Microcystic Adnexal Carcinoma Arising Within a Nevus Sebaceus

Nektarios Lountzis, MD; Jacqueline Junkins-Hopkins, MD; Marie Uberti-Benz, MD; Rosalie Elenitsas, MD

Nevus sebaceus (NS) is a congenital skin lesion arising on the face and scalp that has been linked to the development of various carcinomas. We describe a case of microcystic adnexal carcinoma (MAC) arising in an NS on the scalp of a 62-year-old man. Excisional skin biopsy and hematoxylin and eosin stains were performed to examine the specimen. Serial sections revealed papillomatosis typical of NS, with focal changes consistent with syringocystadenoma papilliferum. Adjacent to the syringocystadenoma papilliferum was an area containing small epithelial islands that extended focally into the subcutaneous layer. The cystic islands were embedded in a desmoplastic stroma with poor circumscription, consistent with MAC. This case presents a rare finding of MAC within an NS.

Cutis. 2007;80:352-356.

Jadassohn[1] first described nevus sebaceus (NS) in 1895 as a hamartomatous locus of embryologically defective pilosebaceous units. Because this lesion involves more than just a sebaceous component, the more encompassing term *organoid nevus* also has been coined. Clinically, the lesion presents in 3 stages. Initially, it is a well-circumscribed, flat, round to oval, hairless patch that progresses into a raised, papillated, yellow plaque under the hormonal influences of puberty. The lesion arises on the face and scalp of children, rarely on the trunk and extremities, and usually is present at birth. During puberty, hormones influence the apocrine glands to mature, sebaceous glands to enlarge, and epidermis to undergo verrucous hyperplasia. The final stage is marked by a propensity for both benign and malignant tumor growth.[2-5] Benign neoplasms, such as syringocystadenoma papilliferum and trichoblastoma, are more likely to occur, whereas malignant neoplasms generally are rare.[3] With this in mind, we report a case of a microcystic adnexal carcinoma (MAC) arising within an NS.

Case Report

A 62-year-old white man presented to his dermatologist for reevaluation of a scalp growth. The patient initially was evaluated in 1998 for the same lesion, which had been present since birth. A biopsy was performed and the results were interpreted elsewhere as multiple follicular infundibular cysts. The lesion gradually recurred, but a complete excision was declined by the patient. In 2002, the growth was treated locally with carbonic acid by another dermatologist. The lesion continued to grow, and the patient presented to us for a reassessment. His past medical history was notable for myelodysplasia and splenectomy. There was a family history of colon cancer.

Physical examination revealed a yellow-beige verrucous plaque on the patient's left temple. An excisional biopsy was performed. Hematoxylin and eosin–stained sections revealed a large lesion with epidermal acanthosis and papillomatosis (Figure 1). Arising in the dermis were endophytic epithelial islands that formed glandular spaces, with decapitation secretion. Together these features were believed to be most consistent with syringocystadenoma papilliferum arising in an NS. Adjacent to the syringocystadenoma papilliferum was a separate dermal adnexal neoplasm that was composed of large and small cystic structures filled with an amorphous material (Figure 2). This proliferation extended deeply into the reticular dermis and focally into the subcutaneous layer (Figures 3 and 4). The small islands were embedded in a desmoplastic stroma with poor circumscription that extended beyond the lateral margins of the specimen. There was focal neurotropism (Figure 5). The luminal surface of the cystic areas stained positively with epithelial

Accepted for publication December 6, 2006.
Dr. Lountzis is from Geisinger Medical Center, Danville, Pennsylvania. Drs. Junkins-Hopkins, Uberti-Benz, and Elenitsas are from the Hospital of the University of Pennsylvania, Philadelphia.
The authors report no conflict of interest.
Reprints: Rosalie Elenitsas, MD, University of Pennsylvania, Department of Dermatology, 3600 Spruce St, 2 Maloney Bldg, Philadelphia, PA 19104-6142 (e-mail: rosalie.elenitsas@uphs.upenn.edu).

