The Korean Journal of Pathology 2010; 44: 92-6
DOI: 10.4132/KoreanJPathol.2010.44.1.92

Adnexal Clear Cell Carcinoma with Comedonecrosis
– A Case Report –

Seo-Hee Kim · Sun-Hee Han
Jung-Suk An · Ju-Han Lee
Eung Seok Lee · Heum-Rye Park
Young-Sik Kim

Department of Pathology, Korea University Ansan Hospital, Ansan, Korea

Received : August 12, 2008
Accepted : June 2, 2009

Corresponding Author
Young-Sik Kim, M.D.
Department of Pathology, Korea University Ansan Hospital, 516 Gojan 1-dong, Danwon-gu, Ansan 425-707, Korea
Tel: 031-412-5322
Fax: 031-412-5324
E-mail: apysk@korea.ac.kr

Adnexal clear cell carcinoma with comedonecrosis (ACCCC) is a very rare malignancy of the skin with an aggressive clinical course and a predilection for the scalp. This is the first reported case of ACCCC in Korea. A 79-year-old male presented with left abdominal masses that proved to be two subcutaneous nodules. The tumors histologically consisted of epithelial nests that showed a distinctive zonal arrangement. The centrally located clear cell areas with comedonecroses were merged with the peripheral squamoid cells, often exhibiting retraction artifacts and an infiltrating border. Nuclear pleomorphism and frequent mitoses were prominent. The clear cells were immunopositive for carcinoembryonic antigen and epithelial membrane antigen. We report here on a case of ACCCC involving the abdominal skin, and this tumor should be distinguished from the more indolent squamous cell and tricholemmal carcinomas.

Key Words : Neoplasms, adnexal and skin appendage; Necrosis; Abdomen

Adnexal clear cell carcinoma with comedonecrosis (ACCCC) is a recently recognized, very rare cutaneous carcinoma.[1] ACCCCs most commonly develop in the head and neck area, especially the scalp, and this tumor exhibits aggressive clinical behavior. Histologically, the tumor nests show a zonal arrangement that is composed of outer squamoid cell layers and inner clear cell layers. The central clear cell areas often contain foci of comedonecrosis. No eccrine, apocrine or sebaceous differentiation is seen. Since ACCCCs have the potential for local recurrence and regional or distant metastases,[1] they should be distinguished from clear cell squamous cell carcinoma (SCC) and tricholemmal carcinomas, which have less aggressive clinical courses.[2,3] We report herein on a case of ACCCC that developed in the abdominal skin, and this is the first reported case in Korea.

CASE REPORT

A 79-year-old man was admitted to Korea University Ansan Hospital for the evaluation of two palpable nodules at the left lower quadrant abdomen, and he had had these nodules for 3 years. Computed tomography revealed two well-enhancing tumors with some necrotic portion in the dermis and subcutaneous fat of the abdominal wall. The tumors were then excised.

Grossly, the specimen consisted of two ovoid masses with the overlying skin. The cross section showed relatively well-demarcated whitish yellow, solid masses with myxoid-like areas, and the tumors measured 3.2 × 2.4 cm and 1.5 × 0.7 cm in cross, respectively (Fig. 1A). Microscopically, the tumor involved the reticular dermis and subcutaneous fat (Fig. 1B). The tumor cells were arranged in discrete nests, trabeculae or interconnecting islands that showed a distinctive zonal arrangement (Fig. 2A). Squamous differentiation was dominant at the periphery of the tumor nests (Fig. 2B). The individual cells had round to oval vesicular nuclei, small prominent nucleoli, eosinophilic cytoplasm, and intercellular bridges, but the cells were without keratin pearls. The squamous cells were merged with the inner clear cells that had centrally located nuclei, small nucleoli, clear cytoplasm

and distinct cell membranes (Fig. 2C). Signet-ring like clear cells were occasionally noted. The clear cell nests showed foci of comedonecrosis that consisted of hydropic degenerated cells, parakeratotic cells, apoptototic cells or tumor necrosis mixed with neu-

