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Case Report

Malignant Transformation of Nodular Hidradenoma in the Lower Leg

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Nodular hidradenoma · Malignant transformation · Lower leg

Abstract
Nodular hidradenoma (NH) is a benign adnexal tumor that arises from either eccrine or apocrine sweat glands. NH can originate from any cutaneous site, but the most common sites are the head and anterior surface of the trunk, with very rare cases in the extremities. Long-standing NH has been reported to undergo malignant transformation to malignant NH (MNH); however, its occurrence in the lower leg is extremely rare with only one other case reported to date. In this report, we present a rare case of MNH occurring in the lower leg which was resected with the intent to make a diagnosis. At the final follow-up after 11 months, no local recurrence or metastasis has been observed.

Introduction

Nodular hidradenoma (NH) is a benign adnexal tumor that arises from the distal excretory duct of eccrine or apocrine sweat glands [1]. Despite its well-defined histological features

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of benignity, long-standing NH has been reported to undergo malignant transformation to malignant NH (MNH) [2]. Contrary to its benign counterpart, MNH has the potential for local recurrence as well as metastasis to lymph node, bone, or visceral organs, and often causes death with a reported survival rate at 5 years of approximately 30% [3]. Accurate diagnosis and appropriate treatment are important to improve the dismal prognosis of MNH. In this report, we present a rare case of MNH and review of the literature to increase the awareness of this clinical entity.

Case Report

A 24-year-old man presented with a recurrent tumor of the right lower leg. The lesion was first noted 9 years earlier and insidious at onset, gradually enlarging, starting as a small nodule. Approximately 2 years before admission, the tumor suddenly increased in size, and the patient had consulted a general practitioner. The lesion was treated by needle puncture and aspiration of red serous fluid several times, all leading to immediate recurrence. The patient was referred to our hospital for further management. There was no history of trauma to his lower leg. Physical examination at the initial visit revealed a hemispheric, firm, mobile, and non-tender mass, measuring 5 × 4 cm on the anterior aspect of the lower leg. The overlying skin was smooth but taut with bluish appearance (Fig. 1). No regional lymphadenopathy was detected.

Plain radiographs demonstrated no involvement of the underlying bone. Magnetic resonance imaging (MRI) scan showed a soft tissue mass in the subcutaneous layer of the anterior aspect of the right lower leg without extension to the adjacent muscular layer or bone. The lesion had a well-delineated margin and was heterogeneous in appearance. T1-weighted image (WI) revealed a hypointense lesion with markedly isointense area. On fat saturation T2WI, the lesion was hyperintense compared to muscle and contained a heterogeneous area inside the mass, measuring 1.5 × 1.5 cm. Postcontrast fat saturation T1WI showed a prominent enhancement of the internal mass and the periphery of the lesion (Fig. 2). Positron emission tomography/computed tomography (PET/CT) scan showed hypermetabolic activity with a maximum SUV of 2.88 in the internal mass of the lesion.

Differential diagnosis included chronic expanding hematoma, hemangioma, schwannoma, and benign skin tumors. Due to disturbance when wearing a shoe, the patient underwent a marginal resection. The tumor was resected with the overlying skin and underlying fascia. Microscopically, the lesion was predominantly cystic with a partial fungiform solid component, measuring 3.4 × 2 × 1.2 cm. The solid component was composed of epithelial cells arranged in lobules and sheets with atypia and sporadic mitosis (Fig. 3). The percentage of Ki-67 positivity, which reflects cell proliferation, was 22%. The histological analysis confirmed the diagnosis of NH with a focus of malignant change, and the surgical margin was free of tumor. At 11 months after surgery, there has been no local recurrence nor any sign of distant metastases.

