American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2018; 19: 1437-1440
DOI: 10.12659/AJCR.911840

Received: 2018.06.28
Accepted: 2018.09.05
Published: 2018.12.04

A Spontaneous Regression of an Isolated Lymph Node Metastasis from a Primary Unknown Merkel Cell Carcinoma in a Patient with an Idiopathic Hyper-Eosinophilic Syndrome

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 Raffaele Longo
ABCE 2 Oana Balasanu
ABCDEF 1 Mathilde Chastenet de Castaing
ABCDEF 3 Eric Chatelain
BCDE 4 Mohammed Yacoubi
BCDEF 1 Marco Campitiello
BDEF 5 Nathalie Marcon
ABCDEF 1 Francesca Plastino

1 Division of Medical Oncology, Centre Hospitalier Régional (CHR) Metz-Thionville, Ars-Laquenexy, France
2 Division of Hematology, Centre Hospitalier Régional (CHR) Metz-Thionville, Ars-Laquenexy, France
3 Division of Surgery, Centre Hospitalier Régional (CHR) Metz-Thionville, Ars-Laquenexy, France
4 Division of Radiotherapy, Centre Hospitalier Régional (CHR) Metz-Thionville, Ars-Laquenexy, France
5 Division of Pathology, Centre Hospitalier Régional (CHR) Metz-Thionville, Ars-Laquenexy, France

Corresponding Author: Raffaele Longo, e-mail: r.longo@chr-metz-thionville.fr
Conflict of interest: None declared

Patient: Male, 69
Final Diagnosis: Spontaneous regression of a Lymph node metastasis
Symptoms: Hypereosinophilia • inguinal mass
Medication: —
Clinical Procedure: —
Specialty: Oncology

Objective: Unusual clinical course

Background: Merkel cell carcinoma (MCC) is a rare, aggressive primary cutaneous neuroendocrine tumor frequently associated with Merkel cell polyomavirus infection. Despite its aggressiveness, a few reports of spontaneous MCC regression have been described in the literature, most of them following incisional biopsy supporting a hypothetical role of surgery-induced inflammation in the process of regression.

Case Report: We report a case of 69-year-old Caucasian male who was followed for an idiopathic hyper-eosinophilic syndrome. A positron emission tomography (PET) scan documented a hyper-metabolic, left, inguinal adenopathy, histologically corresponding to a metastasis of a poorly differentiated neuroendocrine carcinoma. This lesion spontaneously regressed at clinical examination and radiological imaging. After its excisional dissection, histology was negative. Five months later, a nearby adenopathy reappeared. The patient underwent another excisional biopsy. Histology and immunohistochemistry were compatible with a lymph node metastasis of a MCC. As the patient refused radical surgery, a regional radiotherapy was performed. As of a follow-up at 10 months, he was alive and free of tumor recurrence. The hyper-eosinophilic syndrome was stable; however, the serum levels of chromogranin-A were inexplicably elevated in the absence of any tumor evidence at the PET scan.

Conclusions: The particularity of this case relies on the rarity of MCC complete spontaneous regression in a patient without a primary tumor and with a synchronous, idiopathic hyper-eosinophilic syndrome.

MeSH Keywords: Carcinoma, Merkel Cell • Neoplasm Regression, Spontaneous • Polyomavirus

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/911840

994 — 6 28

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

Background

Merkel cell carcinoma (MCC) is a rare, aggressive primary cutaneous neuroendocrine tumor typically occurring on the head and neck of the elderly and generally presenting a poor prognosis [1–3]. Merkel cell polyomavirus (MCPyV) has been identified in up to 80% of cases suggesting its potential role in MCC tumorigenesis [4]. Despite its aggressiveness, a few reports of MCC complete spontaneous regression have been described in the literature, most of them following incisional biopsy, thus supporting the hypothetical role of surgery-induced inflammation in the regression process [5–24].

We report a rare case of an isolated, inguinal lymph node metastasis from a primary unknown MCC, spontaneously regressing after an ultrasound-guided core needle biopsy with a relapse in a nearby lymph node 5 months later, in a patient presenting with synchronous, idiopathic hyper-eosinophilic syndrome.

