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Case Report

Malignant nodular hidradenoma-inguinal region clinically masquerading as squamous cell carcinoma: a case report

Sunita S. Vernekar, Priyadharshini Bargunam*

Department of Pathology, Karnataka Institute of Medical Sciences, Hubballi, Karnataka, India

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***Correspondence:**
Dr. Priyadharshini Bargunam,
E-mail: priyasweetygunam@gmail.com

ABSTRACT

Malignant Nodular hidradenoma is an extremely rare aggressive tumour originating from eccrine sweat glands with an incidence of <.001%. So far less than 80 cases have been reported in the literature. It's known for its local recurrence (50%) and metastasis (60%) and hence early diagnosis and radical treatment is mandatory. But differentiating it from its benign counterparts and other skin tumour mimics is challenging, due to its histopathological similarity & lack of diagnostic immunomarkers. Authors report a case of 65-year-old female who presented with a short 4-month history of rapidly growing ulceroproliferative growth in the right inguinal region with bilateral inguinal node enlargement, associated with pain and discharge. Wedge biopsy of left inguinal lymph node showed malignant cutaneous adnexal tumour deposits, which after excision was typed as malignant nodular hidradenoma. It was confirmed with immunohistochemistry. Patient presented with recurrence 8 months after excision.

Keywords: Hidradenocarcinoma, Malignant nodular Hidradenoma, Sweat gland tumour

INTRODUCTION

Hidradenocarcinomas are tumours of eccrine origin described by Keasby et al, in the year 1954.[1] It is an extremely rare aggressive tumour originating from eccrine sweat glands with an incidence of <.001%.[2] So far less than 80 cases have been reported in the literature.

Several synonyms have been described in the literature, like malignant nodular hidradenoma, malignant acrospiroma, clear cell hidradenocarcinoma, clear cell eccrine carcinoma and malignant eccrine acrospiroma which results in lack of uniformity and confusion in the reporting of these tumours.[3]

Recurrence led to suspicion and diagnosis in most cases, which is due its extreme rarity and lack of awareness about the tumour among pathologists.

CASE REPORT

A 65-year-old female presented with swelling in the right inguinal region since 4 months, which was associated with ulceration, pain and discharge for a month. On examination, she had a hard, tender ulceroproliferative growth measuring 7x5 cm in right inguinal region with restricted mobility. Ulcer had everted edges with a pink base which was discharging seropurulent fluid. Besides, she had bilateral inguinal lymphadenopathy with vulval edema. Per rectal examination showed anterior nodules and hence clinically a presumptive diagnosis of Squamous cell carcinoma was made, and she was investigated. CT abdomen showed a heterogeneously enhancing mass lesion in the right inguinal region with inguinal and external iliac lymphadenopathy. Wedge biopsy of left inguinal lymph node was diagnosed as malignant cutaneous adnexal tumour and hence she

underwent a wide excision of the tumour with lymph node dissection.

Grossly the specimen was skin covered, measuring 6x5.5x4 cm with few areas of ulceration over it (Figure 1A). Cut surface showed a grey white friable granular growth involving the entire specimen except for the margins. Areas of necrosis and hemorrhage were also seen.

Histopathological examination of the tumour revealed tumour cells arranged in nests and broad sheets predominantly in the dermis with pushing borders, extending into the subcutaneous tissue with comedo necrosis and retraction spaces (Figure 1B). Cells were moderate in size showing moderate pleomorphism with clear to vacuolated eosinophilic cytoplasm with vesicular nucleus and distinct nucleoli with increased atypical mitotic figures ranging from 5 to 6 per high power field (Figure 1D). Tumour showed lympho plasmocytic response amidst its lobules along with lymphovascular invasion. Two lymph nodes dissected also showed metastasis from the tumour. Surgical margins were unremarkable. The vacuolated cells were Periodic acid Schiff positive. Based on the above findings, Malignant nodular Hidradenoma and trichelemmal carcinoma were considered as the differentials.

Immunohistochemical analysis revealed that the tumour was positive for EMA (++++), P53 (>5% nuclear staining), KI 67 (>70%) and showed luminal positivity for CEA (Figure 2A-D). It was negative for S100, Her 2 Neu, Androgen and Ber Ep4.

Patient presented with local recurrence after 8 months, which was confirmed by fine needle aspiration from the inguinal swelling. The aspirate was cellular showing tumour cells in clusters and singles. The tumour cells were oval to globoid with clear cytoplasm and indistinct cell membrane, central large round nucleus with coarse granular chromatin and had prominent 1- 2 nucleoli. Also seen were round cells with hyperchromatic nucleus and moderate amount of eosinophilic cytoplasm. Background showed mixed inflammatory cells and hemorrhage (Figure 1C).

