Case Report

"Metastatic malignant nodular hidradenoma": A rare case report with review of literature

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ABSTRACT

Malignant nodular hidradenoma (MNH) also known as hidradenocarcinoma is very rare adnexal tumor with exceedingly low incidence of 0.001%. The recognition is very important because eccrine carcinomas have potential of local destruction and distant metastasis. Given the relative paucity of published data with only just over 50 case reports and small case series, there is little information available on the natural history and appropriate management for this disease. It has been reported most frequently in the head and neck and rarely on the extremities. There is no consensus treatment for metastatic hidradenocarcinoma since it is a rare and aggressive tumor. We report a rare case of MNH in a 70-year-old female presented with inguinal lymphadenopathy and discuss cytological findings and histopathological features with review of literature. Adnexal tumors need thorough histopathological analysis to conclude their biological behavior. This study will highlight the importance of appropriate wide excision of primary adnexal tumors and thereby preventing metastatic presentations in future.

Key words: Cytology, histopathology, hidradenocarcinoma, inguinal mass, metastasis

INTRODUCTION

Malignant nodular hidradenoma (MNH) or nodular hidradenocarcinoma is a rare malignant adnexal tumor that represented <0.001%.[1] It is an aggressive tumor that can metastasize to regional lymph nodes and distant viscera. It has been reported most frequently on the head and neck and rarely on the extremities.[2] There is no consensus treatment for metastatic hidradenocarcinoma since it is a rare and aggressive tumor. We report a case of a metastatic nodular hidradenocarcinoma presented with inguinal lymph node metastasis in a 70-year-old female. With this study, we tried to highlight the clinical, cytological and histopathological features of MNH.

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CASE REPORT

A 70-year-old woman presented to the surgical outpatient department with complaints of mass in the left groin of 3–4 weeks duration. Clinical examination of the left inguinal area showed massively enlarged inguinal lymph node measuring 3 cm × 3 cm [Figure 1a] and few smaller lymph nodes. The largest lymph node was nontender and rubbery in consistency. Past history revealed a skin nodule over left thigh operated 6 months back at a local private clinic. There were no details regarding the diagnosis made either pre- or post-operatively. Examination of left thigh revealed scar mark of previous surgical excision [Figure 1b]. Patient referred for fine-needle aspiration cytology of the left inguinal mass. The aspiration was done from a largest lymph node. The cytology smears studied show high cellularity, composed of the spindle to polygonal cells

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with eosinophilic cytoplasm and moderate to a marked degree of pleomorphism [Figure 2]. The cells were seen in clusters, sheets and singles. There were well-defined granulomas composed of epithelioid cells [Figure 2] without any evidence of caseous necrosis. The cytological impression of metastatic squamous cell carcinoma with the granulomatous response to keratin was issued. Further, a biopsy was advised for confirmation of diagnosis. This was followed by inguinal lymphadenectomy [Figure 1c] with excision of 5 lymph nodes. Gross examination of largest lymph node revealed gray-white friable tumor tissue with papillary excrescences [Figure 3]. The tumor was predominantly composed of solid areas with few tiny cystic spaces scattered in between. Cut section of remaining 4 smaller lymph nodes was gray white. Multiple histopathological sections were submitted from largest lymph node revealed effacement of its normal architecture and replacement of entire lymph node by tumor cells [Figure 4]. The tumor cells were arranged predominantly in papillary fronds with the fibrovascular core. The tumor was composed of fusiform to polygonal cells displaying individual cell keratinization [Figure 5] suggesting squamoid differentiation. Few clear cells were also seen scattered in between these squamoid cells. The papillary projections were seen filling the cystic spaces [Figure 6]. Large areas of keratin with the formation of squamous pearls were seen. High power showed moderate to a marked degree of pleomorphism with the mitotic activity of 1–2/HPF and tumor giant cells [Figure 6]. Cytological atypia and mitotic activity were remarkable. Focal areas of tumor necrosis and apoptotic bodies were also seen. Sections from remaining four smaller lymph nodes showed reactive lymphoid hyperplasia without evidence of metastasis. To summarise, it was metastatic epithelial tumor displaying solid and cystic areas having papillary structures and showing squamous differentiation. Extensive literature search pointed us to offer a diagnosis of MNH. Immunohistochemistry (IHC) carried out at private laboratory confirmed the tumor as epithelial cell origin due to strong positivity for cytokeratin [Figure 5] with focal Ki67 positivity. Final histopathological diagnosis of metastatic malignant nodular hidradenocarcinoma was offered. The postoperative course was uneventful, and patient referred