Discussion

NH was first described in 1949 by Liu [4] as clear cell papillary carcinoma of the skin. NH may have variable histomorphological patterns; therefore, several synonyms have been used

to describe this entity: clear cell hidradenoma, solid–cystic hidradenoma, clear cell acrospiroma, and eccrine acrospiroma. NH are usually seen in the third to fifth decade of life with a slight female predominance. Although the lesion can originate from any cutaneous site, the most common sites are the head and anterior surface of the trunk, with very few cases in the extremities [2]. Clinically, NH usually presents as a solitary, firm, intradermal nodule, up to few centimeters in diameter. There may be various changes in the overlying skin: it may be smooth, thickened, ulcerated, or blue/red colored. Because of the asymptomatic and slow-growing nature of the tumor, it often takes several years before patients present to a clinic. Any rapid growth may indicate trauma, sudden hemorrhage, or malignant transformation. Although NH is a benign tumor, its biological behavior is unpredictable, and it can undergo malignant change to MNH at any time.

A proper understanding of the natural history of MNH is essential for appropriate treatment. MNH is known to arise de novo or after malignant transformation from NH in up to 7% of all cases [2, 5, 6, 7]. In past reports, lesions mostly occurred in the head and neck region. Our case is only the second malignant transformation of NH to be reported in the lower leg [8]. Contrary to its benign counterpart, MNH shows aggressive behavior with a high frequency of local recurrence and metastasis. The local recurrence rate has been reported to be as high as 50% depending on the surgical margin. Metastatic lesions have been reported in the regional lymph nodes and the lung. Once the tumor recurs, it turns highly aggressive with a strong tendency for invasion of surrounding tissues and metastases to distant sites. The prognosis for survival is generally poor with a 5-year disease-free survival rate reported to be <30% [3].

Information on imaging characteristics of NH is scarce because the lesion is usually diagnosed and resected based only on its clinical features. MRI features of NH have been reported to include a well-circumscribed, lobulated, subcutaneous, cystic, or solid mass with low to intermediate signal intensity on T1WI and an intermediate to high signal intensity on T2WI. The variability of the T1WI and T2WI characteristics of the cystic component is probably due to the relative amounts of cholesterol, hemorrhage, and sweat gland secretions expressed in the fluid. To our knowledge, only one MRI study of MNH has been reported where the lesion showed a poorly defined margin with a nearly homogeneous and diffuse-enhanced component [7]. PET/CT imaging of MNH has recently been reported in 2 cases and shown to be useful in differentiating malignant from benign lesions and for excluding distant metastasis [9, 10]. In our case, PET/CT showed hypermetabolic activity in the small area of the lesion, corresponding to the area of malignant transformation.

The initial treatment of MNH is very important to achieve a good result. Most clinicians have concluded that the treatment of choice for this tumor is wide local excision with negative margins. Wide surgical excision with at least 2–3 cm has been advocated in some reports. If wide margins cannot be achieved because of anatomical or functional conditions, Mohs micrographic surgery can be used to control a subtle extension of the tumor [11]. Because of the high tendency for regional lymph node metastasis, prophylactic lymph node dissection has been reported [12], but this aggressive approach has remained controversial since a long-term benefit has not been clearly demonstrated. Further studies are necessary to determine whether this procedure results in a survival benefit or local control.

Due to the high local recurrence rate and poor prognosis, adjuvant chemotherapy and radiotherapy have been reported in some cases. Radiotherapy can be considered when surgery is not feasible or negative surgical margins cannot be achieved, but its impact is still debatable. Recently, reports have shown that radiation therapy may have a role in preventing local recurrence, while in others, radio-resistance has been observed [13, 14]. Chemotherapy

has been used sporadically for residual metastatic disease, but until now, the efficacy of adjuvant chemotherapy has not been demonstrated either alone or in combination with radiation therapy. Estrogen receptor analysis has also been recommended for the treatment of MNH, where patients with positive tests may undergo hormonal therapy. Trastuzumab, a monoclonal antibody against HER2 receptor, was well-tolerated and effective as adjuvant therapy for MNH patients with HER2/neu positivity in some cases [15]. In the present case, although a marginal resection was performed, histological findings showed that the malignant focus was entirely encased in the benign component; therefore, no additional wide resection or adjuvant treatment was performed. Nevertheless, due to the rarity of MNH occurring in the lower leg and poor prognosis reported to date, strict follow-up using MRI and PET/CT is warranted.