Case Report

We report on the case of a 69-year-old Caucasian male who was a smoker and who was regularly followed for an idiopathic hyper-eosinophilic syndrome. The patient had ischemic cardiovascular disease, mellitus diabetes, arterial hypertension, and dyslipidemia as relevant comorbidities. The patient's history was uneventful, and he was asymptomatic. Clinical examination found a hard, irregular, left, inguinal lymph node of 1.5×1.5 cm of diameter.

The positron emission tomography (PET) scan confirmed the presence of an isolated, hyper-metabolic, inguinal adenopathy of 1.9 cm (Figure 1). The patient was referred for a percutaneous ultrasound-guided core biopsy, which revealed a metastasis of a poorly differentiated neuroendocrine carcinoma. The immunohistochemical staining of the biopsy showed that tumor cells were negative for cytokeratin 7 (CK-7), p40, thyroid transcription factor 1 (TTF-1), prostate-specific antigen (PSA), chromogranin-A, weakly positive for cytokeratin 20 (CK-20), moderately positive for synaptophysin, and strongly positive for CD56. The Ki-67 was elevated at 95%. Biochemical tests were in the normal range, but chromogranin-A was persistently elevated at 1400 ng/mL (normal value <101.9 ng/mL). Abdominal and pelvic ultrasound showed a polypoid tumor lesion of the left bladder wall of 2.1×1.5×2.0 cm. Cystoscopy found a low-grade, papillary, noninfiltrating urothelial carcinoma that was completely resected (pTa). Colonoscopy revealed 4 tubular adenomas with a low-grade dysplasia, which were radically resected.

In March 2017, an excisional, inguinal lymph node biopsy was programmed but clinical examination showed a complete

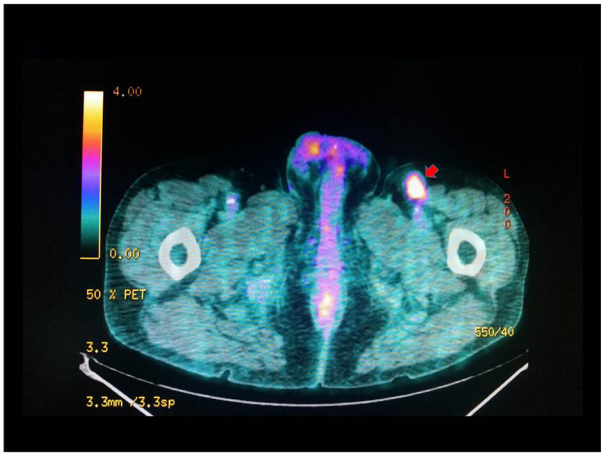

Figure 1. Positron emission tomography scan documents an isolated left, hyper-metabolic, inguinal lymph node lesion (red arrows).

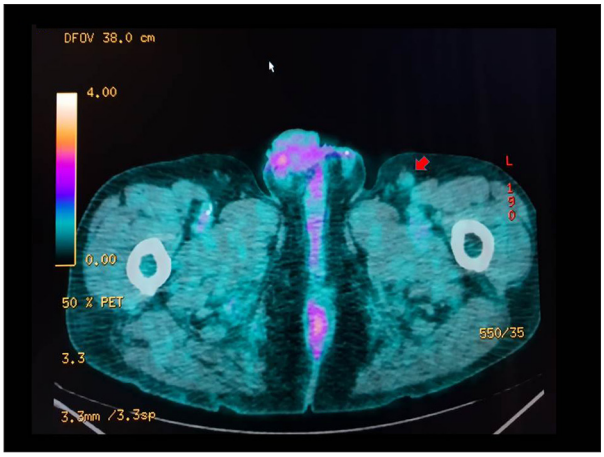

Figure 2. Positron emission tomography scan, performed after the percutaneous, ultrasound-guided core needle biopsy and before the tumor excisional biopsy, reveals a residual, non hyper-metabolic adenopathy (red arrows).

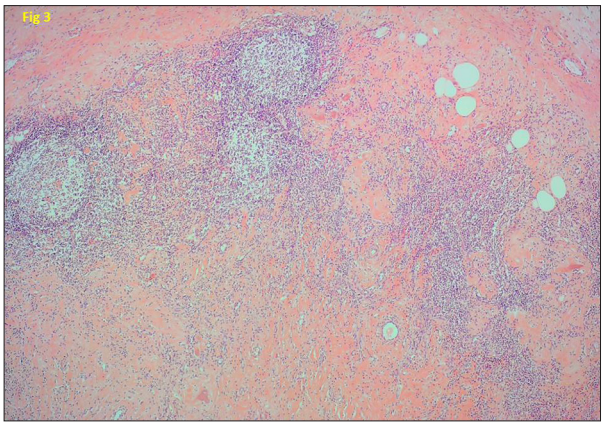

Figure 3. Histology shows a lymph node central sclero-hyalinosis with a normal cortex in the absence of any tumor infiltration (hematoxylin and eosin stain, 100×).