DISCUSSION

Malignant adnexal tumours of the skin originate from the eccrine glands, apocrine glands and the pilosebaceous units. Hidradenocarcinoma are of eccrine origin though apocrine hidradenocarcinomas have been reported.[4]

There is a slight male preponderance and is commonly seen from fifth to seventh decade. It arise *de novo* and rarely results from a pre-existing hidradenoma.[3] It accounts for approximately 6% of malignant eccrine tumours[5] and accounts for less than 0.001% of all tumours[2] Classification, diagnostic criteria, prognostic features, and biologic markers responsible for dysregulated cellular growth that leads to tumorigenesis of hidradenocarcinomas are still undefined and require further studies. Specifically, a detailed understanding of the steps that contribute to the transformation of a benign hidradenoma to a malignant form is lacking.[6]

Generally, lesions present initially on the face or extremities. However, cases have also been reported with lesions described on the abdomen, trunk, and groin and even more unusual presentations have been reported on the scalp, elbow, and digits.[5] They are usually 1 to 5 cm in size and tend to locally expand for a highly variable amount of time. In general, most patients remain asymptomatic except for pain, discomfort, bleeding upon physical contact, or ulceration. At some point, through an unknown mechanism, the tumour assumes an aggressive clinical course with growth at regional or distant metastatic sites, primarily lymph nodes.[5]

Hidradenocarcinomas are usually larger, asymmetric, and tend to show an infiltrative growth pattern or rarely pushing borders into the surrounding tissue. Besides, there may be deep extension and angiolymphatic invasion. Mitoses are usually easily detected, and some may be atypical. Some tumors may contain other cell types, including epidermoid cells, mucinous cells, signet ring cells, and cells with high-grade sarcomatoid change.[7] There have been several cases of low-grade atypical hidradenomas that have metastasized to lymph nodes with subsequent indolent behavior following lymph node resection.[8] Clear cell hidradenoma and hidradenocarcinoma may occasionally mimic metastatic clear cell carcinomas including thyroid, lung or renal cell carcinomas. However, the first two are usually distinguished by their positivity to thyroid transcription factor-1 (TTF-1), and the latter by its prominent vascularity, and the presence of haemorrhage and focal granular necrosis within the lesion.[3] R

enal cell carcinoma also expresses both EMA and CD10. Other differentials include basaloid eccrine carcinoma, eccrine ductal carcinoma, clear cell eccrine carcinoma, and other non-specified sweat gland carcinomas.[3] The distinction between subtypes and even the designation of eccrine tumor is difficult, and requires a stain of eccrine-type enzymes like succinic dehydrogenase or amylophosphorylase and ferritin.[6] They typically stain with AE1/AE3, CK5, and CK6, with high Ki-67 expression helping to distinguish hidradenocarcinoma from atypical hidradenoma.[9] Occasional tumors may demonstrate the[11-19] translocation seen in clear cell hidradenomas.[7] CEA and EMA stain the luminal borders of ductal structures.[7] Less than 20% hidradenocarcinomas harbor mutation in TP53.[7]

A detailed immunohistochemical study of a series of 6 hidradenocarcinomas concluded that Ki- 67 and p53 are useful markers for the diagnosis.[10] Immunohistochemical comparison with various studies is included in Table 1.

Table 1: Immunohistochemical staining results published in various reports.

Study author	ER	PR	AR	HER2 neu	CK AE1/ AE3 PAN keratin	CK 5/6	CAM 5.2	HMW CK (34□E12)	EMA	CEA	P53	KI 67	GCFDP- 15	S100	SMA	VI
Jinnah et al[14]	-	-	-	-	+++	++ +	-	-	-	N	-	-	-	N	-	-
Ko et al[10]	-	-	-	-	+++	++ +	-	-	+++	+++	+++ +	++++	INC	N	-	-
K Balaban et al[15]	N	-	N	-	-	-	++ +	+++	_	_	-	30%	-	-	-	-
Orsaria M et al[16]	-	-	-	-	++++	-	++ ++	FOCAL +	LUMEN +	+++	+++ +	++++	-	N	N	++++
Nazerali et al[17]	-	-	-	+++	-	-	-	-	-	+++	-	-	-	-	-	-
Khan SA et al[18]	++	++	-	N	+++	-	-	-	+++	+++	-	40%	N	-	-	-
Wong et al[19]	-	-	-	-	++++	-	++ ++	-	++++	++	-	-	N	+	N	++
Our case	-	-	N	N	-	-	-	-	++++	+	+++	>70%	-	-	-	-