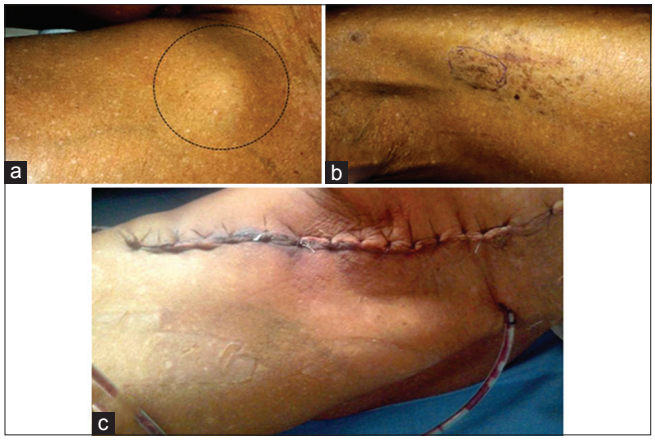

Figure 1: (a) Left inguinal lymphadenopathy. (b) Left thigh showing scar mark of previous surgical excision. (c) Left Inguinal lymphadenectomy

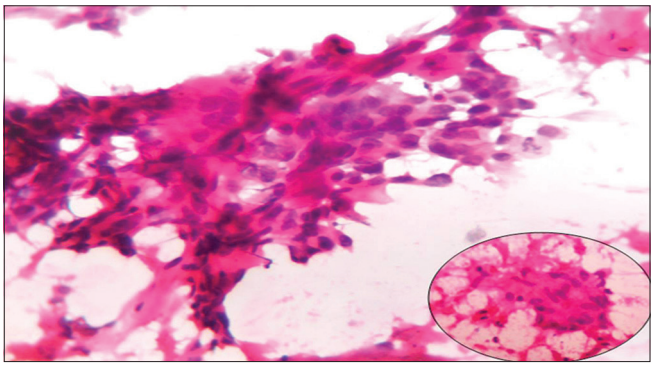

Figure 2: Cytology smear showing high cellularity composed of spindle to polygonal cells with eosinophilic cytoplasm and moderate to marked degree of pleomorphism. Inset shows a granulomatous response to keratin (Pap, ×10)

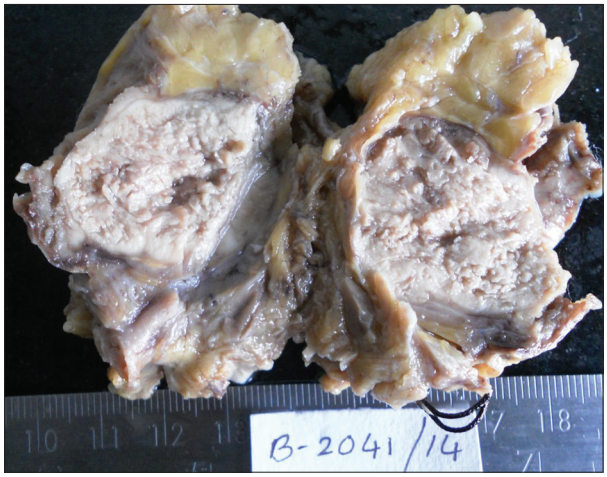

Figure 3: Gross specimen: Cut section of lymph node showing grey white friable tumor with papillary excrescences with solid and cystic spaces

