

7. Sparsa A, Lesaux N, Kessier E, Bonnetblanc JM, Blaise S, Lebrun-Ly V, et al. Treatment of cutaneous calcinosis in CREST syndrome by extracorporeal shock wave lithotripsy. *J Am Acad Dermatol*. 2005;53:263–5.
8. Sultan-Bichat N, Menard J, Perceau G, Staerman F, Bernard P, Reguiat Z. Treatment of calcinosis cutis by extracorporeal shock-wave lithotripsy. *J Am Acad Dermatol*. 2012;66:424–9.
9. Chan AY, Li E. Electric shock wave lithotripsy (ESWL) as a pain control measure in dermatomyositis with calcinosis cutis—old method, new discovery. *Clin Rheumatol*. 2005;24:172–3.
10. Schaden W, Thiele R, Köpl C, Pusch M, Nissan A, Attinger C, et al. Shock wave therapy for acute and chronic soft tissue wounds: A feasibility study. *J Surg Res*. 2007;143:1–12.

A.M. Delgado-Márquez,^{a,*} M. Carmona,^b F. Vanaclocha,^a C. Postigo^a

^a *Departamento de Dermatología, Hospital 12 de Octubre, Madrid, Spain*

^b *Departamento de Rehabilitación, Hospital 12 de Octubre, Madrid, Spain*

*Corresponding author.

E-mail address: anadelgadam13@gmail.com (A.M. Delgado-Márquez).

<http://dx.doi.org/10.1016/j.adengl.2014.12.004>

Small-Cell Neuroendocrine Carcinoma, Not Merkel Cell Carcinoma, in the Sinonasal Region: A Case Report[☆]



Carcinoma neuroendocrino de células pequeñas de la región nasosinusal no carcinoma de células de Merkel: presentación de un caso

Small-cell neuroendocrine carcinoma (SCNC) in the sinonasal region is a relatively rare, aggressive tumor with a high rate of recurrence and metastasis. It was first described in 1965 by Raychowdhuri¹ and approximately 50 cases have been published since that time. The majority of SCNCs affect the lungs and only around 4% are located at other sites.²

We present the case of a 32-year-old woman with no past history of interest. She consulted for progressively increasing pain and inflammation on the dorsum of the nose that

had started 2 months earlier. Physical examination revealed a solid, fixed nodule with a smooth surface on the right lateral surface of the dorsum of the nose. The nodule measured approximately 3 cm in its longest diameter (Figure 1); in addition, there was a palpable right jugulodigastric lymph node. Magnetic resonance imaging of the paranasal sinuses revealed a nodular lesion of the external nose that eroded the right nasal bones. On skin biopsy, a diffuse infiltration of neoplastic cells was observed in the deep dermis, hypodermis, and muscle layer. The cells were small and round, with scant cytoplasm and basophilic nuclei (Figure 2A and B). Immunohistochemistry (Figure 3) showed a phenotypic profile positive for neuroendocrine (chromogranin A and CD56) and epithelial (cytokeratin AE1/AE3) markers and for thyroid transcription factor 1 (TTF-1) and negative for cytokeratin 20 (CK20), cytokeratin 7 (CK7), protein S-100, glial fibrillary acidic protein (GFAP), neurofilaments, and Epstein Barr virus (EBV) antigen. The cervical lymph node was biopsied and the histologic and immunohistochemical findings were consistent with SCNC arising from the seromu-

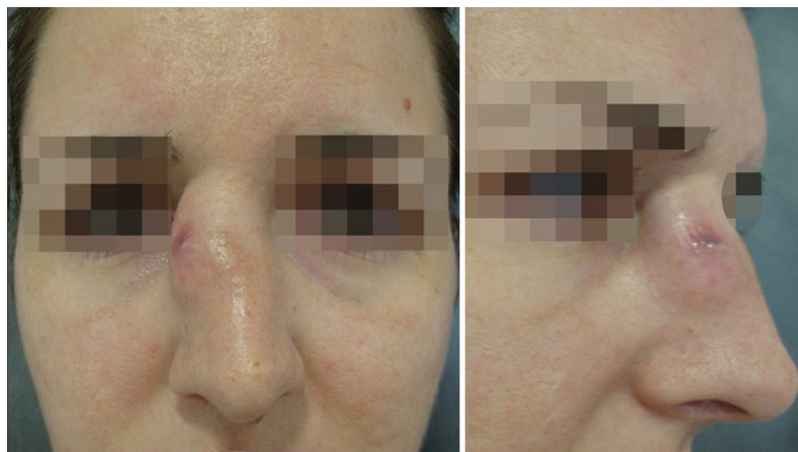


Figure 1 A solid nodule with a smooth surface and irregular outline on the right lateral surface of the dorsum of the nose.

[☆] Please cite this article as: Rivas-Tolosa N, Llombart B, Traves V, Guillén C. Carcinoma neuroendocrino de células pequeñas de la región nasosinusal no carcinoma de células de Merkel: presentación de un caso. *Actas Dermosifiliogr*. 2015;106:143–145.

