

Case Report

A Rare Incidence of Malignant Eccrine Spiradenoma in a Male's Breast

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Abstract

Introduction: Malignant eccrine spiradenoma is a rare cutaneous tumor of sweat gland origin. It is even more rare to develop malignant eccrine spiradenoma located in the breast. Eccrine spiradenoma is a benign sweat-gland tumor which can arise on skin surfaces of the head, neck, limbs, and trunk [1]. Kersting and Helwig were the first to describe spiradenoma as a skin adnexal neoplasm with a very slow growth pattern [2]. Malignant eccrine spiradenoma (MES) is one of the rarest sweat-gland tumors and can arise from benign eccrine spiradenoma [3] or, less frequently, develop de novo.

Case Presentation: We encountered a 74 year old male with a two centimeter malignant eccrine spiradenoma located at the six o'clock position three centimeters from the right nipple with no skin changes present.

Conclusion: The development of MES in a male's breast is a very rare condition. A high index of clinical suspicion is required to reach a diagnosis. Furthermore, no gold standard management option exists and treatment should be individualized.

Keywords: Malignant eccrine spiradenoma; differentiated invasive ductal cancer; modified radical mastectomy; breast cancer in a male

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Introduction

Malignant eccrine spiradenoma is a rare cutaneous tumor of sweat gland origin. The majority of presorted cases occur in the extremities or upper trunk, with only a handful of cases arising in the breast. Here we report a malignant eccrine spiradenoma of the breast in a 74 year old male. He was successfully treated with a modified radical mastectomy.

Case Report

A 74 year old male sought evaluation for a palpable lump which had been gradually increasing in size over a period of 3 months. Physical examination revealed a non-tender, firm, mobile 2 cm nodule located at the six o'clock position 3 cm from the right nipple with no skin changes present.

An ultrasound confirmed a 1.6 x 1.2 x 1.7-cm solid lobulated mass (Figure 1). Mammography demonstrated a 1.8 cm mass with lobulated margins in the retroareolar region and did not reveal any microcalcifications (Figure 2). A right breast core needle biopsy revealed the mass morphologically resembled a well to moderately differentiated invasive ductal cancer which was positive for immunostains GCDFP-15, E-Cadherin and S-100. The mass stained negative for CK903, CK7, CK5 & 6, CK20, MSA, PSA, and PSAP. Estrogen and progesterone receptors were negative.



Figure 1 High-resolution sonography of the right breast was performed utilizing a real-time sector scanner. The study was analyzed in conjunction with the breast-CAD (computer aided detection) system. Image shows a solid lobulated mass that is wider than tall within the retroareolar region. It measured 1.6 x 1.2 x 1.7 cm.



Figure 2 Craniocaudad and mediolateral oblique views of both breasts were obtained utilizing low dose mammographic technique. Computer assisted detection (CAD) was utilized in interpretation. Image of the right breast shows a mass within the retroareolar region. It measures approximately 1.8 cm with lobulated margins.

Due to the initial impression as an invasive ductal carcinoma, the patient underwent a modified radical mastectomy of the right breast. The surgical specimen demonstrated a 1.9 x 1.4-cm well-differentiated invasive carcinoma. The axillary dissection revealed 12 negative nodes. Microscopic examination revealed the tumor consisted of circumscribed cellular proliferation of epithelial and myoepithelial cells (Figure 3 and Figure 4). The carcinomatous component displayed ductal/glandular formation with intertwining cords of epithelial cells (Figure 5 and Figure 6).

Immunohistochemistry demonstrated absence of chromogranin, synaptophysin, CD34, and calponin staining. Myoepithelial cells were visible with immunohistochemical analysis (Figure 7 and Figure 8). The overall morphology was consistent with an eccrine spiradenoma. No adjuvant therapy was recommended by both medical and radiation oncology consultants. The patient is doing well at 42 months status post diagnosis, with no evidence of recurrence or metastasis.