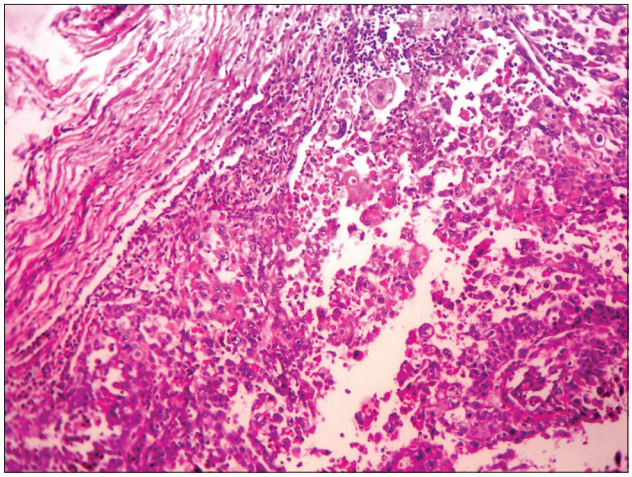

Figure 4: Histopathology section showing lymph node with effacement of architecture and replacement by tumor cells (H and E, ×10)

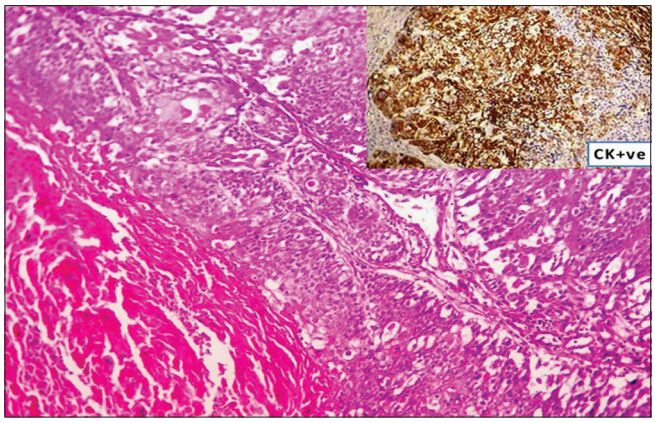

Figure 5: Histopathology section showing tumor cells arranged in papillary fronds with fibrovascular core and presence of extensive keratin (H and E, ×10). Inset showing immunohistochemistry stain for cytokeratin positivity

to the higher center for further treatment. The patient did not come for follow-up after 6 months of discharge.

DISCUSSION

The first reported case of sweat gland tumor dates back to 1865; however, it was not until the late 1950s that interest had sparked the development of a classification system.[1] The largest case series of malignant sweat gland tumors was provided by Berg and McDivitt in 1968 with a total of 101 cases included and till today it remains the largest case series published.[2] However, there remains a significant deficit in the form of a reliable classification system and a set of guidelines for the management of these tumors, particularly when considering the malignant variants such as hidradenocarcinoma. This is somewhat a reflection of the rarity and thus the relative paucity of published data beyond a hand full of case series and reports.

Hidradenocarcinoma also referred to as MNH is a malignant intradermal tumor of the sweat gland with a reported incidence of <0.001%.[1,2] It represents the malignant equivalent of the hidradenoma. The overall incidence of all eccrine carcinomas is 6% which represent <1% of all skin neoplasms. MNH has peak incidence in the sixth decade of life; with an equal male/female distribution; the tumor has a high local recurrence rate (50%), metastases to lymph nodes, bones or visceral organs (60% of cases) recurs within the first 2 years from diagnosis.[2]

Typically the tumor originates in the ductal or secretary part of the sweat gland and presents clinically as an asymptomatic solitary skin lesion measuring approximately 1–5 cm.[3] Generally it is slow-growing but may undergo a rapid phase of growth in a short period of time. Clinically there are no uniquely distinguishable features, and patients are often asymptomatic. At an unknown point in time, the tumor transitions into an aggressive form with expansion

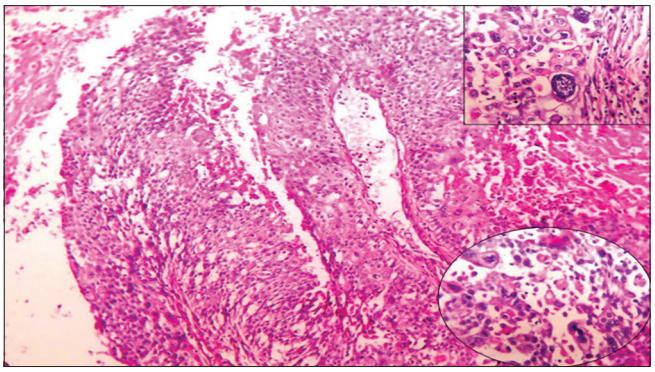

Figure 6: Microphotograph showing papillary structures projecting into cystic spaces and lined by polyhedral cells and few clear cells (H and E, ×10). Insets showing tumor cells with marked degree of pleomorphism with atypical mitotic figures and tumor giant cells (H and E, ×40)

to regional or distant metastatic sites, most commonly to lymph nodes.