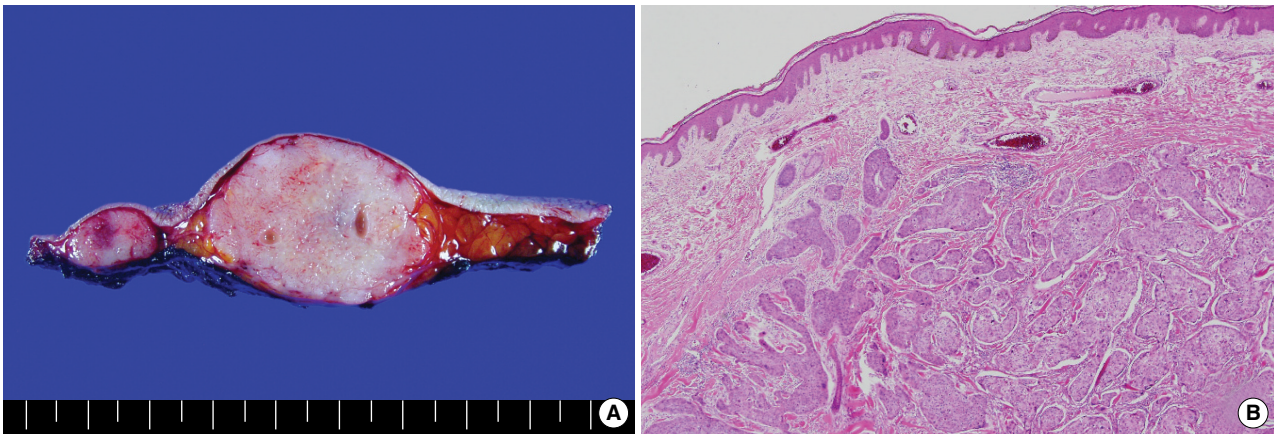

Fig. 1. Grossly, two ovoid, whitish yellow, solid masses, measuring 3.2 × 2.4 cm and 1.5 × 0.7 cm, respectively, are seen (A). At low power view, the tumor involves the superficial and deep reticular dermis without epidermal connection (B).

