Clear cell hidradenocarcinoma

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SUMMARY

A case of eccrine clear cell hydradenocarcinoma of sweat gland origin is presented, disclosing its clinical behavior and morphologic characteristics as evidenced by fine needle aspiration biopsy and tissue section histology. The patient was a 53-years old male who had a tumor on his fifth toe for 16 years. The tumor recurred 18 months after excision and metastasized widely 17 months following the amputation of the toe due to the recurrence. In spite of chemotherapy the patient died 37 months after the excision of the primary tumor. In aspirates, the tumor cells had no nuclear anaplasia and only numerous mitotic figures pointed to the malignant nature. Histologic features of malignancy were aggressive local growth, focal necrosis, angioinvasion and high mitotic index.

KEY WORDS

eccrine carcinoma, hidradenocarcinoma, skin tumors, cytology, fine needle aspiration biopsy, pathology

Introduction

Clear cell hidradenocarcinoma (CCHC) is a rare skin tumor of eccrine sweat gland origin that has been described in the literature under various names: malignant clear cell myoepithelioma, malignant clear cell hydradenoma, clear cell eccrine carcinoma, malignant clear cell acrospiroma, to only mention a few. During the course of years no single term has been universally accepted. The patients with CCHC are usually in their fourth decade or older. The tumor grows slowly and can be present for several years without apparent change. The estimated recurrence rate is 50% despite agressive surgery.(1) Metastases appear first in regional lymph nodes while the most common hematogenic metastases appear in lungs.(2) In widespread disease chemo and radiotherapy have not proven effective.(3)

In this paper we report on the clinical, cytological and histological findings of a skin tumor that corresponds to the description of malignant clear cell hydradenoma as described by Lever. (4)

Case report

A 53-year old male had a swelling on the fifth toe of his right foot for 16 years that reached a size of 30x25x20mm. Since it had been growing for the last two years it was removed at a local hospital. The histology report was malignant tumor of the skin adnexa and the patient was referred to the Institute of Oncology.

Since no signs of dissemination were found no further treatment was given. The tumor recurred after 18 months and amputation of the fifth toe was necessary. Histologic report at that time was malignant acrospiroma (hydradenocarcinoma). Seventeen months later the patient returned with unilateral pleural effusion, ascites, unilateral cervical lymphadenopaty, a lump in the breast and two subcutaneous nodules in the abdominal wall. Fine needle aspiration biopsy (FNAB) of the affected sites confirmed the malignancy. The morphology was in accordance with the primary tumor. The patient received three cycles of chemotherapy, each one consisting of 500 mg of 5-fluorouracil per day for 4 days. The disease progressed and he died in uremia two months later (28 months after excision of primary tumor). In addition to to the metastases already mentioned, additional ones were found at autopsy in the lungs, on the epicardium, in both thyroid lobes, in the left adrenal gland, in both kidneys, and in the mediastinal, hilar and mesenteric lymph nodes.

Cytologic findings

Smears were partly air dried and Giemsa stained and partly wet fixed in Delaunay solution and stained by the Papanicolaou method. All smears were highly cellular, containing cell groups, dissociated cells and naked nuclei, lying in abundant, viscous material which stained intensely pink with Giemsa but was not noticable in Papanicolaou stained smears. Cell groups were well organized, branching structures with a fibrous core (Figure 1). Nuclei were round to oval with minimal anisonucleosis, finely granular chromatin and multiple nucleoli. There were occasional bi- and multinucleated cells. The cytoplasm was pale and scant. The overall picture was rather uniform, however, numerous mitotic figures were seen (Figure 2).

Histologic findings

The primary tumor which was obtained for review was identical to the recurrent one. Lobulated mases were situated in the dermis and extending into the subcutaneous tissue. The tumor's only connection with the epidermis was at the site of the ulceration. Some of the lobules were solid, some made up of tubular structures lined with one row of cells, and still others contained large cystic spaces filled with homogenous, eosinophilic material and lined with a thick coat of tumor cells (Figure 3). There was focal nuclear palisading at the periphery of some lobules and foci of keratinized cells with pearl formations within walls of cystic spaces. Parts of the tumor were necrotic. Interstitial hyaline collagen changes were present around lobules. The cell population was made up roughly of two cell types: the fusiform cell type with basophilic cytoplasm and the clear cell type. There was very little nuclear pleomorphism, but the number of mitotic figures was high, averaging 8.2 mitoses/10 high power fields (HPF) (range 4-14). Angioinvasion was readily visible in various fields. Glycogen was demonstrated only focally by PAS-positive diastase – digestible material in the cytoplasm of tumor cells. There was, however, a considerable amount of PAS-positive diastase resistant material in the interstitial spaces between cells, between lobules and inside the cystic spaces. This same material was also Kreyberg and alcian blue-positive, meaning that it contained also acid mucopolysacharides. Immunohistochemical reaction for carcinoembryonic antigen (CEA), Glostrup, Denmark, was negative in sections from several blocks.