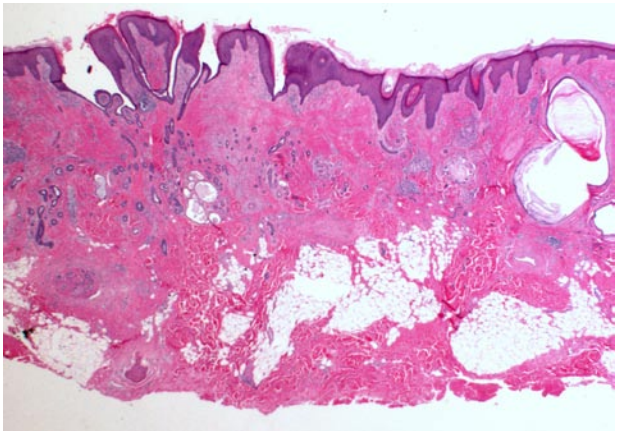

Figure 1. A large lesion with irregular verrucous epidermal hyperplasia with variably sized cystic and glandular structures in the dermis (H&E, original magnification ×12.5).

membrane and carcinoembryonic antigens. This atypical sclerosing lesion was most consistent with features of MAC. A reexcision subsequently was performed, with pathology that revealed a residual MAC with clear margins.

Comment

With a penchant for developing both benign and malignant neoplasms as well as an association with NS syndrome, NS has held a traditionally small threshold for prophylactic excision.[6,7] Neoplasms occur mostly in the fourth decade of life in approximately 10% to 30% of lesions, with trichoblastoma and syringocystadenoma papilliferum being the most common tumors.[4,6,8] Although rare, NS also may experience multiple growths.[9,10] The premalignant nature of NS was first described in 1962 by Michalowski,[11] and basal cell carcinoma (BCC) was believed to be the most common tumor. However, some researchers theorized that the most BCCs found within NS were in fact benign trichoblastomas,[12] and a study by Cribier et al[3] confirmed this finding using silhouette analysis and stromal examination. Currently, trichoblastomas are believed to be the most common follicular tumors associated with NS.[3,8]

Nevertheless, malignant tumors do occur in NS, including squamous cell carcinoma (SCC), malignant melanoma, apocrine carcinoma, and sebaceous carcinoma.[4,13] Underlying malignancy within NS is suggested by the acute appearance of large, discrete, ulcerating nodules within the lesion.[4,6,14] Primary epithelial germ cell defects may explain the abnormalities found in follicular, apocrine, and sebaceous structures, and the tendency for neoplastic growth. Moreover, few cases of MAC have been reported within an NS; this is the second documented case to date.[15] However, there are reports of adnexal carcinomas arising in NS that could have features that overlap with our case.[16,17]

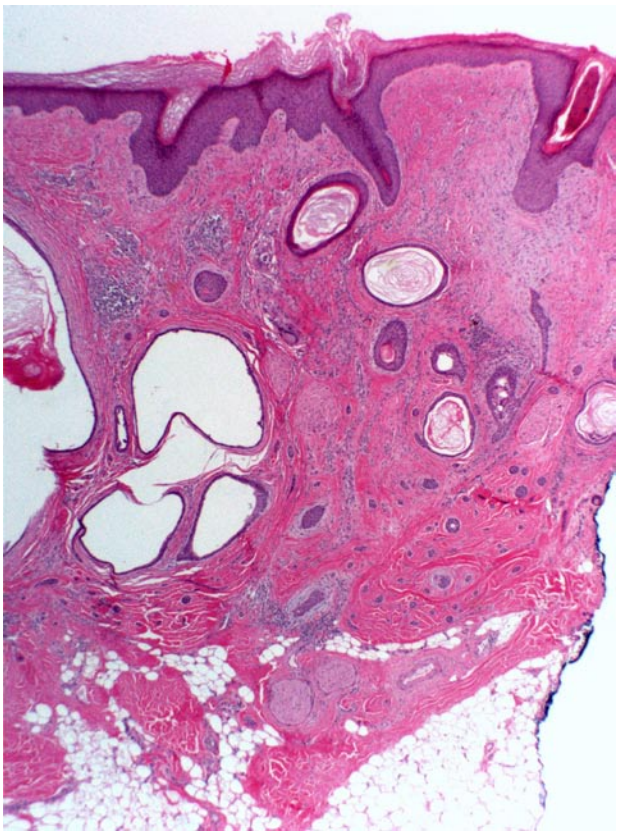

Figure 2. Microcystic adnexal carcinoma. An infiltrative dermal adnexal neoplasm, which is adjacent to the syringocystadenoma papilliferum (H&E, original magnification ×5).

