
Clear Cell and Signet-Ring Cell Squamous Cell Carcinoma

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Introduction

Clear cell squamous cell carcinoma (clear cell SCC) was first described by Kuo in 1980 as a rare variant of squamous cell carcinoma (SCC). It appears predominantly on sun-exposed sites in elderly. The neoplasm is formed by sheets or islands of clear cells with empty-appearing or “bubbled” cytoplasm. Signet-ring cell squamous cell carcinoma (signet-ring cell SCC) is a very rare histopathological variant of SCC with only a few cases reported. It can be exceedingly difficult to differentiate this neoplasm from both primary cutaneous and secondary adenocarcinomas.

Clinical Features

The lesions of clear cell SCC and signet-ring cell SCC appear as nodules or ulcerated tumors on sun-exposed areas, especially on the head and neck region of elderly people with chronic sun exposure (Fig. 2.1).

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Pathology

Originally, Kuo described three types of clear cell SCC, namely, keratinizing (type I), nonkeratinizing (type II), and pleomorphic (type III). Type I tumors are described as neoplasms formed by sheets or islands of clear cells with empty-appearing or “bubbled” cytoplasm with foci of keratinization and keratin pearl formation. Type II tumors are described as predominantly dermal neoplasms with parallel and anastomosing cords of cells with central nuclei and finely reticulated clear cytoplasm, without keratinization and ductal or glandular differentiation (Figs. 2.2, 2.3, 2.4, 2.5, and 2.6). In Kuo’s opinion, these could represent either recurrent SCCs or primary adnexal tumors of undetermined histogenesis. Type III tumors are described as pleomorphic neoplasms with clear cells arising from the epidermis, which show foci of squamous differentiation, dyskeratotic cells, and acantholysis and considerable perineural and vascular involvement. Kuo’s examples showed no evidence of either glycogen or mucin within the tumor cells which would support his hypothesis that clear cell changes are degenerative. However, in recent studies, examples of clear cell SCC have been shown to demonstrate glycogen accumulation in the cytoplasm of the clear cells. Only a few cases of authentic cutaneous signet-ring cell SCC have been reported. Apart from the areas with signet-ring cell appearance of the neoplastic intraepidermal or invasive cells, the tumors may show foci of



Fig. 2.1 An ulcerated vegetating tumor on the cheek of an 83-year-old woman

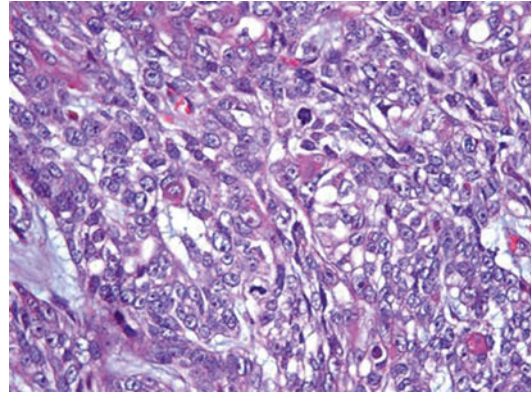


Fig. 2.4 Very focally, the cells show individual keratinization. The cells are large, with vesicular and pleomorphic nuclei and prominent nucleoli. Many mitotic figures are easily identified

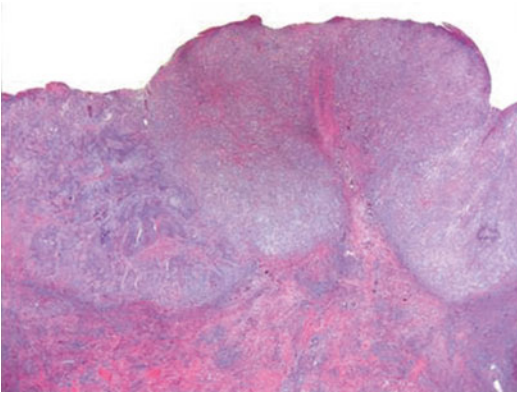


Fig. 2.2 The ulcerated epithelial neoplasm displays large areas of clear cells recognizable even at low magnification