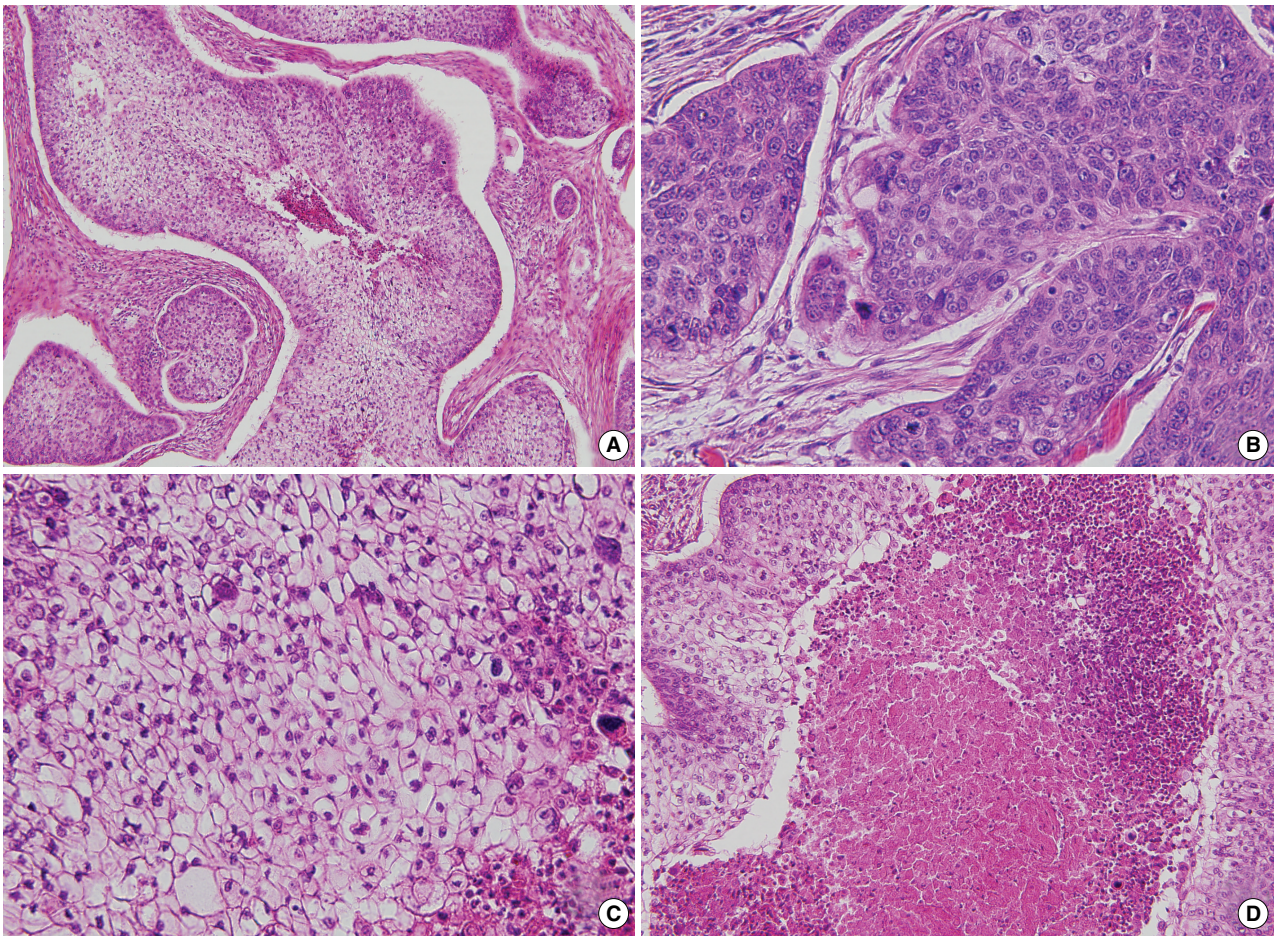

Fig. 2. The tumor nests demonstrate a distinctive zonal arrangement, consisting of outer squamous cell layers and inner clear cell layers, and retraction artifacts (A). Squamous differentiation is dominant at the periphery of tumor nests (B). The centrally located clear cells with occasional signet-ring like form are noted (C). The clear cells surround a large amount of comedonecrosis in the center of tumor islands (D).

trophils in the central area (Fig 2D). The clear cells contained a large amount of glycogen, which stained positive with periodic acid-Schiff (PAS) (Fig. 3A) and it was digested with diastase (Fig. 3B). There was no evidence of intracytoplasmic lipid deposition or cytoplasmic microvacuolization that would suggest sebaceous differentiation. Nuclear pleomorphism was observed in both the squamous and clear cell areas. Bizarre giant cells or multinucleated cells were also noted. The mitotic count was 2-3/high power field. The connective tissue surrounding the tumor nests varied from a loose inflamed stroma to dense fibrosis. Characteristically, there were retraction artifacts of the tumor islands from the surrounding stroma.

Immunohistochemistry was performed using a ChemMate EnVision Kit (Dako, Carpinteria, CA, USA). The antibodies we used are listed in Table 1. The tumor cells were positive for cytokeratin (AE1/AE3) and cytokeratin 7, but they were negative for S-100 protein, CD34, and cytokeratin 20. Most of the clear

Table 1. Antibodies used for immunohistochemistry

Antibody	Clone	Source	Tumor
EMA	E29	Dako	+
CEA	85A12	Signet	+
Cytokeratin	AE1/AE3	Zymed	+
CAM 5.2	UCD/PR-10.11	Zymed	+, focal
CK5/6	D5/16B4	Dako	+
HMW cytokeratin	34 beta E12	Dako	+
Cytokeratin 7	OV-TL12/30	Dako	+
Cytokeratin 20	K_s 20.8	Dako	–
Calretinin	DAK-Calret1	Dako	–
S100	4C4.9	Labvision	–
CD34	QBEnd/10	Labvision	No emboli
D2-40	D2-40	Dako	No emboli
$p16^{INK4A}$	E6H4	Dako	–
p53	DO-7	Novocastra	+, focal
p63	4A4	Dako	+
Ki-67	MIB-1	Dako	20%

EMA, epithelial membrane antigen; CEA, carcinoembryonic antigen; HMW, high molecular weight.