MAC is an infiltrative adnexal neoplasm occurring on the centrofacial region. The median age of onset is 56 years, with an incidence equal in men and women.[18] Predominance is seen in the white population, but a few cases in the black population have been documented.[19-22] Sun exposure, genetics, immunosuppression, and radiation have been implicated as risks for MAC.[18,19,23-25] Numerous cases of MAC (8%–12%) involve patients with previous radiation exposure for treatment of acne, tinea capitis, or thyroid carcinoma several years prior to presentation.[18,26-28] Only one death has been attributed to MAC.[29] Metastases also are uncharacteristic, but cases have been reported.[24,29,30] Clinically, the lesion presents as a flesh-colored to yellow nodule, cyst, or plaque, with a strong predilection for the lips (52%) and nasal area (14%).[18] Lesions of the axilla and trunk rarely have been reported.[19,31,32] Delay of several years from onset to diagnosis is often observed because of the lesion's slow growth and bland clinical appearance of MAC.[18,30,33]

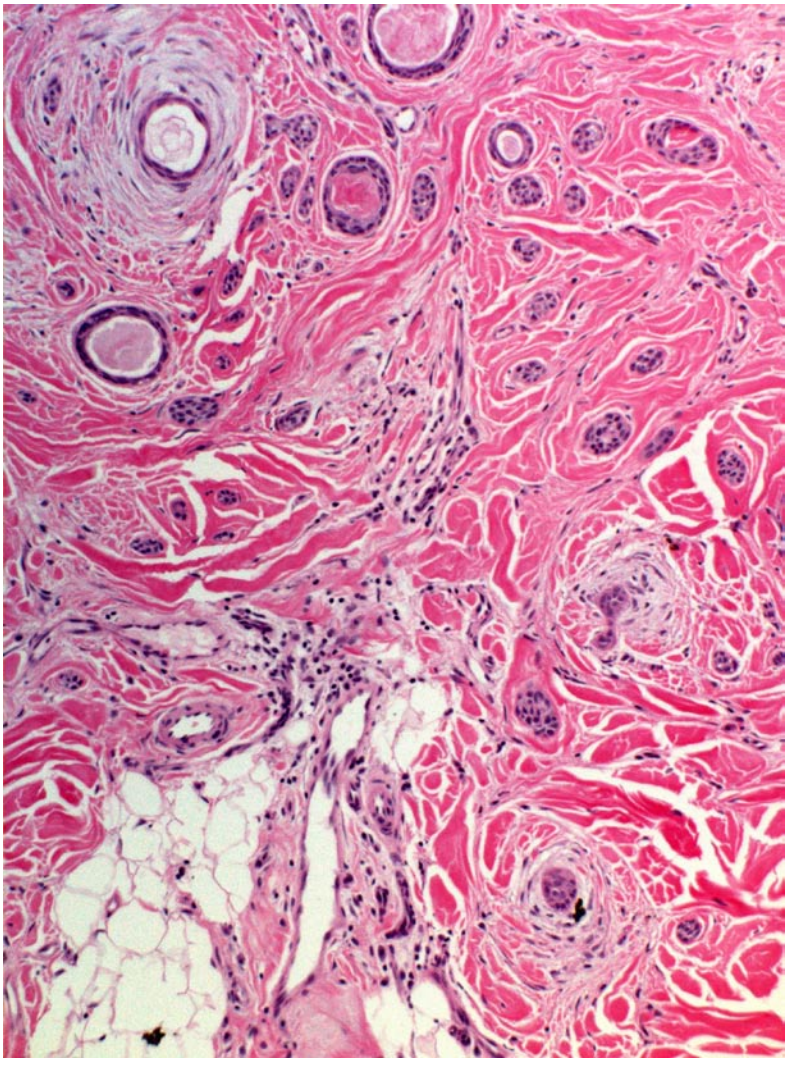

Figure 3. Microcystic adnexal carcinoma. Small infiltrative epithelial islands and ducts extending into the subcutaneous tissue (H&E, original magnification ×200).

