

# Giant Clear Cell Nodular Hidradenoma of the Thigh Mimicking Cutaneous Malignancy

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## ABSTRACT

Clear cell nodular hidradenoma is an exceedingly rare cutaneous adnexal neoplasm arising from the eccrine sweat glands and is typically benign in nature. Although it has special predilection for the head, trunk and the extremities, it can involve any part of the body. We are reporting a case of a 47-year man who presented with progressively enlarging painless pedunculated growth on the outer aspect of left thigh. Clinical impression was consistent with a primary cutaneous malignancy. MRI of the thigh showed a multiloculated cystic lesion arising from the

dermal layer of skin with no deeper infiltration. Fine needle aspiration cytology was inconclusive as multiple attempts on sampling the tumour revealed nothing except frank blood because of the hypervascular nature of the tumour. Wide-excision of the growth was followed by an uneventful recovery of the patient. Histopathological evaluation of the resected specimen supplemented by immunohistochemistry was consistent with the diagnosis of clear cell nodular hidradenoma with no evidence of atypia or malignancy.

**Keywords:** Clear cell nodular hidradenoma; Thigh; Malignancy

## INTRODUCTION

Clear cell nodular hidradenoma (CCNH) was first described by Liu in 1949 as eccrine acrospiroma; where "acro" means the top most or distal end while "spiroma" means adenoma arising from spiral ducts of the sweat glands [1]. CCNH is an extremely rare skin adnexal tumour. There are three histologic variants of sweat glands in the body; eccrine, apocrine and mixed. Eccrine sweat glands are present everywhere in the skin except vermilion zone of the lips and the nail beds whereas apocrine glands occur only in the axilla and the anogenital region [2]. CCNH has been described by a conundrum of synonyms such as clear cell adenoma, clear cell hidradenoma, nodular hidradenoma, solid-cystic hidradenoma, clear cell myoepithelioma, acrospiroma, poroma, syringoma, porosyringoma, hidroacanthoma etc [3]. Although it can occur anywhere in the body, CCNH has special predilection for the head, trunk and extremities. Despite well-defined cytomorphological features of benignity, CCNH possesses an inherent risk for loco-regional nodal spread and systemic dissemination. CCNH, due to angiolymphatic invasion but no nodal or systemic metastasis, is labelled as atypical hidradenoma. Long-standing CCNH has strong

likelihood of malignant transformation (hidradenocarcinoma). The prime rationale of reporting this case scenario is to familiarize the healthcare professionals with biological behaviour, clinical characteristics, diagnostic work-up and therapeutic strategies of this rare dermal adnexal neoplasm.

## CASE REPORT

A 47-year old man presented with gradually enlarging painless growth on the outer aspect of his left thigh for ten years duration. To begin with, it was slow in growth but over a period of six months, it rapidly increased in size. Because of its rapid growth and ugly appearance, medical advice was sought. Clinical evaluation revealed an unsightly-looking, non-tender, firm, bosselated and pedunculated with a wide base growth, measuring 8x7x6 cm located on the outer aspect of left thigh. The overlying skin was bronze in colour with two microscopic ulcerations with serous discharge (Figures 1 and 2). Substantial degree of basal induration imparting the impression of deeper soft tissue infiltration was noted on palpation. However, there was no regional lymphadenopathy. Based on its size and clinical characteristics, it was difficult to distinguish this growth from a

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**Figure 1:** Pedunculated growth (Anterior aspect of left thigh)



