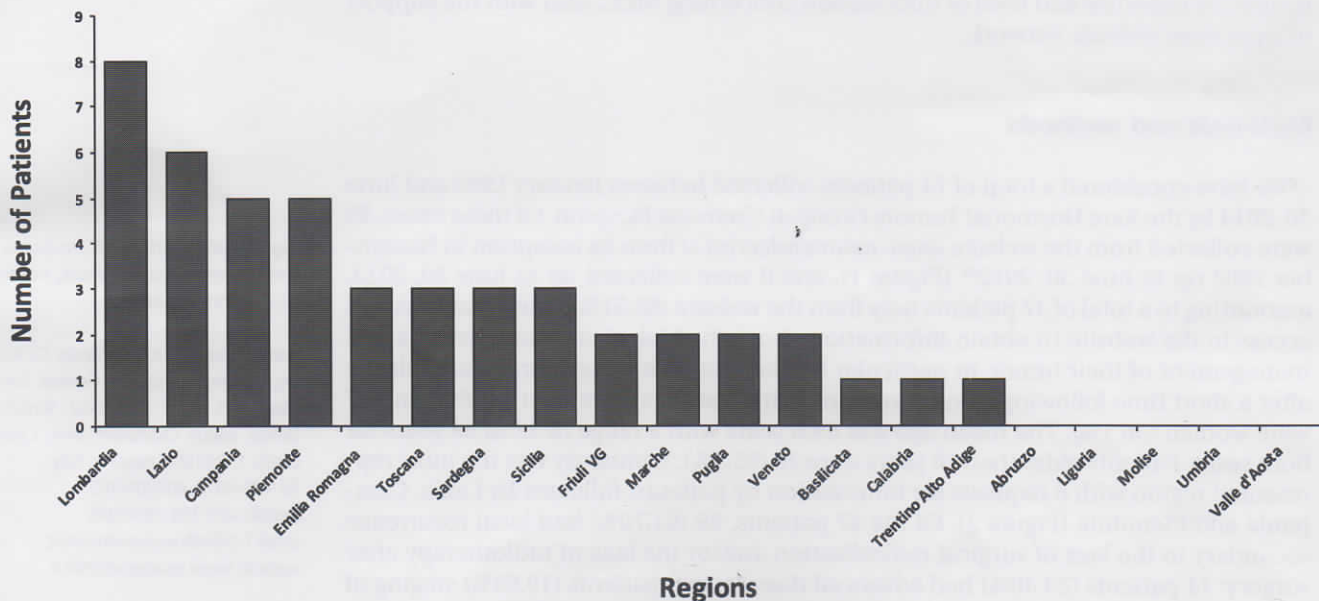


Figure 2 - Merkel cell carcinoma stratified by region up to June 30, 2013 (47 patients).

MCC, although considered a low-incidence tumor, is not quite so rare¹¹. Secondly, given that a considerable proportion of patients contacted the website because of local or distant relapse, it appears that not enough attention is paid to a tumor that tends to be underestimated, and for this reason mishandled. Sometimes this may occur because of the wrong timing: in 4 cases we observed a delay between the onset of the lesion and its excision, in 12 cases a delay between the histological diagnosis and the treatment decision, and in 2 cases a delay in delivery of the histological examination up to 60 days. In 1 case there was no histological examination of the primary lesion, and in another no histological examination for recurrence was carried out. These observations point to organizational issues from which the clinician cannot be considered extraneous. With regard to the treatment of metastatic disease, it is assumed that chemotherapy should be considered at present the standard treatment in advanced disease¹⁵; however, in our series we observed the choice of different molecules (somatostatin analogues in 4 cases and imiquimod in 1 case) without any clear, definitive scientific evidence. This could be due to a lack of adherence to shared recommendations.

It should be possible to find solutions to these issues. If the most recent reports suggest that MCC may not be an uncommon neoplasm, then it is necessary to pay more attention to these skin lesions, as is currently done for melanoma. Such surveillance should also involve general practitioners, who should recommend early excision of skin lesions to patients.

Timing is an integral part of an appropriate pathway in the management of MCC. The dermatologist and the surgeon should cooperate to reduce the delay between excision and pathological diagnosis in order to favor an early start of other therapies, if necessary, and a better quality of life of the patient.

There are guidelines for clinicians from the US National Comprehensive Cancer Network (NCCN)¹⁶ and in Italy from Rete Oncologica Lombarda¹⁷. The former have the advantage of being clear and concise, even without entering into the details of drug therapy; the latter provide recommendations concerning standard therapy and individualized therapy, as well as a complete and comprehensive overview of experimental therapies. Widespread circulation of the recommendations regarding experimental therapies is warranted in order to limit the use of therapies that have not been corroborated by scientific evidence, with a consequent decrease in costs and waiting times.

In the current situation, MCC must be considered an

aggressive tumor whose behavior is in most cases underestimated, as illustrated by the significant number of second opinion requests in our series. More attention should be paid to this relatively uncommon but highly malignant tumor, with the aim of improving patient survival and quality of life, and reducing costs. Therefore, new strategies and more extensive information, also not strictly in specialized areas, are necessary. We consider the role of information from dedicated websites useful, and we want to believe that in some cases our website may have contributed to improving the management of patients suffering from MCC.

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