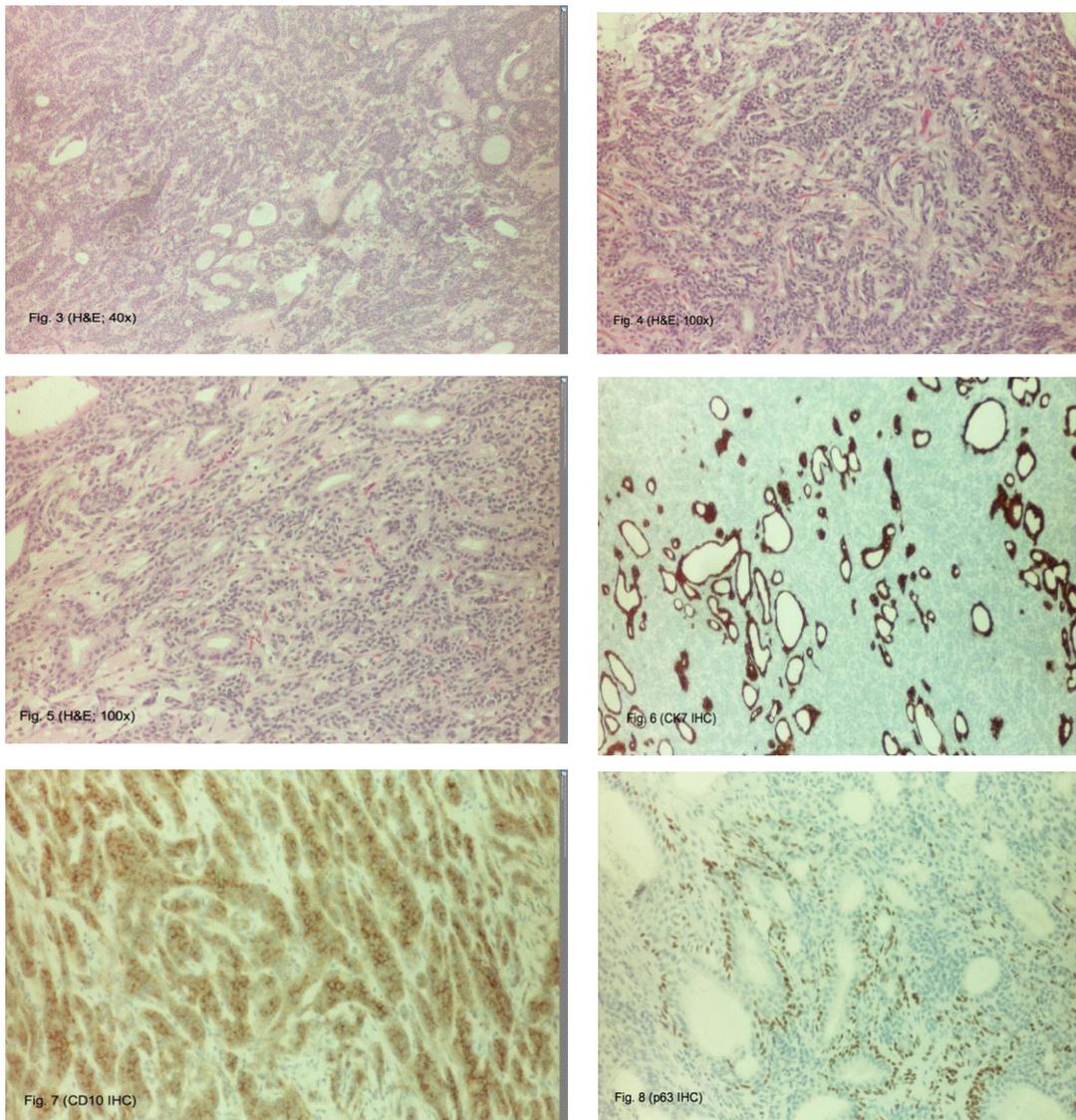


Fig 3-8 Malignant Eccrine Spiradenoma (Eccrine Spiradenocarcinoma) results from rare malignant transformation from benign eccrine spiradenoma. It is an adnexal tumor of eccrine sweat glands. Usually presents as a painful, slow growing solitary nodule. The tumor consists of a circumscribed cellular proliferation of two cell types composed of epithelial and myoepithelial cells (Fig. 3 and Fig. 4). Malignant eccrine spiradenoma typically originate from previous spiradenomas with malignant transformation based on architectural features including cellular atypia and increased mitotic rate. The carcinomatous component in a malignant eccrine spiradenoma may display ductal/glandular formation (Fig.5 and Fig. 6) with intertwining cords of epithelial cells, which can be mistaken for infiltrating mammary carcinoma. However, unlike infiltrating mammary carcinoma, myoepithelial cells can be demonstrated with immunohistochemical analysis (in malignant eccrine spiradenocarcinoma).

Discussion

Eccrine spiradenoma is a benign sweat-gland tumor which can arise on skin surfaces of the head, neck, limbs, and trunk [1]. Kersting and Helwig were the first to describe spiradenoma as a skin adnexal neoplasm with a very slow growth pattern [2]. Malignant eccrine spiradenoma (MES) is one of the rarest sweat-gland tumors and can arise from benign eccrine spiradenoma [3] or, less frequently, develop de novo. They are usually located in the superficial or deep dermis. The typical size of these tumors is 1-2 cm and tumors are, occasionally, painful and tender to palpation [4]. The average age of eccrine spiradenoma occurrence is 59 years (range 21-92) with no gender predilection [5]. The latency period before transformation into malignant disease can range from 6 months to 70 years [6]. MES presents a skin mass with recent growth and may have a combination of the following signs and symptoms: ulceration, bleeding, tenderness, and erythema of the affected area. Spiradenocarcinomas are classified as well differentiated, moderately differentiated, and undifferentiated [7]. These tumors have a tendency to metastasize to lymph nodes, bones, lungs, liver, and brain [8-9].

