

Carcinoma Avançado de Células de Merkel: Um Novo Caso de Regressão Espontânea

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RESUMO – O carcinoma de células de Merkel é uma neoplasia cutânea agressiva que afecta predominantemente indivíduos idosos ou imunodeprimidos. A progressão para doença metastática é frequente, enquanto a regressão espontânea é bastante rara. A exposição crónica à radiação solar e a infecção pelo poliomavírus das células de Merkel são reconhecidos factores etiopatogénicos. Uma mulher de 89 anos foi observada com um carcinoma de células de Merkel localmente avançado na asa esquerda do nariz. Tinha doença ganglionar metastática na região submandibular clinicamente evidente, confirmada por punção aspirativa com agulha fina. Uma metástase hepática isolada foi detectada por estudo tomográfico por emissão de positrões com (68)Ga-DOTATOC. Enquanto aguardava por radioterapia paliativa, observou-se regressão do tumor primário e das metástases ganglionares, clinicamente completa ao fim de 6 semanas. Uma ecografia hepática demonstrou regressão concomitante da metástase hepática. Os relatos de regressão espontânea de carcinoma de Merkel são muito escassos na literatura. Após a revisão realizada pelos autores, este é o primeiro caso descrito em Portugal. O mecanismo subjacente à remissão espontânea é desconhecido, embora possa ser teoricamente explicado pelo desenvolvimento de uma resposta immune eficaz contra o tumor.

PALAVRAS-CHAVE – Carcinoma de Células de Merkel; Idoso; Regressão Neoplásica Espontânea.

Advanced Merkel Cell Carcinoma: A New Case of Spontaneous Regression

ABSTRACT – Merkel cell carcinoma is an aggressive skin neoplasm affecting predominantly older or immunosuppressed patients. The progression to metastatic disease is frequent while spontaneous regression is quite uncommon. Chronic sun exposure and infection by Merkel cell polyomavirus are known etiopathogenic factors.

An 89-year-old female was observed with a locally advanced Merkel cell carcinoma of the left nasal ala. Lymph node metastases in left submandibular region were clinically apparent and confirmed by fine-needle aspiration. A solitary metastasis in the liver was identified by positron-emission tomography/computed tomography with (68)Ga-DOTATOC.

While she was waiting for palliative radiation therapy, the patient experienced a complete clinical remission of the primary tumor and regional lymph nodes metastases occurring after 6 weeks. A liver ultrasonography disclosed remission of the liver metastasis as well. The spontaneous remission is rarely reported in medical literature. As far as we know, this is the first report in Portugal. The underlying mechanism of the spontaneous remission remains unknown, although theoretically it can be explained by the development of an efficient immune response against the tumor.

KEYWORDS – Aged; Carcinoma, Merkel Cell; Neoplasm Regression, Spontaneous.

INTRODUCTION

Merkel cell carcinoma is an aggressive skin malignancy with a relatively high recurrence rate and propensity for metastatic spread. This neoplasm affects predominantly older men, arising mainly in head and neck skin. Ultraviolet-induced

skin damage, immunosuppression and the recently discovered Merkel cell polyomavirus were identified as pathogenic factors.¹ Spontaneous regression is a very rare occurrence in Merkel cell carcinoma with very few cases reported so far, none of them in Portugal.²⁻⁶

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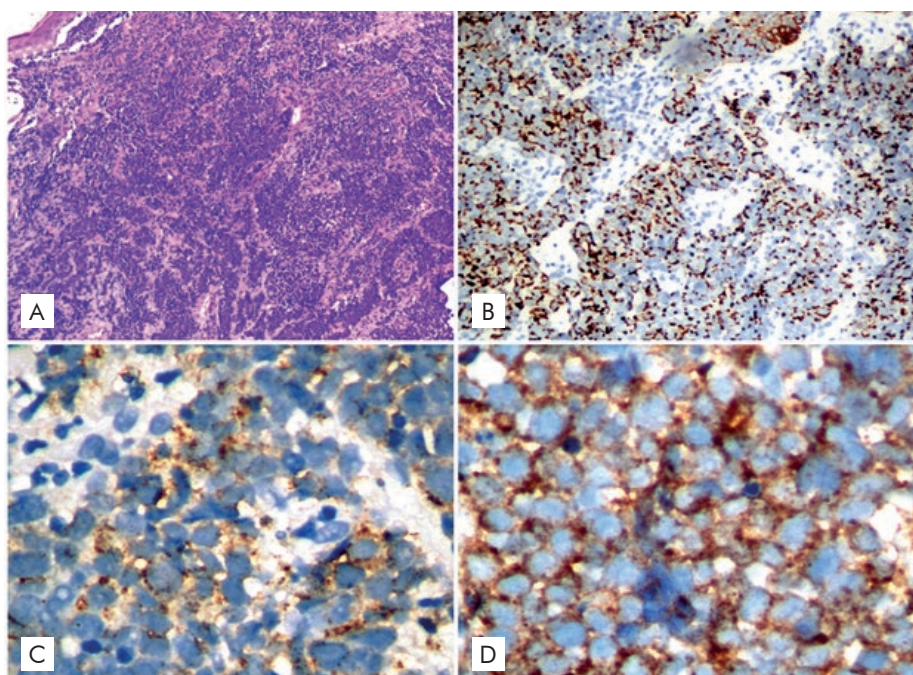