Microscopically, MAC has a deceivingly banal appearance without cytologic atypia, mitoses, or necrosis. However, it is a locally destructive neoplasm with a high recurrence rate that is secondary to hidden invasion of deeper perineural, perichondrial, perimuscular, and perivascular structures.[18,27,31,34] Moreover, microscopic borders can extend to up to twice the size of clinically visible margins, which makes simple local excision difficult.[23] Biopsy results generally reveal poorly demarcated epithelial nests, strands, and cords of tumor cells that infiltrate deep into the dermis and subcutaneous layer, with areas of keratinized cysts and well-differentiated ductules. No variation in histology is seen between irradiated and nonirradiated skin.[35]

Differentiation of MAC is controversial; Goldstein et al[36] originally hypothesized both a follicular and eccrine origin. Squamoid aggregations with keratin cysts resemble hair matrix differentiation, and basaloid cords, nests, and ducts resemble sweat glands, with both components present in variable proportions.[32,36] Some authors also contend that an apocrine or sebaceous differentiation is plausible.[15,18,37] However, immunohistochemistry has been used to identify the origin of MAC, which has shown a strong penchant for carcinoembryonic antigen, epithelial membrane antigen, and cytokeratin, which suggest an eccrine and follicular origin, as speculated by Goldstein et al.[36] MAC also shows immunoreactivity with cystic fibrosis-1, a monoclonal antibody specific for eccrine ducts, and acrosyringium.[32] Electron microscopy has further supported the notion of follicular and eccrine differentiation.[18] Light microscopy is the gold standard for diagnosis, with a differential that includes trichoadenoma; morpheaform BCC; syringoma; eccrine carcinoma; desmoplastic SCC; metastatic breast cancer; and desmoplastic trichoepithelioma, which is the most difficult to discern from MAC.[18,27,38]

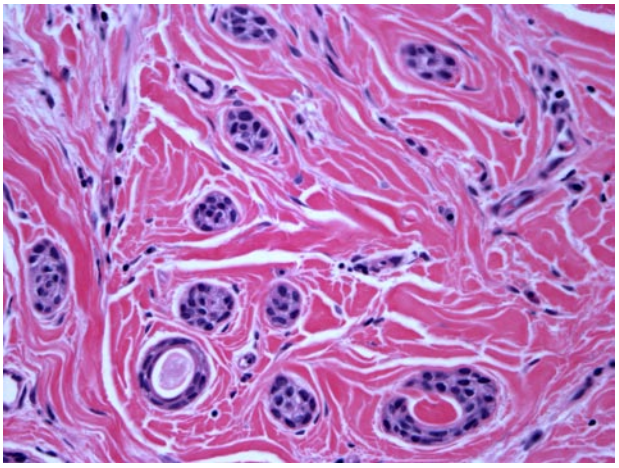

Figure 4. Microcystic adnexal carcinoma. Focal duct formation deep in the dermis (H&E, original magnification ×400).

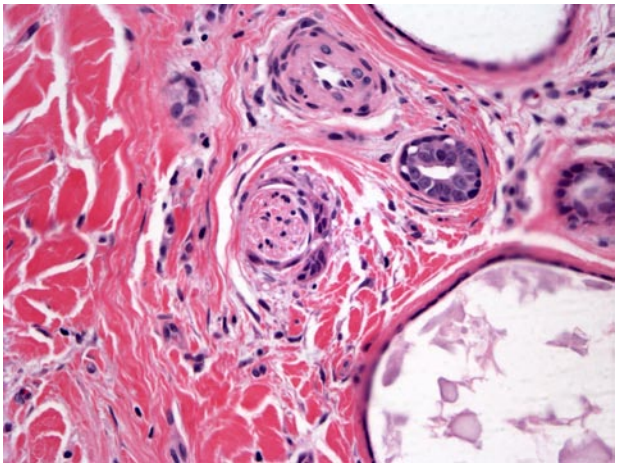

Figure 5. Epithelial tumor cells surround a small cutaneous nerve (H&E, original magnification ×400).