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

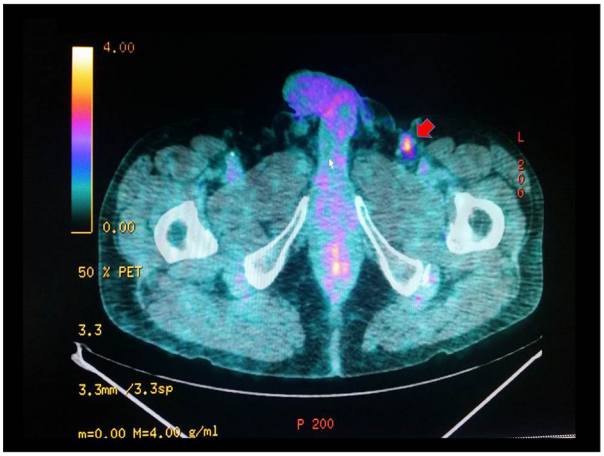

Figure 4. Positron emission tomography scan confirms the presence of a new, inguinal, hyper-metabolic lymph node (red arrows).

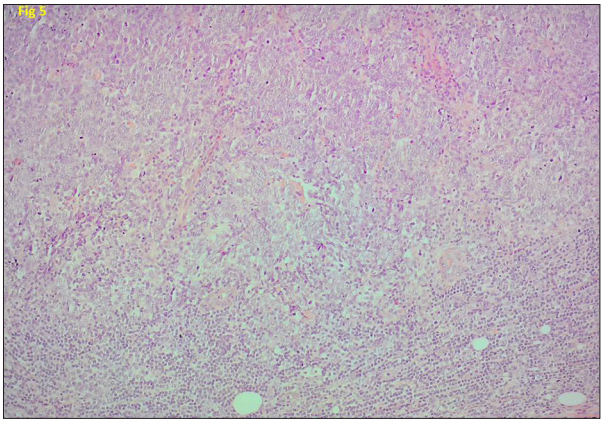

Figure 5. Histology reveals a massive tumor infiltration of poorly differentiated cells with scant cytoplasm, coarse chromatin, prominent mitotic and apoptotic figures, associated to a diffuse necrosis (hematoxylin and eosin stain, 100×).

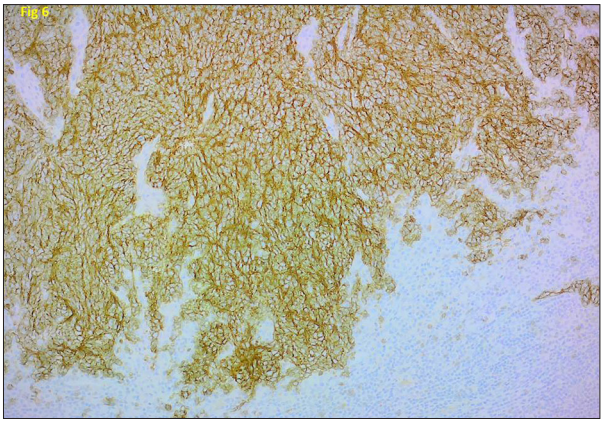

Figure 6. At the immunohistochemistry, tumor cells are positive for CD56 (400×).

regression of the lesion, confirmed by a PET scan revealing a residual, not hyper-metabolic adenopathy (Figure 2), histologically corresponding to a lymph node with a central sclero-hyalinosis and a normal cortex in the absence of any tumor infiltration (Figure 3). Five months later, another left, inguinal lymph node was clinically documented and confirmed by a PET scan, showing a hyper-metabolic adenopathy of 1.2 cm (Figure 4). The patient underwent another excisional biopsy. Histology revealed a massive infiltration of poorly differentiated, small, neuroendocrine tumor cells with a scant cytoplasm and prominent mitotic figures (Figure 5). Immunohistochemistry showed that tumor cells were positive for CD56 (Figure 6), synaptophysin, and cytokeratin AE1/AE3, and negative for CK-7, CK-20, chromogranin-A, and CM2B4 (anti-polyomavirus), according with the diagnosis of MCC metastasis.