Figure 1 - Histopathological features of the tumor under hematoxylin-eosin stain (A) and with immunocytochemical stains for cytokeratin-20 with a typical paranuclear dot-like pattern (B), synaptophysin (C) and chromograninA (D).

CASE REPORT

An 89-year-old woman, Fitzpatrick phototype III, farmer during 40 years and with no relevant past medical history was observed with a rapidly-growing nodule (evolution of 3 months) with 3 cm in the left nasal ala. Histopathological examination of a skin biopsy specimen revealed a tumour composed by medium-sized cells with scant cytoplasm and hyperchromatic nucleus. Focal necrosis and frequent mitosis were also observed. The immunostainings for cytokeratin-20, synaptophysin and chromogranin A were positive, highly suggestive of Merkel cell carcinoma (Fig. 1). The immunostaining for S100 protein was negative. Detection of DNA of Merkel cell polyomavirus in paraffin-embedded lesional skin was negative under quantitative real-time polymerase chain reaction analysis.

An enlarged lymph node with 3 cm was identified in the left submandibular region corresponding to lymphatic metastases

of Merkel cell carcinoma proven by fine needle aspiration. Furthermore, a positron-emission tomography/computed tomography with $(68)\text{Ga-DOTATOC}$ detected a single liver metastasis with 2 cm in diameter localized in the segment IV (Fig. 2). The patient was staged in the stage IV (T4 N1b M1c) of the American Joint Committee on Cancer 7th edition.

Due to the poor performance status of the patient (score 3 in the Eastern Cooperative Oncology Group Performance Scale), palliative radiation therapy applied to the primary tumour and to the regional metastases was proposed. However, 6 weeks after the biopsy and before radiation therapy was initiated, spontaneous reduction of the primary tumor and the cervical metastatic lymph node were noticed (Fig. 3). Hepatic ultrasonography also revealed the concomitant disappearance of liver metastasis. The patient remains disease-free after a 9-month follow-up.

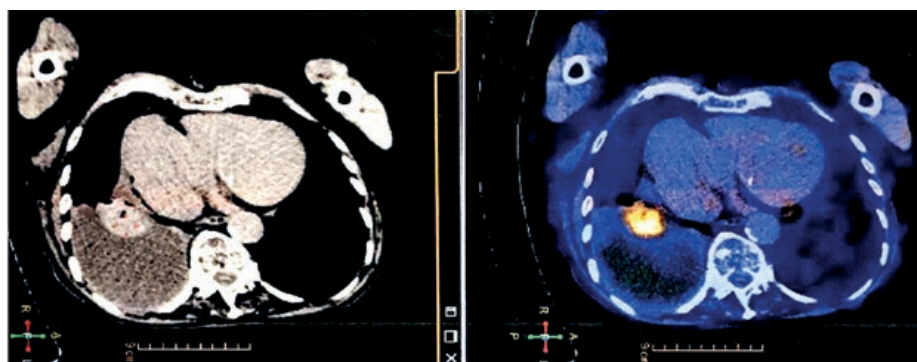


Figure 2 - Liver metastasis disclosed by $(68)\text{Ga-DOTATOC}$ PET-CT.

Table 1 - Complete spontaneous regression of Merkel cell carcinoma: review of the literature (n=34 cases)^{4,6}.