Immunohistochemistry may be useful in differentiating SCCs and BCCs from MAC.[19,39]

The definitive treatment of MAC includes Mohs micrographic surgery.[27] Wide excision alone may be inadequate because MAC has a tendency to recur even with margins as wide as 5 cm.[18] Radiation therapy has not shown much success, even when combined with wide excision.[18,36,40,41]

Overall, the occurrence of MAC within NS is a rare incident that is just recently being recognized. Our case reinforces this event and underscores the importance of adequate biopsy specimens that involve a suspected MAC to reveal all architectural features of the neoplasm, such as deep dermal and/or subcutaneous infiltration and neurotropism. Poor specimens can lead to misdiagnosis, which may delay proper treatment and lead to further tissue destruction and morbidity.

REFERENCES

1. Jadassohn J. Bemerkungen zur histologie der systematisierten naevi und über "Talgdrüsen-Naevi." *Arch Derm Syph.* 1895;33:355-408.
2. Mehregan AH, Pinkus H. Life history of organoid nevus. *Arch Dermatol.* 1965;91:574-588.
3. Cribier B, Scrivener Y, Grosshans E. Tumors arising in nevus sebaceus: a study of 596 cases. *J Am Acad Dermatol.* 2000;42:263-268.
4. Domingo J, Helwig EB. Malignant lesions associated with the nevus sebaceus of Jadassohn. *J Am Acad Dermatol.* 1979;1:545-556.
5. Tarkan II, Domingo J. Metastasizing eccrine porocarcinoma developing in a sebaceous nevus of Jadassohn. report of a case. *Arch Dermatol.* 1985;121:413-415.
6. Shapiro M, Johnson B, Witmer W, et al. Spiradenoma arising in a nevus sebaceus of Jadassohn. *Am J Dermatopathol.* 1999;21:462-467.
7. Rogers M, McCrossin I, Commens C. Epidermal nevi and the epidermal nevus syndrome. *J Am Acad Dermatol.* 1989;20:476-478.
8. Jaqueti G, Requena L, Sanchez Yus E. Trichoblastoma is the most common neoplasm developed in nevus sebaceus of Jadassohn: a clinicopathologic study of a series of 155 cases. *Am J Dermatopathol.* 2000;22:108-118.
9. Stavrianeas NG, Katoulis AC, Stratigeas NP, et al. Development of multiple tumors in a sebaceous nevus of Jadassohn. *Dermatology.* 1997;195:155-158.
10. Rosenblum GA. Nevus sebaceus, syringocystadenoma papilliferum, and basal cell epithelioma. *J Dermatol Surg Oncol.* 1985;11:1018-1120.
11. Michalowski R. Jadassohn's sebaceous nervus a precancerous state [in French]. *Dermatologica.* 1962;124:326-340.
12. Ackerman AB, Steffen C. *Neoplasms With Sebaceous Differentiation.* Philadelphia, Pa: Lea & Febiger; 1994.
13. Abe S, Yamamoto Y, Uno S, et al. Malignant melanoma arising in a sebaceous nevus of the scalp. *Br J Plast Surg.* 2003;56:171-173.
14. Constant E, Davis DG. The premalignant nature of the nevus sebaceus of Jadassohn. *Plast Reconstr Surg.* 1972;50:257-259.
15. Ongenae KC, Verhaegh ME, Vermeulen AH, et al. Microcystic adnexal carcinoma: an uncommon tumor with debatable origin. *Dermatol Surg.* 2001;27:979-984.
16. Martin PC, Smith JL, Pulitzer DR, et al. Compound (primordial) adnexal carcinoma arising in a systematized compound epithelial nevus. *Am J Surg Pathol.* 1992;16:417-425.
17. Hugel H, Requena L. Ductal carcinoma arising from a syringocystadenoma papilliferum in a nevus sebaceus of Jadassohn. *Am J Dermatopathol.* 2003;25:490-493.
18. Sebastien TS, Nelson BR, Lowe L, et al. Microcystic adnexal carcinoma. *J Am Acad Dermatol.* 1993;29:840-845.
19. Abate M, Zeitouni NC, Seyler M, et al. Clinical course, risk factors, and treatment of microcystic adnexal carcinoma; a short series report. *Dermatol Surg.* 2003;29:1035-1038.