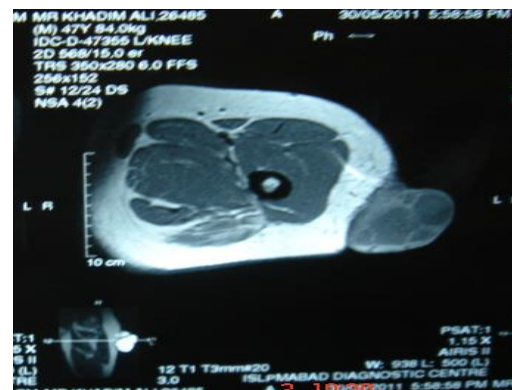
**Figure 2:** Pedunculated growth (Posterior aspect of left thigh)



dermatological malignancy. Haematological and biochemical profiles were within normal ranges. X-rays of the left femur showed no cortical involvement. MRI of the left thigh demonstrated a 8x7x6 cm exophytic, multiloculated lesion arising from the dermal layer of skin with no deeper fascial or muscular penetration (Figure 3 and Figure 4). Several attempts at fine needle aspiration to take samples for preoperative cytological diagnosis revealed nothing except frank blood owing to hypervascularity of the growth. Accordingly, wide-excision of the growth with 2 cm clear margins was carried out keeping in view significant basal induration, hypervascular nature of the tumour, inconclusive

cytological results and clinical diagnostic uncertainty (Figures 5). Grossly, the specimen was covered with tanned and thickened skin with two tiny ulcerations over its fundic area. The cut-sections of the growth exhibited multiloculated architecture consisting of cystic and solid areas. The cystic spaces were filled with dark-brown gelatinous material. Histopathological evaluation of the hematoxylin and eosin stained tissue sections revealed rudimentary ductal differentiation and existence of nests and cords of eosinophilic and clear cells with no nuclear anaplasia, mitotic figures or tumour necrosis. The nests and cords of eosinophilic and clear cells were interspersed with fibrovascular stroma that was demonstrating collagenous, hyalinized, keratinized, sclerotic and myxoid patterns. Papillary excrescences extending into the cystic spaces were also discernible. These microscopic features were consistent with the diagnosis of CCNH. Immunohistochemical analysis revealed that the tissue sections exhibited positivity for epithelial membrane antigen (EMA), cytokeratins, p63, S100 Protein and HMB45 but negativity for vimentin, smooth muscle actin (SMA), CD10 and CD34; thus confirming the diagnosis of CCNH.

**Figure 3:** MRI of left thigh (coronal view)



**Figure 4:** MRI of left thigh (sagittal view)



## DISCUSSION

CCNH is an exceedingly rare dermal adenexal tumour that exhibits diversified morphologies and wide-ranging histologic spectra of cellular differentiation; hence there are ample chances of being misguided for other primary and metastatic skin tumours [4]. Vast majority of CCNH originate from spiral ducts of the eccrine sweat glands (eccrine derivation) but origin from the folliculo-sebaceous-apocrine units is possible (apocrine derivation). Although no age is exempt, CCNH predominantly afflicts the adult population in their 4th and 5th decades of life with slight female predominance (M:F=2:1). There is no distinct racial, familial or ethnic predilection [3-6].

Clinically, CCNH appears as painless, solitary, firm, small intradermal nodule (usually 0.5-1 cm in size) slightly elevated above the surrounding skin. CCNH has special predilection for the head (30.3%), trunk (20.2%) and extremities (25.8%) [5]. Nevertheless, it can originate from any part of the body such as scalp, eyelid, ear, face, oral cavity, shoulder, breast, buttocks, scrotum, palms, soles and digits [4]. Even though it is a slow growing tumour, neglected cases of CCNH can acquire prodigious size and become polypoidal and even pedunculated like that of our case. Sudden increase in the size of CCNH may indicate trauma, sudden haemorrhage or malignant transformation. The biological behaviour of CCNH is unpredictable and it can undergo malignant change (hidradenocarcinoma) at any time. Clear cell hidradenocarcinoma may arise de novo or after malignant transformation of its benign counterpart. The exact frequency of malignant transformation of CCNH is unknown but has been reported in the range of 6%-7% [4, 6]. The clinical criteria suggestive of malignant transformation are unexpected rapid growth, hyperpigmentation and ulceration of overlying skin, locoregional lymphadenopathy and systemic dissemination while histologic criteria include overt nuclear atypia, brisk mitotic figures, preponderance of solid islands, infiltrative growth patterns (poor circumscription), existence of tumour necrosis and angio-lymphatic invasion and perineural permeation [6]. CCNH with histologic features of benignity and angiolymphatic invasion but no nodal or systemic spread is known as atypical CCNH or hidradenoma of indeterminate malignant potential. CCNH with locoregional nodal infiltration and systemic metastasis are considered as frank malignant CCNH. CCNH