Author	Age	Sex	Location	Bx	LN	Met	MCPyV	Time to regression	Follow-up
Kayashima et al.	68	F	Forehead	Yes	No	No	-	2 mo	132 mo
	86	F	Cheek	Yes	No	No	-	1.5 mo	32 mo
Dijlali-Bouzina et al.	83	F	Cheek	Yes	No	No	-	1 mo	12 mo
Hashimoto et al.	69	F	Cheek	Yes	No	No	-	-	12 mo
Umezawa et al.	89	F	Nose	-	No	No	-	-	-
Ogiyama et al.	54	F	Eyelid	-	No	No	-	-	-
Tanita et al.	75	F	Cheek	Yes	No	No	-	-	12 mo
Satoh et al.	87	M	Cheek	Yes	No	No	-	-	2 mo
Okamoto et al.	79	F	Cheek	-	-	-	-	-	-
Inoue et al.	58	M	Cheek	-	-	-	-	-	-
	77	F	Cheek	-	-	-	-	-	-
	74	F	Cheek	-	-	-	-	-	-
	83	F	Cheek	-	-	-	-	-	-
Maruo et al.	82	F	Cheek	Yes	No	No	-	5 mo	12 mo
Connelly et al.	71	F	Cheek	Yes	No	No	-	2 mo	11 mo
Junquera et al.	79	F	Cheek	Yes	No	No	-	3 mo	72 mo
Vesely et al.	67	F	Cheek	Yes	No	No	-	7 wk	6 mo
Missoten	90	M	Eyelid	Yes	No	No	-	2 wk	18 mo
	81	M	Eyelid	Yes	-	-	-	4 mo	24 mo
Yagi et al.	73	F	Forearm	Yes	No	No	-	-	-
Turk et al.	70	F	Forearm	No	No	No	-	3 wk	6 mo
Ciudad et al.	86	F	Cheek	Yes	No	No	-	4 wk	18 mo
	92	M	Scalp	Yes	No	No	-	7 wk	23 mo
Val-Bernal et al.	86	F	Forearm	Yes	No	No	-	10 wk	-
Morand et al.	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-	-
Higaki-Mori et al.	94	F	Nose	Yes	No	No	Yes	-	8 mo
Ishiji et al.	43	F	Cheek	Yes	No	No	Yes	10 mo	96 mo
Pang et al.	86	F	Nose	Yes	No	No	-	8 wk	-
Khader et al.	40	F	Knee	Yes	No	No	-	1 mo	24 mo
Fujimoto et al.	76	F	Cheek	Yes	No	No	Yes	1 mo	60 mo
Moghaddam et al.	79	M	Jaw	Yes	No	-	No	8 wk	12 mo
Cirillo	89	M	Scalp	Yes	Yes	No	-	1 mo	24 mo
Current report	89	F	Nose	Yes	Yes	Yes	No	6 wk	9 mo

Bx: biopsy previous to the spontaneous regression. LN: lymph node metastases. Met: distant metastases. MCPyV: presence of Merkel cell carcinoma polyomavirus.

Caso Clínico

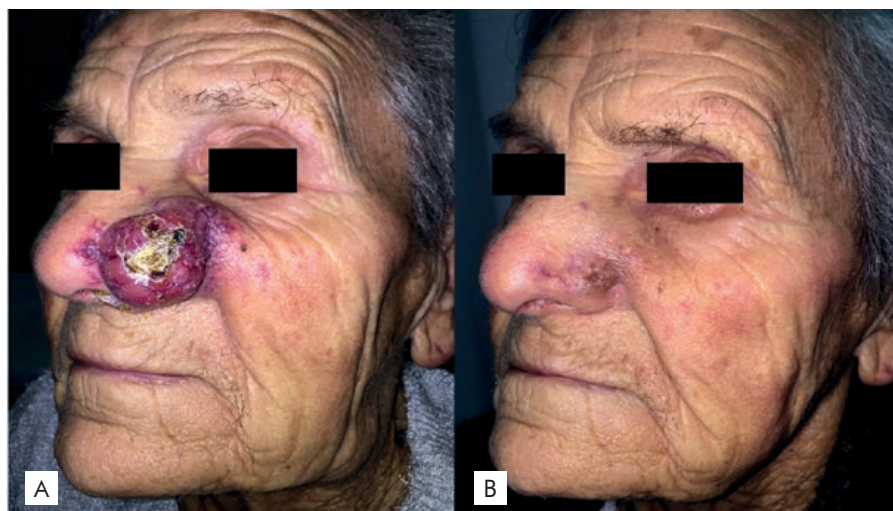


Figure 3 - Clinical features of the primary tumour prior (A) and after (B) the spontaneous regression.

DISCUSSION

Spontaneous regression of Merkel cell carcinoma was rarely described, generally occurring after the biopsy of the primary tumour.^{3,4} The underlying mechanism for this occurrence is unclear but there is scarce evidence suggesting a relevant role of T-cell mediated immune response.^{3,4} The review of previous reports in the literature is summarized in Table 1. The presence of Merkel cell polyomavirus was analysed in only few previous reports and the DNA of the virus was found in three out of four cases.^{4,6} The current case contributes to this count with an additional negative result. Further investigation is required to confirm whether the presence of the virus has any influence in the likelihood of complete spontaneous remission, as mentioned by some authors.^{3,4} It is remarkable that the complete spontaneous regression of this aggressive skin neoplasm is usually definitive, with no recurrences reported (the patients who did not survive during the follow-up died of other causes not related with Merkel cell carcinoma).^{4,6} The authors emphasize that this is the first report of complete spontaneous regression of a primary Merkel cell carcinoma with synchronous complete regression of nodal and distant metastases.

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