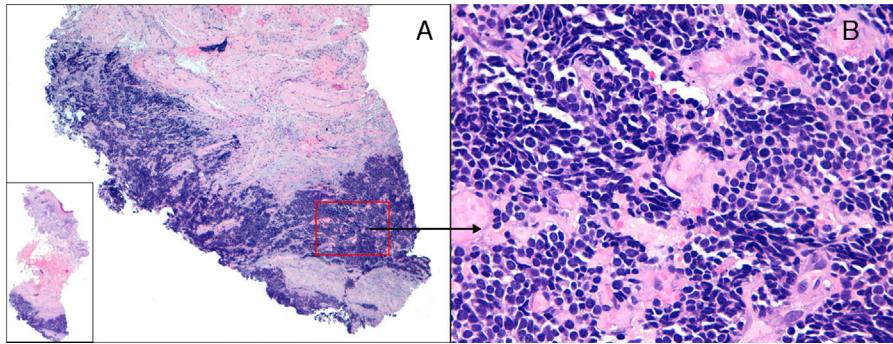


Figure 2 A, A 5-mm biopsy of the nasal nodule. A diffuse proliferation of neoplastic cells is visible in the deep dermis, hypodermis, and muscle layer. Hematoxylin and eosin, original magnification $\times 10$. B, The neoplastic cells are small, round, and monomorphic, with scant cytoplasm and basophilic nuclei. Hematoxylin and eosin, original magnification $\times 400$.

cous glands of the sinonasal region. Study of tumor spread by cervical-thoracic-abdominopelvic computed tomography (CT) revealed multiple proliferative malignant implants in the liver. The case was discussed in the tumor committee and, in view of the presence of disseminated disease, salvage surgical treatment of the primary tumor was excluded and it was decided to start chemotherapy with cisplatin and etoposide, combined with radiation therapy. Six months

after the diagnosis of the carcinoma, after 8 cycles of chemotherapy, the patient died of liver failure secondary to metastatic infiltration by the tumor.

SCNC of the sinonasal region arises from the APUD cells of the neuroendocrine system that are occasionally present in the seromucous glands of the nasal cavity and in the accessory salivary glands.³ These tumors affect men and women equally, and the mean age at onset is 50 years. No

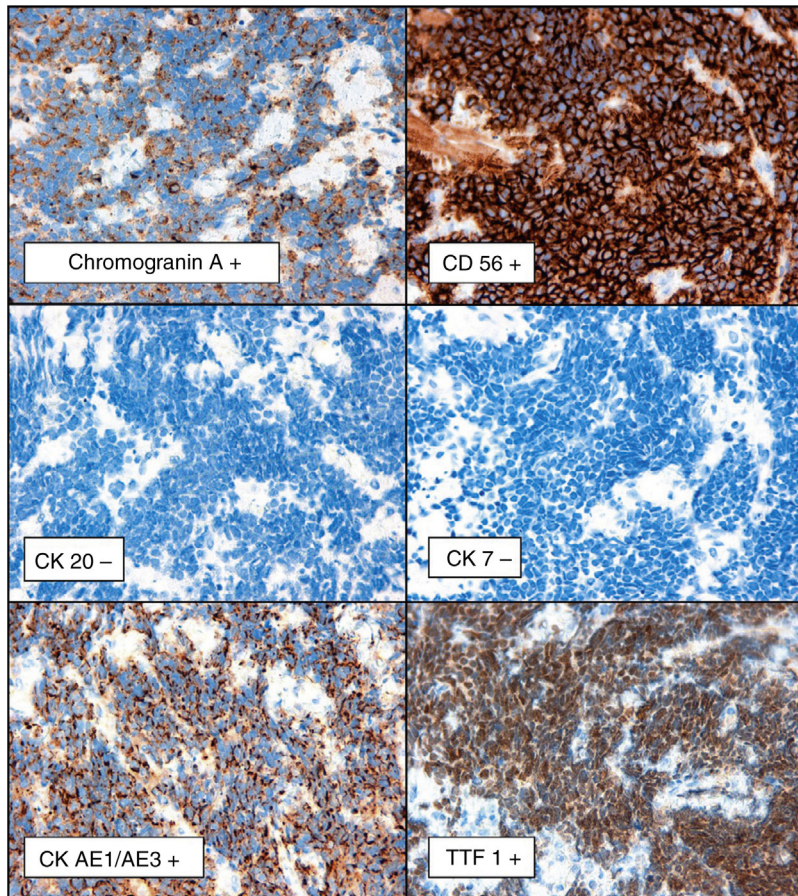


Figure 3 Immunohistochemistry shows that the cells are positive for epithelial and neuroendocrine markers; negativity for cyto-keratin (CK) and CK7 associated with positivity for thyroid transcription factor (TTF) 1 helps to exclude other diagnoses such as Merkel cell tumor.

risk factors have been identified, nor is there evidence to suggest that the presence of EBV is related to the pathogenesis of this tumor; infection by this virus has been well documented in other types of sinonasal carcinoma.⁴

Histopathology study using hematoxylin and eosin (H&E) stain reveals a diffuse infiltration of neoplastic cells that mainly affects the dermis and that is formed of small cells with scant cytoplasm and large, densely hyperchromatic nuclei; mitotic figures and areas of necrosis can be seen.