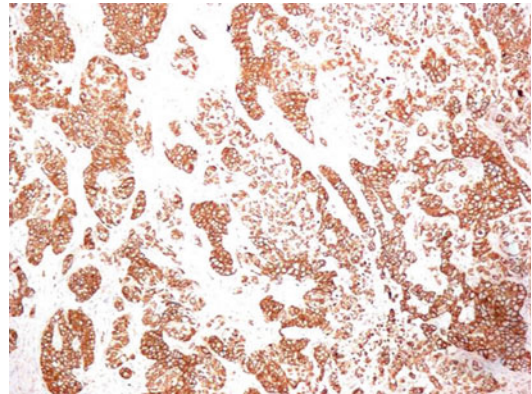


Fig. 2.5 The neoplasm, including the clear cell areas, stains positive for cytokeratin 34βE12

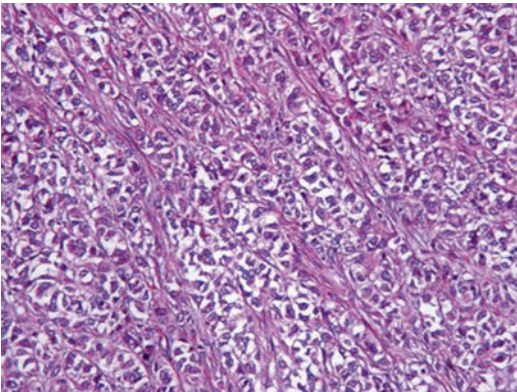


Fig. 2.3 At higher magnification, these areas show parallel and anastomosing cords of cells with central nuclei and clear cytoplasm, without keratinization and ductal or glandular differentiation

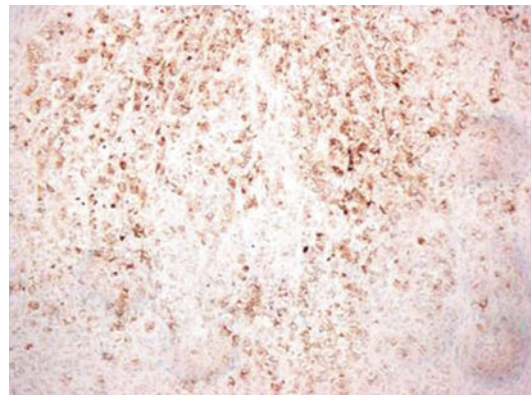


Fig. 2.6 Most of the cells are EMA positive

conventional squamous cell carcinoma that point to the real nature of the neoplasm. The results of the studied cases indicated that mechanisms responsible for the formation of the signet-ring cells are diverse. In some cases, cytosolic accumulation of glycogen was found. In other cases, intracytoplasmic material was shown to be negative for both PAS and mucicarmine.

Differential Diagnosis

SCC with extensive clear cell changes can pose difficulties in differentiation from other neoplasms with clear cells, such as clear cell acanthoma, clear cell hidradenoma, trichilemmoma, balloon cell nevus, proliferating pilar tumor, clear cell basal cell carcinoma, clear cell hidradenocarcinoma, clear cell porocarcinoma, sebaceous carcinoma, clear cell atypical fibroxanthoma, balloon cell melanoma, and metastatic renal cell carcinoma. The presence of more typical areas of SCC (foci of squamous differentiation with horn cyst formation) and identification of a preexisting lesion of actinic keratosis or Bowen's disease should enable the pathologist to establish a correct diagnosis. Clear cell basal cell carcinoma (BCC) is differentiated by the presence of typical areas of BCC with peripheral palisading and retraction artifact. Unlike SCC with clear cells, the rare examples of authentic trichilemmal carcinoma display true trichilemmal differentiation (peripheral columnar cells with clear cytoplasm arranged in a palisade resting on a hyaline basement membrane). Identification of ductal structures by histology and immunohistochemistry (EMA and CEA) allows separation of clear cell hidradenocarcinoma or clear cell porocarcinoma from clear cell SCC.

Signet-ring cell cutaneous SCC should be differentiated from primary cutaneous or secondary adenocarcinomas using special stains (PAS-D,

mucicarmine), immunohistochemistry (EMA, CEA, etc.), and clinical data.

Prognosis

Due to the rarity of these variants of SCC, it is difficult to ascertain its malignant potential. The prognosis depends especially on the tumor size, degree of differentiation, and the presence of intravascular and perineural invasion.

Treatment

Complete surgical excision of the tumor is the treatment of choice.

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