Case Report

# Low grade malignant eccrinespiradenoma with florid squamous differentiation: A Potential Diagnostic Pitfall

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## ABSTRACT

Malignant eccrinespiradenomas (MES) are rare, fatal neoplasmsand typically manifest as rapid enlargement of long-standing benign eccrinespiradenomas. Low grade malignancyarising in benign eccrinespiradenomas are difficult to diagnose as the morphological changes are subtle and needs careful examination by the pathologist. MES frequently shows focal squamous differentiation, which may be florid in rare instances. We herein report a case of low grade malignancy in an eccrinespiradenoma with florid squamous differentiation. The present tumor was removed twomonths after rapid increase in size of a long standing nodule over the left forearm was noted by the patient. Histopathological examination showed the earliest stage of malignant transformation within eccrinespiradenoma. The early changes of malignant transformation was characterized by nuclear pleomorphism, loss of two cell types, increased mitotic activity with atypical mitoses, partial loss of PAS positive basement membrane material and florid squamous differentiation. Immunostaining for p53 revealed absent staining in benign areas and increased expression in malignant areas. Ki 67 score was less than 1% in benign areas and was increased (4-5%) in the malignant area. Since patient had tumor free margin, no palpable lymph node in the axilla or evidence ofdistant metastasis, he was not put on any adjuvant therapy. Such cases must be followed up carefully. In conclusion, we need more information about low grade malignant eccrinespiradenoma, its biological behavior, and treatment modalities.

**Key words:** Eccrinespiradenoma, malignant, squamous differentiation

## INTRODUCTION

Eccrinespiradenoma is a well recognized benign sweat gland tumor arising from the intradermal straight part of the duct of eccrine sweat glands. Although benign forms are not uncommon, malignant transformation of this tumor is rare[1] and typically manifest as rapid enlargement in long-standing spiradenomas.[2] We present a patient with spiradenoma in the left forearm with early changes of malignant transformation and florid squamous differentiation.

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## CASE REPORT

A 29 year old male presented with rapidly increasing nodular mass over the left forearm. The mass was small and painless initially and patient noticed it since two years. There was increase in the size of mass since twomonths and it was associated with pain. On examination, there was a nodular, firm mass over the upper part of left forearm measuring 3 × 2 cms in size. The mass was tender and was not fixed to the underlying structures. There was no palpable lymph node in the axilla. The mass was excised and sent to us for histopathological examination.

Histopathological examination revealed a nodular tumor located in the dermis. The overlying epidermis demonstrated hyperplastic changes. At higher magnification, one of the nodule comprised of intertwining cords of cells separated by edematous connective tissue. These cords were made up of two cell types, consisting of peripheral row of cells with small dark nuclei and center of the cords consisted of cells with large pale nuclei. These larger cells were frequently arranged around lumina containing eosinophilic PAS

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positive diastase resistant material. A heavy lymphocytic infiltration was present mainly at the peripheral portions of the tumor, but some were also scattered between the tumor cells. Mitotic figures were absent. These features were suggestive of eccrinespiradenoma. One of the nodules showed cystic degeneration. But largest of the nodule was poorly circumscribed and showed extensive squamous differentiation throughout the nodule [Figure 1]. In addition, there was loss of differentiation between two cell types with single type of tumor cells revealing mild pleomorphism, slight nuclear irregularity, numerous apoptotic bodies and increased mitotic figures (5-6/10 HPF) [Figure 2]. Occasional mitotic figures were atypical. There were focal areas revealing typical spiradenoma at the periphery.There was no evidence of tumor necrosis or vascular invasion by tumor cells.PAS outlined partial loss of PAS positive basement membrane in the malignant area.p53 was not expressed in benign areas,wheras increased nuclear p53 expression was noted in malignant areas [Figure 3]. Ki 67 score was less than 1% in benign areas and was increased (4-5%) in the malignant area [Figure 4]. These histological features were suggestive of the earliest stage of malignant transformation within spiradenoma. A diagnosis of low grade malignant eccrinespiradenoma with florid squamous differentiation was rendered. Chest radiographs and abdominal ultrasound failed to reveal any evidence of metastatic lesion.

## DISCUSSION

Eccrinespiradenoma is a well-differentiated benign tumor of the sweat glands. Malignant change arising within eccrinespiradenoma is rare.[1,3] The malignant change in eccrinespiradenoma occurs after a variable latent period, which may be as long as 75 years.[3] It generally begets medical attention when a pre-existing undiagnosed lesion rapidly enlarges, changes color, ulcerates, or becomes painful and tender. According to the estimates of Marenda and Otto,[4] malignant sweat gland tumors account for only 0.005% of all skin tumors.