Immunohistochemistry, though nonspecific, is the most useful diagnostic tool and is based on positivity for markers of epithelial differentiation (CK, AE1/AE3, and CAM 5.2) and neuroendocrine differentiation (chromogranin A, synaptophysin, and/or neuron-specific enolase [NSE]). Immunohistochemistry is negative for protein S-100 and neurofilaments, which helps to exclude other diseases that can have a similar appearance with H&E stain, such as small cell melanoma and stesioneuroblastoma.⁴

The diagnostic challenge, because of the similar clinical and histological characteristics, arises with 2 diseases: Merkel cell carcinoma, which is usually CK20-positive⁵ and TTF-1-negative⁶; and skin metastases of small-cell lung cancer,⁷ whose cells stain positive for CK7 and TTF-1. In the case of SCNC of the sinonasal region, CK7 and CK20 are negative and, if the cells are positive for TTF-1, imaging studies must be performed to confirm the absence of lung disease. In our patient, we confirmed the absence of a lung tumor by CT, which was performed as part of the workup for tumor spread.

Although there is little experience in the management of this type of tumor, neoadjuvant cytoreductive chemotherapy with cisplatin and etoposide is considered to be the treatment of choice.⁸ Other authors recommend wide excision of the lesion as the initial treatment, associated with radiation therapy and chemotherapy,⁹ as long as metastatic disease has been excluded at the time of diagnosis.

Metastases usually affect the brain, lung, and skeleton. Mean survival after diagnosis is between 2 and 3 years, and the most unfavorable prognostic factors are locoregional invasion and associated paraneoplastic endocrine syndromes.¹⁰

It is important for dermatologists to be aware of the existence, characteristics, and clinical course of SCNC of the sinonasal region in order to differentiate it from other neu-

roendocrine tumors that can be clinically and histologically indistinguishable, such as Merkel cell tumor.

References

1. Raychowdhuri R. Oat cell carcinoma and paranasal sinuses. *J Laryngol Otol.* 1965;79:253–5.
2. Ibrahim NB, Briggs JC, Corbishley CM. Extrapulmonary oat cell carcinoma. *Cancer.* 1984;15:1645–61.
3. Koss LG, Spiro RH, Hajdu S. Small cell (oat cell) carcinoma of minor salivary gland origin. *Cancer.* 1972;30:737–41.
4. Perez-Ordóñez B, Caruana SM, Huvos AG, Shah JP. Small cell neuroendocrine carcinoma of the nasal cavity and paranasal sinuses. *Hum Pathol.* 1998;29:826–32.
5. Aneiros-Fernández J, Almodóvar-Real A, Caba-Molina M. Carcinoma de células de Merkel: estudio histopatológico, inmunohistoquímico, ultraestructural y molecular. *Monogr Dermatol.* 2013;26:57–63.
6. Ordóñez NG. Value of thyroid transcription factor-1 immunostaining in distinguishing small cell lung carcinomas from other small cell carcinomas. *Am J Surg Pathol.* 2000;24:1217–23.
7. Arrue I, Arregui MA, Catón B, Soloeta R. Neuroendocrine tumor with an atypical clinical course: A description of 2 cases. *Actas Dermosifiliogr.* 2014;105:94–6.
8. Soussi AC, Bengeriat A, Holgate CS, Majumdar B. Neuroendocrine tumours of the head and neck. *J Laryngol Otol.* 1990;104:504–7.
9. Rejowski JE, Campanella RS, Block LJ. Small cell carcinoma of the nose and paranasal sinuses. *Otolaryngol Head Neck Surg.* 1982;90:516–7.
10. Babin E, Rouleau V, Vedrine PO, Toussaint B, de Raucourt D, Malard O, et al. Small cell neuroendocrine carcinoma of the nasal cavity and paranasal sinuses. *J Laryngol Otol.* 2006; 120:289–97.

N. Rivas-Tolosa,^{a,*} B. Llombart,^a V. Traves,^b C. Guillén^a

^a *Servicio de Dermatología, Fundación Instituto Valenciano de Oncología, Valencia, Spain*

^b *Servicio de Anatomía Patológica, Fundación Instituto Valenciano de Oncología, Valencia, Spain*

* Corresponding author.

E-mail address: nancyrivastolosa@yahoo.com (N. Rivas-Tolosa).

<http://dx.doi.org/10.1016/j.adengl.2014.12.003>