It can be mistaken clinically with the more common infundibular and pilar cysts; other entities to consider are cutaneous tuberculosis or dermatofibrosarcoma protuberans.[3] Probably in our case, a previous operation done by local practitioner considered the tumor as benign one and not submitted it for histopathological study after excision. This might have resulted in the metastatic presentation now. MNH has been reported most frequently in the head and neck and rarely on the extremities as in our case.

Although sweat-glands neoplasms generally arise from the eccrine cellular lineage, they exhibit cellular growth patterns that may further influence the neoplasm's architecture. Hidradenoma may exhibit both cystic and solid features, and that is why it enters on differential diagnosis with apocrine tumors; in fact there are divergent opinions on the primitive cellular lineage. The issue is complicated by the coexistence of eccrine and apocrine cells inside cutaneous hamartomas or inside adnexal tumors with mixed differentiation (follicular and sebaceous).[4]

On histological examination, hidradenocarcinoma shows two distinct cell types: Darker fusiform cells with eosinophilic cytoplasm and larger cells exhibit nuclear pleomorphism and atypical mitotic figures.[5] Cystic spaces may show papillary fronds. Hidradenocarcinoma can be difficult to distinguish histologically from hidradenoma, which is a benign tumor. Histological criteria used to distinguish these two entities include greater mitotic activity, atypical mitotic figures, angiolymphatic invasion into surrounding tissue and loss of circumscription.[6] However, the absence of these criteria should not reassure the pathologist because the diagnostic of hidradenocarcinoma may rest solely on the presence of tumor cords invading peripherally or metastasis.

IHC of MNH will reveal strong positivity for epithelial membrane antigen, cytokeratin, estrogen and progesterone receptors (EPRs) and CEA. P63 and C-erbB2 will be usually negative. Ki67 may show high index rate.[7] The skin tumors with eccrine differentiation often express positivity for EPR. The positivity of some eccrine carcinomas to EPR has important clinical implications, as affected patients may be treated with hormonal therapy.[8]

Standard treatment for hidradenocarcinoma is surgical excision, but local recurrence rates range from 10% to 50%.[9] Adjuvant therapies included radiation has been used in the setting of positive margins, recurrent tumors, and positive lymph nodes when further surgery has not been an option. Various chemotherapy regimens containing 5-fluorouracil based regimes have been used. Targeted therapy like Herceptin is also used in the treatment of metastatic hidradenocarcinoma for stabilization of the disease.[9] There is no consensus treatment for hidradenocarcinoma since it is a rare and aggressive tumor. It seems important to use adjuvant therapies particularly for recurrent and metastatic forms.

There is not an established consensus on lymph node dissection. The 5-year postsurgical survival rate for MNH is reported to be <30%.[8,9] At the time of excision of eccrine tumors, some researchers have utilized the sentinel lymph node biopsy to detect the possible regional microscopic lymph node metastasis. The lymph node dissection is certainly indicated when there are signs of lymph node local invasion; prophylactic dissection otherwise has not yet proved to increase the free disease interval. Positivity of sentinel lymph node also permits to assess the indication for a radical lymphadenectomy.[9] Whether early detection and treatment of lymph node metastases could improve overall survival or not, however, is not clear at this time.

CONCLUSION

This case allowed us to learn more about MNH, which is very rare eccrine carcinoma. The presence of peculiar and confusing histopathological features like neoplastic cells with eosinophilic to clear cytoplasm, presence of papillary structures (masquerading adenocarcinoma) lined by cells with squamous differentiation (mimicking squamous cell carcinoma) projecting into cystic spaces, led us to the extensive literature search offering final diagnosis of MNH. In view of the aggressive behavior of these adnexal tumors, they should be deeply investigated and treated with utmost precaution to prevent metastatic presentation.

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Conflicts of interest

There are no conflicts of interest.

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