In 1972 Dabska reported the first case of malignant transformation of an eccrine spiradenoma [10]. Marena and Otto estimated malignant sweat gland tumors account for only 0.005 % of all skin tumors [11]. Urso et al. did not find malignant eccrine spiradenoma in a large series of 60 sweat gland carcinomas [12]. Of the reported cases in the breast, malignant changes and systemic metastasis of malignant eccrine spiradenoma have been observed [13-14].

From 1972, when it was first reported, to 2010, a total of 102 MES cases have been reported [6]. In a review of five published cases of MES of the breast, the most common reason patients sought medical evaluation was a long standing nodule which began enlarging over time, ranging from a few weeks to a few months. The average age of disease in the reviewed cases was 51 with a range of 42-68 years of age. Physical examination typically revealed a palpable and moveable mass with or without pain or nipple discharge. One case revealed a lesion which had ulcerated the skin with a friable and bleeding appearance, while another case presented with erythematous discoloration of the overlying skin and a serosanguineous nipple discharge [15-16]. Due to varied presentation of MES, before making the diagnosis of an adnexal tumor arising in the breast parenchyma, the possibility of a cutaneous tumor infiltrating breast tissue must be ruled out [3].

The diagnosis of an eccrine spiradenoma is based on histopathologic examination of the lesion and requires finding a focus of benign spiradenoma within or adjacent to the malignant tumor [16]. The classic histopathology of MES shows solid islands of anaplastic basaloid cells arranged in cords and nodules, with highly pleomorphic cells containing abundant mitotic figures [6]. In the absence of a benign focus, the tumor can be microscopically confused with other skin malignancies [16]. The malignant proliferation will histologically show proliferation of cells with hyperchromatic nuclei, increased mitoses, loss of periodic acid-Schiff-positive basement membrane and invasion of the surrounding tissue [16]. Immunohistochemistry (IHC) studies show the tumor cells exhibit a variable expression of cytokeratin, carcinoembryonic antigen, epithelial membrane antigen and, as seen in this case, S-100 protein [16]. Over-expression of P53 and Ki67 have been associated with malignant transformation [17].