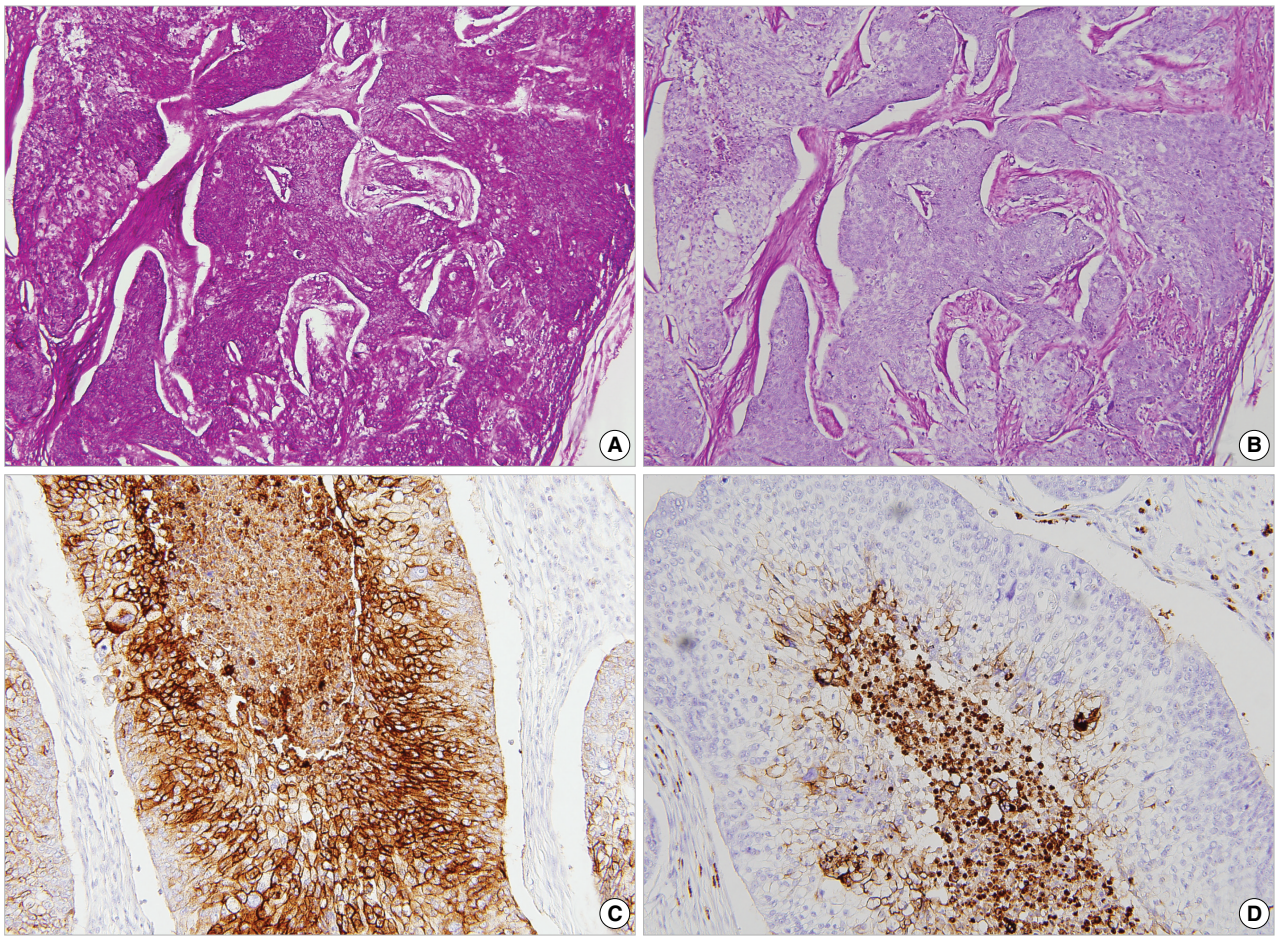

Fig. 3. The clear cells show intracellular accumulation of glycogen, as indicated by staining of periodic acid-Schiff reagents (A) and digestion with diastase (B). Immunohistochemically, most of the clear cells stain positive for epithelial membrane antigen (C) and carcinoembryonic antigen (D).

cells stained positive for epithelial membrane antigen (EMA) (Fig. 3C), and the clear cells adjacent to the comedonecroses stained for carcinoembryonic antigen (CEA) (Fig. 3D). The Ki-67 labeling index rate was about 20%.

DISCUSSION

ACCCC is a distinctive clinicopathologic entity that has a predilection for older individuals (median age, 71 years) and hair-bearing skin, especially the head and neck area.[1] The tumors are usually ulcerated or crusted papules, nodules or plaques that range from 0.5 to 3 cm in size. All the reported cases have presented as a single lesion, which is different from our case.

The characteristic histologic features are the zonal arrangement that is comprised of peripheral squamoid cells, central clear cells, and comedo-type necrosis.[1] The present case had the largest tumor (3.2 cm) among the reported cases and the tumor showed an eccentric location on the abdominal skin. In addition, the tumor presented as two separated nodules infiltrating the subcutaneous fat, suggesting the possibility of subepidermal metastasis. Clinically, these nodules were more like benign soft tissue lesions.