may mimic a multitude of dermatological lesions and at times, it becomes difficult to decipher its differentiation from these lesions on clinical grounds. The following lesions must always be kept in mind in the differential diagnosis of CCNH; seborrheic keratosis, pyogenic granulomas, hemangioma, pedunculated lipoma, leiomyoma, pedunculated neurofibroma, fibrosarcoma, dermatofibroma protuberance, basal cell epithelioma, squamous cell carcinoma, amelanotic malignant melanoma [6].

CCNH is primarily diagnosed on clinical evaluation by an experienced dermatologist. Routine laboratory and biochemical investigation(s) usually do not help in reaching preoperative diagnosis of CCNH. The imaging modalities such as MRI are only required when there is strong suspicion of malignancy and for exclusion of deeper tissue infiltration. Fine needle aspiration cytology has no definite role in identifying cytomorphologic features of CCNH. Nonetheless, the following cytological findings on cytology may be helpful; a cystic component to the aspirate represented by amorphous background material with or without foam cells and epithelial duct-like and tubular structures [7]. More often than not, exact diagnosis of CCNH is achieved only on painstaking efforts during histopathological evaluation of the tumour sections supplemented by immunohistochemistry [8-10]

Histopathologically, CCNH is a well-circumscribed and well-encapsulated multilobular lesion lying in the dermis. The lesion consists of solid areas and cystic spaces. The cystic spaces are outcomes of tumour degeneration and are lined by low cuboidal cells

**Figure 5:** Resected Specimen



and are filled with eosinophilic granular mucoid material and papillary excrescences. In contrast, the solid areas consist of nests, cords or lobules separated by delicate intervening fibrovascular stroma. Foci of hyalinized, keratinized, myxoid and chondroid stroma may be scattered here and there in the tissue sections. Ductal differentiation is seen as slit-like lumina in the whorls (morules) of squamous and sebaceous differentiation [2, 4]. Cytologically, the solid areas contain biphasic cellular population. The predominant cells (60%-70%) are large polyhedral cells containing faintly granular eosinophilic cytoplasm, prominent nucleoli and round to oval nuclei. The other variety is clear cells with abundant intracytoplasmic accumulation of glycogen and eccentrically placed inconspicuous nuclei and accounting only for 5%-30% of cell populace [2]. Many psammoma bodies or chunks of calcification may be detectable in some histologic fields. No areas of necrosis, nuclear pleomorphism or mitotic figures have been described. Nevertheless, existence of mitotic figures doesn't necessarily signify presence or onset of malignancy. The eosinophilic cells exhibit intracytoplasmic substance that shows positivity with periodic acid-Schiff stain and is diastase-resistant. Owing to significant similarities of CCNH to cutaneous metastasis from conventional clear cell renal carcinoma, clear cell variant of squamous cell carcinoma and clear cell sarcoma, immunohistochemical analysis is mandatory for validation of CCNH. Immunohistochemically, the tumour cells display positivity for cytokeratins, p53, CEA, epithelial membrane antigen (EMA), S-00 protein and HMB45 and negativity for vimentin, smooth muscle actin (SMA), CD10, CD34 and Ki-67. No procedures lesser than wide excision with negative margins is the foremost therapeutic strategy for CCNH [8-10]. In a nutshell, CCNH is a deceptive dermatological tumour that can pose perplexing diagnostic challenges even to an experienced clinician.

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