N- Negative - Test not done, + - Positive INC- Inconsistent, ER- Estrogen; PR- Progesterone; AR- Androgen; CK- Cytokeratin; EMA- Epithelial membrane Antigen; CEA- Carcino Embryonic Antigen; GCDFP- 15- Gross cystic disease fluid protein 15; SMA- Smooth Muscle Actin; VI- Vimentin

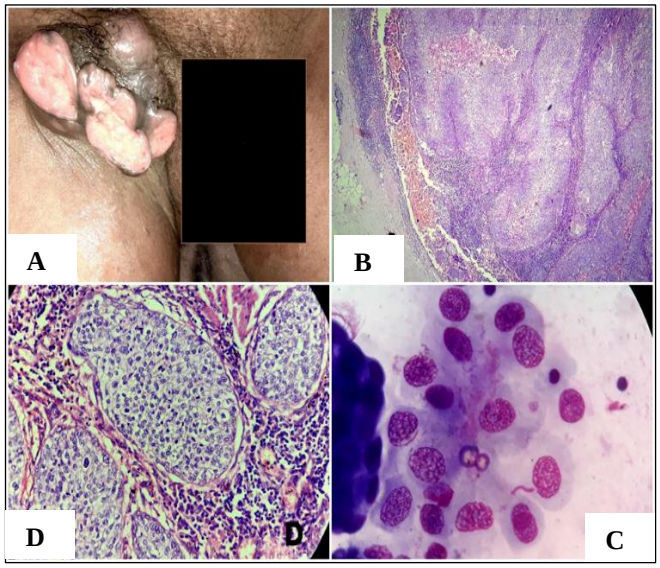

Figure 1: (A): Ulceroproliferative growth in the right inguinal, (B): Tumour cells arranged in broad sheets with comedo necrosis (H &E 4x), (C): Aspiration cytology from the recurrent swelling showing globoid to oval tumour cells in clusters with clear cytoplasm, central large round nucleus and prominent 1 to 2 nucleoli (Wrights stain 200x), (D): Tumour cells having clear to vacuolated eosinophilic cytoplasm with vesicular nucleus and distinct nucleoli. They show increased atypical mitotic figures and lympho plasmocytic response around (H & E 40x).

Cytologically, the aspirates are cellular with 2 populations of cells forming vague acini, sheets and pseudopapillary formations.

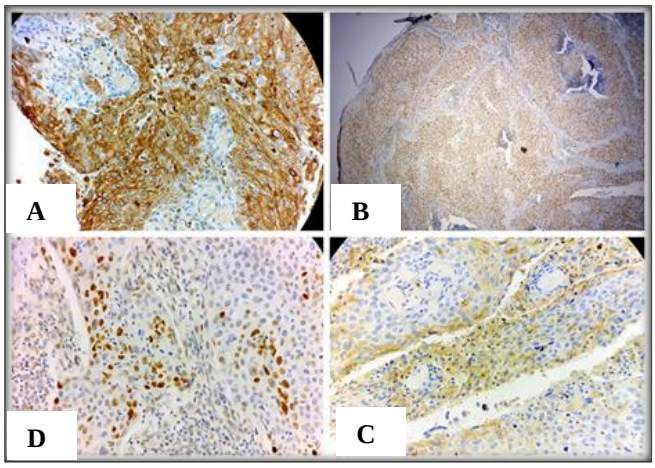

Figure 2: (A): Epithelial membrane Antigen showing strong Membrane and cytoplasmic staining (40x), (B): Scanner view of a part of the tumour showing >70% positivity for Ki-67(4x), (C): Cacinoembryonic Antigen mild luminal positivity (40x), (D): p53 showing >5% strongly positive nuclear staining (40x).

The clear cells are globoid to cylindrical with round relatively bland nucleus. Also seen are round cells having moderate basophilic cytoplasm, round nucleus and

uniformly distributed granular chromatin, a thin nuclear membrane and small nucleolus.[11]

Classical carcinoma surgery may be used but two-step surgery may enhance the quality of the margin control and excellent control can be achieved by Mohs micrographic surgery.[12] Investigators have proved the usefulness of tamoxifen in metastatic hidradenocarcinomas with positive estrogen receptor and Trastuzumab can be added depending on HER-2/neu status.[6]

The prognosis for survival with newly diagnosed nodular hidradenocarcinoma is generally poor and, notably, the 5-year disease-free survival rate is less than 30%.[5] Tumors demonstrate up to 50% local recurrence, despite aggressive surgical management.[5] In addition, metastases have been reported in more than 60% of patients within the first 2 years, commonly through regional lymph nodes.[13]

CONCLUSION

Hidradenocarcinoma is a rare aggressive cutaneous adnexal tumour which mimics other malignant tumours of the skin. Pathologists should have a high degree of suspicion for early diagnosis of these tumours, as these mandates an extensive resection.

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