In our present case, there were conspicuous microscopic nuclear pleomorphism and mitoses that unequivocally indicated a malignancy. The Ki-67 labeling index was up to 20%. Approximately 30% of ACCCCs show local recurrence and/or lymph node and lung metastases.[1] In our case, lymphatic or vascular tumor emboli were not found on immunohistochemistry for CD34 and D2-40. The clear cell changes of ACCCC are due to the intracellular accumulation of glycogen. Together with the absence of cytoplasmic microvacuolization, the diastase-sensitive PAS positivity suggests that sebaceous differentiation can be excluded. The additional consistent features of ACCCC are the immunohistochemical expression of CEA and EMA in the clear cells.[1] Although immunopositivity for CEA and EMA usually indicates ductal or acrosyringeal differentiation among the skin adnexal tumors, it is also known that both antigens can be expressed in epithelial cells with squamous differentiation or degenerative changes.[1] Considering this tumor's frequent occurrence in the scalp and its expressions of EMA and CEA, it is likely that ACCCC has more follicular differentiation than sweat gland differentiation. However, despite its putative differentiation toward the outer root sheath of hair follicles, the prefix "adnexal" of ACCCC is designated because there is a significant overlap of follicular and sweat gland differentiation.[1]

The main differential diagnoses of ACCCC include clear cell SCC[4,5] and tricholemmal carcinoma.[6,7] ACCCC should also be distinguished from clear cell tumors, including clear cell hidradenocarcinoma, clear cell porocarcinoma, amelanotic clear cell melanoma, clear cell sarcoma, clear cell proliferating tricholemmal tumor, clear cell basal cell carcinoma, and metatstatic clear cell carcinomas. ACCCC can be distinguished from clear cell hidradenocarcinoma and porocarcinoma by the fact that these carcinomas show tubule formation or cystic lumina in their tumor nests. ACCCC is immunohistochemically different from malignant melanoma. Amelanotic clear cell melanomas are immunoreactive for Fontana-Masson, S-100 protein and HMB-45. Clear cell proliferating tricholemmal tumor is usually well demarcated from the surrounding tissue, and it displays characteristic tricholemmal keratinization. Basal cell carcinoma shows a peripheral palisading of the tumor cells. Metastastatic clear cell carcinoma can be distinguished from ACCCC by the clinical history and the histologic findings of well formed cords, alveoli or tubules that are composed of uniform clear cells.

Clear cell SCC can be differentiated from ACCCC by the fact that the latter has characteristic features that include a zonal arrangement of tumor nests with central comedonecrosis, a predominant involvement of the reticular dermis and the immunoexpressions of EMA and CEA that are limited to the clear cell areas.[1] In contrast to ACCCC, the clear cells of SCC are mixed with squamoid cells without a zonal arrangement and they have no intracellular glycogen or mucin.[3]

Tricholemmal carcinoma is a low-grade cutaneous malignancy despite its aggressive histologic features, including cytologic atypia, frequent mitoses and dermal invasion.[2] Tricholemmal carcinoma shows a lobular proliferation of pale to clear squamoid cells with peripheral palisading, but it is without a zonal arrangement. Typically, this tumor is centered on a pilosebaceous unit and it frequently shows follicular and epidermal connections.[2,6,7]

In summary, we report here on a case of ACCCC that involved an unusual site. ACCCC is a distinctive adnexal carcinoma with potentially aggressive behavior. Although any lymphovascular invasion was not found in this case, the presence of these double tumors suggested a possibility of intradermal metastasis, and so this patient is receiving close follow-up.

REFERENCES

1. Chaudhry IH, Zembowicz A. Adnexal clear cell carcinoma with comedonecrosis: clinicopathologic analysis of 12 cases. Arch Pathol Lab

Med 2007; 131: 1655-64.
2. Cassarino DS, Derienzo DP, Barr RJ. Cutaneous squamous cell carcinoma: a comprehensive clinicopathologic classification. Part one. J Cutan Pathol 2006; 33: 191-206.
3. Cassarino DS, Derienzo DP, Barr RJ. Cutaneous squamous cell carcinoma: a comprehensive clinicopathologic classification. Part two. J Cutan Pathol 2006; 33: 261-79.
4. Kuo T. Clear cell carcinoma of the skin. A variant of the squamous cell carcinoma that simulates sebaceous carcinoma. Am J Surg Pathol 1980; 4: 573-83.
5. Requena L, Sànchez M, Requena I, Alegre V, Sanchez Yus E. Clear cell squamous cell carcinoma: a histologic, immunohistologic, and ultrastructural study. J Dermatol Surg Oncol 1991; 17: 656-60.
6. Swanson PE, Marrogi AJ, Williams DJ, Cherwitz DL, Wick MR. Tricholemmal carcinoma: clinicopathologic study of 10 cases. J Cutan Pathol 1992; 19: 100-9.
7. Wong TY, Suster S. Tricholemmal carcinoma: a clinicopathologic study of 13 cases. Am J Dermatopathol 1994; 16: 463-73.