As the patient refused the radical lymph node dissection, a regional radiotherapy was performed (50 Gy/25 fractions).

Ten months later, the patient was in good clinical conditions and free of tumor recurrence. The hyper-eosinophilic syndrome was stable; however, the serum levels of chromogranin-A were inexplicably elevated in the absence of any tumor evidence at the PET scan.

Discussion

First described by Toker in 1972 as “trabecular carcinoma” of the skin [1], MCC is an aggressive neuroendocrine skin tumor most commonly appearing on sun-exposed areas, particularly in the head and neck region [1–3].

MCC presents a poor prognosis, with a 5-year overall survival of 60% [3]. At diagnosis, the involvement of regional lymph nodes is reported in 10–45% of the cases and is strongly related to the prognosis [3]. Distant metastases have been described in 50% of patients, the common sites being lymph nodes, liver, bone, brain, lung, and skin [3]. The incidence of MCC has tripled over the last 15 years [3].

A new human polyomavirus (Merkel cell polyomavirus: MCPyV) was detected in 2008 in 80% of MCC tumors and subsequently confirmed by many studies [4]. Its role in MCC prognosis is still controversial and not well established [4].

The risk for MCC is highly increased in patients with chronic T-cell dysfunctions such as solid organ transplantation, HIV infection, and chronic lymphocytic leukemia [1–3].

Despite its aggressiveness, several reports have documented MCC complete spontaneous regression in the absence of any specific treatment [5–24].

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

First described by O'Rouke and Bell in 1986 [5], MCC complete spontaneous regression accounts for approximately 1.4% of all reported cases (15 out of 1100) as compared to all other cancers, which present an incidence rate of 1 out of 60 000 to 100 000 [5–24].

Interestingly, MCC complete spontaneous regression typically has rapid onset (1 to 5 months) and is persistent, with a few reported cases of recurrence; it occurs more frequent in women, and is usually associated with better disease-specific survival [5–24].

The complete spontaneous regression pathogenesis remains unclear. It has been suggested that T-cell-mediated immunity could play an important role in complete spontaneous regression pathogenesis. Several histopathologic studies showed accumulation of chronic inflammatory cells, mainly T-cells and foamy macrophages, after tumor biopsy. Furthermore, T-cell-related cytokines, such as interferons, can promote effective immune responses against neuroendocrine tumors [24–28]. Several reports suggest a potential role for diagnostic biopsy that could stimulate a T-cell mediated immune response, but data concerning the prognostic value of intra-tumoral and/or peri-tumoral CD8+ lymphocyte infiltration are still controversial [24–28].

Conclusions

In our case, the patient presented with a spontaneous regression of an isolated inguinal lymph node metastasis from an unknown primary MCC after a percutaneous, ultrasound-guided core needle biopsy, with a relapse in a nearby lymph node 5 months later.

The particularity of this case relies on the rarity of the MCC complete spontaneous regression in a patient without a primary tumor, which probably spontaneously regressed, and who had a synchronous idiopathic hyper-eosinophilic syndrome.

Conflict of interests

None.

References:

1. Toker C: Trabecular carcinoma of the skin. Arch Dermatol, 1972; 105: 107–10
2. Okamoto O, Yoshiyama M, Takayasu S, Yokoyama S: Merkel cell carcinoma: Report of three cases. J Dermatol, 1998; 25(1): 45–50
3. Majewska H, Biernat W: Merkel cell carcinoma. Pathological and molecular aspects of diagnosis and clinical features. Pol J Pathol, 2010; 61: 117–23
4. Higaki-Mori H, Kuwamoto S, Iwasaki T et al: Association of Merkel cell polyomavirus infection with clinicopathological differences in Merkel cell carcinoma. Hum Pathol, 2012; 43(12): 2282–91
5. O'Rourke MG, Bell JR: Merkel cell tumor with spontaneous regression. J Dermatol Surg Oncol, 1986; 12: 994–96
6. Ahmadi Moghaddam P, Cornejo KM, Hutchinson L et al: Complete spontaneous regression of Merkel Cell Carcinoma after biopsy: A case report and review of the literature. Am J Dermatopathol, 2016; 38(11): e154–58
7. Duncan WC, Tschen JA: Spontaneous regression of Merkel cell (neuroendocrine) carcinoma of the skin. J Am Acad Dermatol, 1993; 29: 653–54
8. Tanita M, Tabata N, Kato T: Merkel cell carcinoma with spontaneous regression. Skin Cancer, 1996; 11: 70–72
9. Yanguas I, Goday JJ, González-Güemes M et al: Spontaneous regression of Merkel cell carcinoma of the skin. Br J Dermatol, 1997; 137: 296–98
10. Brown TJ, Jackson BA, Macfarlane DF, Goldberg LH: Merkel cell carcinoma: Spontaneous resolution and management of metastatic disease. Dermatol Surg, 1999; 25: 23–25
11. Maruo K, Kayashima KI, Ono T: Regressing Merkel cell carcinoma – a case showing replacement of tumour cells by foamy cells. Br J Dermatol, 2000; 142: 1184–89
12. Connelly TJ, Cribier B, Brown TJ, Yanguas I: Complete spontaneous regression of Merkel cell carcinoma: A review of the 10 reported cases. Dermatol Surg, 2000; 26: 853–56
13. Sais G, Admella C, Soler T: Spontaneous regression in primary cutaneous neuroen-docrine (Merkel cell) carcinoma: A rare immune phenomenon? J Eur Acad Dermatol Venereol, 2002; 16: 82–83
14. Junquera L, Torre A, Vicente JC et al: Complete spontaneous regression of Merkel cell carcinoma. Ann Otol Rhinol Laryngol, 2005; 114: 376–80
15. Pang C, Sharma D, Sankarc T: Spontaneous regression of Merkel cell carcinoma: A case report and review of the literature. Int J Surg Case Rep, 2015; 7C: 104–8
16. Sugamata A, Goya K, Yoshizawa N: A case of complete spontaneous regression of extremely advanced Merkel cell carcinoma. J Surg Case Rep, 2011; (10): 7
17. Cirillo F: Spontaneous regression of primitive Merkel cell carcinoma. Rare Tumors, 2015; 7(4): 5961
18. Terui H, Fujimura T, Kakizaki A et al: Merkel cell carcinoma with spontaneous regression: A case report and immunohistochemical study. Case Rep Dermatol, 2016; 8(1): 52–58
19. Kubo H, Matsushita S, Fukushige T et al: Spontaneous regression of recurrent and metastatic Merkel cell carcinoma. J Dermatol, 2007; 34: 773–77
20. Karkos PD, Sastry A, Hampal S, Al-Jafari M: Spontaneous regression of Merkel cell carcinoma of the nose. Head Neck, 2010; 32: 411–14
21. Ciudad C, Avilés JA, Alfageme F et al: Spontaneous regression in Merkel cell carcinoma: Report of two cases with a description of dermoscopic features and review of the literature. Dermatol Surg, 2010; 36: 68793
22. Wooff JC, Trites JR, Walsh NM, Bullock MJ: Complete spontaneous regression of metastatic Merkel cell carcinoma: A case report and review of the literature. Am J Dermatopathol, 2010; 32: 614–17
23. Val-Bernal JF, García-Castaño A, García-Barredo R et al: Spontaneous complete regression in Merkel cell carcinoma after biopsy. Adv Anat Pathol, 2011; 18: 174–77
24. Takenaka H, Kishimoto S, Shibagaki R et al: Merkel cell carcinoma with partial spontaneous regression: An immunohisto-chemical, ultrastructural and TUNEL labeling study. Am J Dermatopathol, 1997; 19: 614–18
25. Haag ML, Glass LF, Fenske NA: Merkel cell carcinoma. Diagnosis and treatment. Dermatol Surg, 1995; 21: 669–83
26. Sihto H, Bohling T, Kavola H et al: Tumor infiltrating immune cells and outcome of Merkel cell carcinoma: A population-based study. Clin Cancer Res, 2012; 18: 2872–88
27. Vandeven N, Nghiem P: Complete spontaneous regression of Merkel cell carcinoma metastatic to the liver: Did lifestyle modifications and dietary supplements play a role? Glob Adv Health Med, 2012; 1: 20–21
28. Koba S, Paulson KG, Nagase K et al: Diagnostic biopsy does not commonly induce intratumoral CD8 T cell infiltration in Merkel cell carcinoma. PLoS One, 2012; 7: e41465

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]