20. Park JY, Parry EL. Microcystic adnexal carcinoma: first reported case in a black patient. *Dermatol Surg.* 1998;24:905-907.
21. Gardner ES, Goldberg LH. Neglected microcystic adnexal carcinoma: the second reported case in a black patient. *Dermatol Surg.* 2001;27:678-680.
22. Peterson CM, Ratz JL, Sangueza OP. Microcystic adnexal carcinoma: first reported case in an African American man. *J Am Acad Dermatol.* 2001;45:283-285.
23. Snow S, Madjar DD, Hardy S, et al. Microcystic adnexal carcinoma: report of 13 cases and review of literature. *Dermatol Surg.* 2001;27:401-408.
24. Carroll P, Goldstein GD, Brown CW Jr. Metastatic microcystic adnexal carcinoma in an immunocompromised patient. *Dermatol Surg.* 2000;26:531-534.
25. Brookes JL, Bentley C, Verma S, et al. Microcystic adnexal carcinoma masquerading as a chalazion. *Br J Ophthalmol.* 1998;82:196-199.
26. Burns MK, Chen SP, Goldberg LH. Microcystic adnexal carcinoma: ten cases treated by Mohs micrographic surgery. *J Dermatol Surg Oncol.* 1994;20:429-434.
27. Billingsley EM, Fedok F, Maloney ME. Microcystic adnexal carcinoma. case report and review of the literature. *Arch Otolaryngol Head Neck Surg.* 1996;122:179-182.
28. Hamm JC, Argenta LC, Swanson NA. Microcystic adnexal carcinoma: an unpredictable aggressive neoplasm. *Ann Plast Surg.* 1987;19:173-180.
29. Yugueros P, Kane WJ, Goellner JR. Sweat gland carcinoma: a clinicopathologic analysis of an expanded series in a single institution. *Plast Reconstr Surg.* 1998;102:705-710.
30. Bier-Lansing CM, Hom DB, Gapany M, et al. Microcystic adnexal carcinoma: management options based on long-term follow-up. *Laryngoscope.* 1995;105:1197-1201.
31. Cooper PH, Mills SE. Microcystic adnexal carcinoma. *J Am Acad Dermatol.* 1984;10:908-914.
32. Ceballos PI, Penneys NS, Cohen BH. Microcystic adnexal carcinoma: a case showing eccrine duct differentiation. *J Dermatol Surg Oncol.* 1988;14:1236-1239.
33. Borenstein A, Seidman DS, Trau H, et al. Case report: microcystic adnexal carcinoma following radiotherapy in childhood. *Am J Med Sci.* 1991;301:259-261.
34. Cooper PH, Mills SE, Leonard DD, et al. Sclerosing sweat duct (syringomatous) carcinoma. *Am J Surg Pathol.* 1985;9:422-433.
35. Friedman PM, Friedman RH, Jiang SB, et al. Microcystic adnexal carcinoma: collaborative series review and update. *J Am Acad Dermatol.* 1999;41:225-231.
36. Goldstein DJ, Barr RJ, Santa Cruz DJ. Microcystic adnexal carcinoma. *Cancer.* 1982;50:566-572.
37. Leboit PE, Sexton M. Microcystic adnexal carcinoma of the skin. *J Am Acad Dermatol.* 1993;29:609-618.
38. Smith KJ, Williams J, Corbett D, et al. Microcystic adnexal carcinoma: in an immunohistochemical study including markers of proliferation and apoptosis. *Am J Surg Pathol.* 2001;25:464-471.
39. Wick MR, Cooper PH, Swanson PE, et al. Microcystic adnexal carcinoma. an immunohistochemical comparison with other cutaneous appendage tumors. *Arch Dermatol.* 1990;126:189-194.
40. Yuh WT, Engelken JD, Whitaker DC, et al. Bone marrow invasion of microcystic adnexal carcinoma. *Ann Otol Rhino Laryngol.* 1991;100:601-603.
41. Birkby CS, Argenyi ZB, Whitaker DC. Microcystic adnexal carcinoma with mandibular invasion and bone marrow replacement. *J Dermatol Surg Oncol.* 1989;15:308-312.