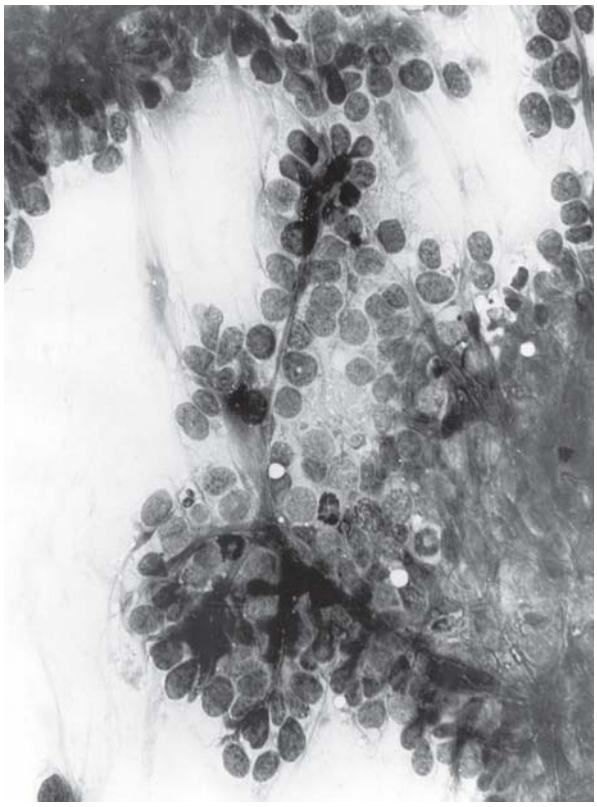

Figure 1. Fine needle aspiration biopsy (FNAB) of clear cell hidradenocarcinoma (CCHC) featuring a well organised cell group in wich cells are attached to a fibrous core. (Giemsa, x 500)

Discussion

In 1996 Gamboa-Dominguez (5) reported that he has found 47 cases of clear cell eccrine carcinomas of the skin in the literature. With the help of PubMed Ser-

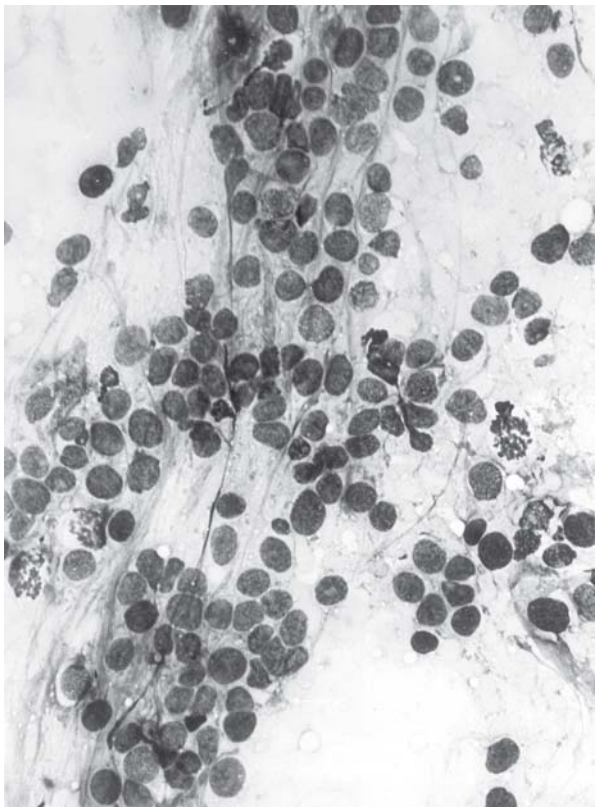

Figure 2. Cytologic smear showing a uniform picture of dissociated cells and naked nuclei lying in abundant, viscous material. Notice mitotic figures. (Giemsa, x 400)