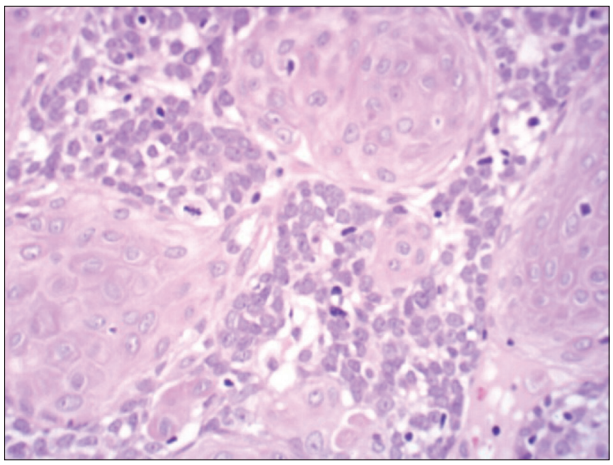

**Figure 1:** Photomicrograph revealing florid squamous differentiation throughout the tumor (H and E, ×20)

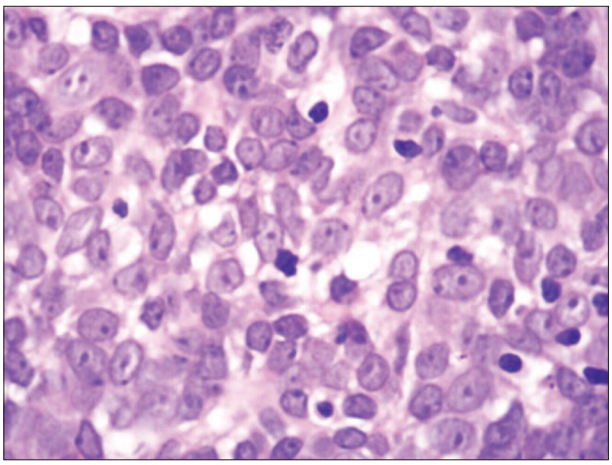

**Figure 2:** Higher magnification revealing loss of two cell types, mild pleomorphism and increased mitotic figures (H and E, ×40)

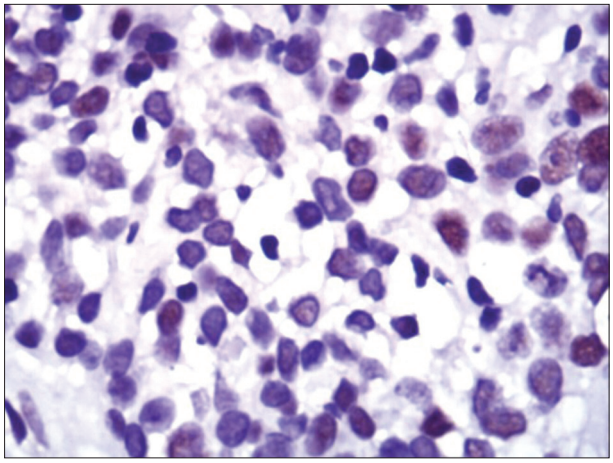

**Figure 3:** increased p53 expression in area of low grade malignant change (IHC, ×40)

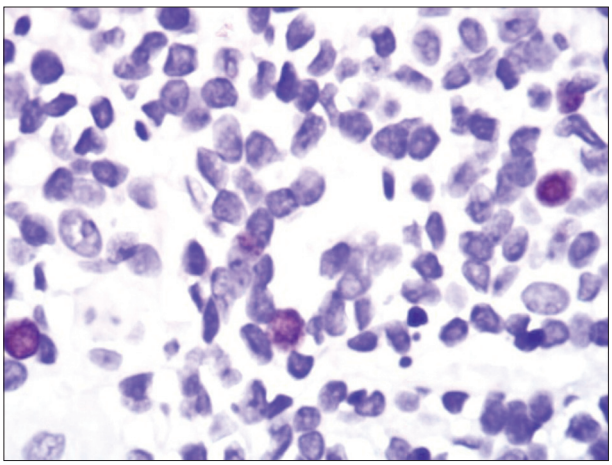

**Figure 4:** Ki 67 score, up to 5% in malignant area (IHC, ×40)

MES is a histologically heterogenous tumor and, it has two distinct paterns; high-grade carcinoma and low-grade tumor imitating benign spiradenoma. The latter is difficult to diagnose as it presents with subtle histological changes. Therefore, pathologists must examine all eccrinespiradenomas carefully in view of malignant transformation.Histologically, proliferation of cells with hyperchromatic nuclei, increased mitoses, atypical mitoses, loss of Periodic-Acid-Schiff positive basement membrane, and invasion of the surrounding tissues characterize malignant transformation in eccrinespiradenoma.