A needle core biopsy initially diagnosed the patient with well to moderately differentiated invasive ductal carcinoma. The carcinomatous component in a malignant eccrine spiradenoma may display ductal/glandular formation with intertwining cords of epithelial cells, which can be mistaken for invasive carcinoma (Figure 5 and Figure 6). Invasive Ductal Carcinoma lesions are typically hard, gray-white, gritty masses which invade the surrounding tissue in a haphazard fashion to create the characteristic irregular, stellate shape. They are microscopically characterized by cords and nests of tumor cells with

varying amounts of gland formation, and cytologic features that range from bland to highly malignant. The malignant cells induce a fibrous response as they infiltrate the breast parenchyma, and this reaction is, in large part, responsible for the clinically and grossly palpable mass, the radiologic density, and solid sonographic characteristics of typical invasive carcinomas [18]. However, unlike invasive carcinoma, myoepithelial cells can be demonstrated with immunohistochemical analysis in MES (Figure 7 and Figure 8).

Due to the rarity of the disease in the breast, imaging findings have not been clearly demonstrated. However, Jin *et al.* [18] and Lee *et al.* [19] have reported the ultrasonography findings of eccrine spiradenoma in the upper arm and breast respectively. Jin *et al.* [19] showed a well-defined, lobulated mass with heterogeneous hypoechogenicity in the deep portion of the dermis and superficial subcutaneous fat layer without connections to the epidermis, with no extension into the muscular structures. Lee *et al.* [19] described ultrasonography findings as well-circumscribed, oval shaped, hypoechoic masses in the cutaneous and subcutaneous layer with all masses surrounded by echogenic lines that represent the dermal layer, such findings are suggestive of a cutaneous origin.

The imaging findings of the present case correlate with Jin *et al.* and Lee *et al.* Ultrasonography findings demonstrate a solid, mildly lobulated heterogeneous mass in the superficial layer of the skin with minimal central vascularity (Figure 2). Mammography showed a hyper-dense mildly lobulated mass within the retroareolar region. There were no suspicious microcalcifications or abnormal skin thickening present (Figure 1). Jin *et al.* concluded that although the sonographic findings may not specify the diagnoses of MES, it should indeed be included in the differential diagnosis of a well-circumscribed hypervascularized hypoechoic subcutaneous tissue tumor [19].

The accepted treatment for MES is wide local excision with a regional lymph node dissection, if tumor metastasis is clinically suspected [16]. MES metastasizes to regional lymph nodes, lungs, brain, and liver (in descending order of frequency) [16]. Distant metastases of MES are uncommon and generally signal an ominous prognosis [16].

Radiotherapy alone or in combination with chemotherapy has been used unsuccessfully in the treatment of patients with metastatic MES [20]. The role of hormonal therapy, localized postoperative radiation therapy, prophylactic lymph node dissection and chemotherapy, still remain to be determined. However, hormonal therapy (Tamoxifen) was well tolerated in estrogen receptor-positive eccrine adenocarcinoma as described by Mirza *et al.* [19] with no distant metastases detected after 41 months follow up. Recurrences are reported in 17.5% to 57% of cases and metastases in lymph node or in distant organs are observed in 40% of cases after a mean follow-up period of 35.23 months [21]. 17.5% of patients develop distant metastases and die after an average time period of 11 months following initial diagnosis [16, 22, 23].

Conclusion

To summarize, MES is a rare malignant tumor that usually arises from a benign tumor after a varied period of latency. The tumor has a tendency to metastasize but generally does not. Due to the rarity of this disease, optimal therapy is still undefined. To our knowledge, this the first reported case of MES of the breast in a male patient.

List of Abbreviations

CAD, Computer assisted detection; MES, Malignant eccrine spiradenoma; IHC, Immunohistochemistry.

Authors Contributions

NP, SK, RP all contributed to drafting and designing of the manuscript. SA served as the Primary Oncologist and reviewed manuscript. HP served as the Primary Care Doctor and ES was the Primary Pathologist.

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