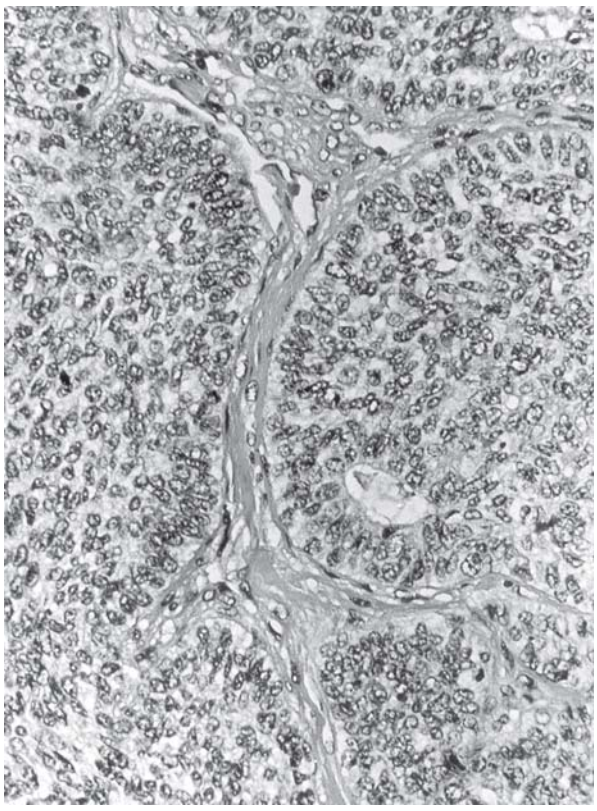

Figure 3. Histology of the tumor from the amputated toe showing mostly solid lobules of fusiform cells. (HE, x 250)

vices we have located additional eight cases reported since 1996 under the names of malignant acrospiroma, (3, 6,7) malignant nodular hidradenoma,(8,9) and malignant clear cell hidradenoma (10, 11, 12). In the commentary to the article of Long et al. from 1998, (3) Geisse et al. point out that in the series of case reports describing the above mentioned tumors, the authors have been reporting microscopically diverse patterns under the same name. Therefore, they say, one cannot derive guidelines for management of such neoplasms until we have reproducible diagnoses, using consise and uniform nomenclature. In their opinion the term »malignant acrospiroma« is confusing and they advocate the use of the term hidradenocarcinoma.

Besides the confusion in nomenclature there seams to be some disagreement also as to the most common location sites of the CCHC. While some authors report head and neck to be the most common location followed by extremities (1), others believe the trunk is the main location (9). We find it interesting that among the nine cases found in the literature since 1996 and adding our own, four CCHC were located in the foot.

In diagnosing an eccrine carcinoma from tissue sections a pathologists has to differentiate it from metastatic carcinomas, from non-adnexal skin tumors, to distinguish various subtypes of eccrine carcinoma and to separate malignant variants from their benign counterparts. The difficuly in recognizing CCHC as an adnexal tumor is illustrated in the fact that in three out of 10 reported cases since 1996 the initial histopathologic diagnoses were seborrheic keratosis (7), basalioma (13) and leiomyosarcoma (3). Immunohistochemical positivity for CEA could help solve the dilemma. However, all tumors of adnexal glandular lineage are not CEA positive. (14) Furthermore, positivity for CEA does not rule out a metastatic carcinoma. Distinguishing the CCHC from other eccrine carcinomas is difficult in poorly differentiated cases when all the characteristic features are not present. Recognising the biological potential of eccrine skin neoplasms is not always possible. Infiltrative growth, nuclear pleomorphism, number of mitotic figures as well as perineural and angiolymphatic invasion have been proposed as criteria of malignancy, however, they are not absolutely reliable. Some authors have proposed a subclassification of CCHC into high grade, low grade and atypical hidradenoma with focal atypia (15). The recurrent clear cell hidradenoma of the foot reported by Will et al. (16) could represent a case of the last cathegory. The authors have reported the tumor as benign. However, since

the follow-up has been only 11 months after the recurrence it is possible the tumor will prove to be malignant in future.

Very little is known about the appearance of CCHC in FNAB samples. We have found only two reports on the benign counterpart, the hidradenoma (17, 18). Based on the morphology of our present case we believe the malignant nature of CCHC cannot be positively assessed from an FNAB smear. Among the characteristics of malignancy proposed for eccrine carcinoma to be used for tissue sections, only a few could be applied in cytology: mitotic activity and nuclear anaplasia. In our case of CHCC there was no nuclear pleomorphism, no hyperchromasia or nucleolar prominence. We only observed high nucleocytoplasmatic ratio and numerous mitotic figures. Except for these, the tumor had a perfectly benign appearance. Unfortunately, high mitotic rate does not seem to be a reliable criterion of malignancy. According to Cooper, high mitotic index has been described in benign clear cell hydradenomas as well as in malignant ones (19).

In conclusion we can say that the tumor we have described seams to be a typical case of CCHC both clinically and histologically. However, after analyzing the morphological characteristics of FNAB smear from our present case, we believe that a definitive diagnosis of CCHC cannot be given. We can probably suggest the origin of the tumor to be from skin adnexa, but a definitive answer as to its biological potential should not be attempted.

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