Cooper *et al*.[5] evaluated mitotic figures in a series of sweat gland adenomas, providing baseline data that could be of value in estimating the importance of estimating mitotic figure as a criterion of malignancy in sweat gland neoplasms. In eccrinespiradenomas, mean number of mitotic figure was 0.51/10 HPF and mitotic figures are confined to the basal cells and are absent in pale cells lining the ducts. Mitotic rates are usually between 4 and 32/10 HPF in high grade MES and 2-12/10 HPF low- grade lesions.[2] In our case no mitotic figures were found in benign areas and whereas increased number of mitotic figures including atypical ones up to 5-6/10 HPF were found in malignant areas.

In histopathological examination of our case, features suggesting benign eccrinespiradenomawere found at the periphery of one of the nodules and also low grade MES in the center of the nodule. Lack of encapsulation, irregular borders, lack of double population of cells with monomorphous population of tumor cells with mild pleomorphism, slight nuclear atypia, increased mitotic count, loss of PAS positive basement membrane material in these areas, lack of vascular invasion suggest that this lesion is low-grade MES. Low grades MESs are more difficult to diagnose and are said to have a better prognosis.

MES frequently shows focal squamous differentiation, which may be florid in rare instances.[3] The significance of squamous differentiation in eccrine neoplasms has been a subject of much debate.[6,7] While some believe that this differentiation delineates a subtype of eccrine neoplasms with a more aggressive biologic behavior, others believe that it is an incidental finding and one of no real clinical significance as it does not appear to have an impact on the biology of the disease.[8] In support of the latter is the study by Kohda *et al*.[7] in which both benign and malignant eccrine neoplasms (46% of 24 cases) had foci of squamous differentiation. Squamous islands occurring in eccrine neoplasms are classified into three types, according to their location, histologic characteristics and degrees of cellular atypia. Type I squamous islands resemble normal epidermis and are present in the superficial to middle portion of eccrineporomas. Type II squamous islands are localised in the deeper portion of eccrineporomas and show lumen formation suggestive of acrosyringeal differentiation. Type III squamous islands show atypical features and are limited to malignant eccrine tumors.[8]

The cause of malignant transformation is unknown. Beirnat *et al*.[9] demonstrated overexpression of p53 protein in the malignant portion of eccrinespiradenoma. Immunostaining for p53 remained negative in benign portion. Similar results for p53 staining were also observed in our case, supporting their conclusion that the accumulation of p53 protein,which resulted from alteration in its turnover, accompanied the malignant transformation. These results also suggested the usefulness of p53 staining in the detection of malignant transformation.

Malignant eccrinespiradenoma metastasizes to regional lymph nodes, lungs, brain, and liver in a descending order of frequency.[10] While distant metastases of MES are uncommon, they generally portend an ominous prognosis. Appropriate therapy of malignant eccrinespiradenoma consists of a wide local excision with resection of clinically suspicious lymph nodes. Irradiation of the resection site can be useful in preventing local recurrence. The role of chemotherapy is not yet clearly defined. Symptomatic improvement and shrinkage of the tumor with tamoxifen therapy in a patient with estrogen receptor-positive eccrine adenocarcinoma has also been reported.[10] However, the roles of hormonal therapy and other modalities, such as localized postoperative radiation therapy, prophylactic lymph node dissection and chemotherapy still remain to be determined. Close follow-up of these patients for early detection of recurrence and metastases is recommended. Our patient has tumor free margin, no palpable lymph node in the axilla or evidence of distant metastasis; therefore, he was not put on any adjuvant therapy.

In conclusion, rapid changes of appearance of the benign skin lesions, rapid growth, color change, and ulcerations are clues to the malignant transformation. All such lesions should be carefully examined for early changes of malignant transformation. It is important to diagnose these low grade MES, since they are said to have a better prognosis. However; we need more information about low grade MES, its biological behavior, and treatment modalities.

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