Conclusions

NH is a benign adnexal tumor, but it must be borne in mind that the clinical behavior is unpredictable. Early diagnosis and appropriate treatment are crucial to prevent local recurrence and malignant transformation. Surgical resection emphasizing tumor-free margin is considered the mainstay of treatment for NH. On the contrary, management of MNH should be more aggressive with wide resection. Although the importance of surgery has been established, the role of loco-regional lymphadenectomy and adjuvant therapy has yet to be fully determined.

Statement of Ethics

The authors have no ethical conflicts to disclose. Informed consent was obtained from the patient for this case report and any accompanying images.

Disclosure Statement

The authors have no conflicts of interest to declare.

References

1 Winkelmann RK, Wolff K. Solid-cystic hidradenoma of the skin. Clinical and histopathologic study. Arch Dermatol. 1968 Jun;97(6):651–61.
2 Hernández-Pérez E, Cestoni-Parducci R. Nodular hidradenoma and hidradenocarcinoma. A 10-year review. J Am Acad Dermatol. 1985 Jan;12(1 Pt 1):15–20.
3 Görtler I, Köppl H, Stark GB, Horch RE. Metastatic malignant acrospiroma of the hand. Eur J Surg Oncol. 2001 Jun;27(4):431–5.
4 Liu Y. The histogenesis of clear cell papillary carcinoma of the skin. Am J Pathol. 1949 Jan;25(1):93–103.
5 Ashley I, Smith-Reed M, Chernys A. Sweat gland carcinoma. Case report and review of the literature. Dermatol Surg. 1997 Feb;23(2):129–33.
6 Biddlestone LR, Mclaren KM, Tidman MJ. Malignant hidradenoma—a case report demonstrating insidious histological and clinical progression. Clin Exp Dermatol. 1991 Nov;16(6):474–7.
7 Lim SC, Lee MJ, Lee MS, Kee KH, Suh CH. Giant hidradenocarcinoma: a report of malignant transformation from nodular hidradenoma. Pathol Int. 1998 Oct;48(10):818–23.
8 Kane B, Adler E, Bhandari T, Rose M, DiGuglielmo N, Sun X. Malignant hidradenocarcinoma in the lower extremity: A case report of a rare tumor. J Foot Ankle Surg. 2018 Feb;57(3):618–621.

9 Patel TV, Oldan J. 18F-FDG PET/CT Imaging of Hidradenocarcinoma Arising From Preexisting Hidradenoma of the Knee. Clin Nucl Med. 2018 Jan;43(1):55–6.
10 Surasi DS, Lam S, Subramaniam RM. F-18 FDG PET/CT imaging of a hidradenocarcinoma of head and neck. Clin Nucl Med. 2011 Oct;36(10):945–7.
11 Tolkachjov SN, Hocker TL, Hochwalt PC, Camilleri MJ, Arpey CJ, Brewer JD et al. Mohs micrographic surgery for the treatment of hidradenocarcinoma: the Mayo Clinic experience from 1993 to 2013. Dermatol Surg. 2015 Feb;41(2):226–31.
12 Delgado R, Kraus D, Coit DG, Busam KJ. Sentinel lymph node analysis in patients with sweat gland carcinoma. Cancer. 2003 May;97(9):2279–84.
13 Harari PM, Shimm DS, Bangert JL, Cassady JR. The role of radiotherapy in the treatment of malignant sweat gland neoplasms. Cancer. 1990 Apr;65(8):1737–40.
14 Keasbey LE, Hadley GG. Clearcell hidradenoma; report of three cases with widespread metastases. Cancer. 1954 Sep;7(5):934–52.
15 Nash JW, Barrett TL, Kies M, Ross MI, Sneige N, Diwan AH et al. Metastatic hidradenocarcinoma with demonstration of Her-2/neu gene amplification by fluorescence in situ hybridization: potential treatment implications. J Cutan Pathol. 2007 Jan;34(1):49–54.

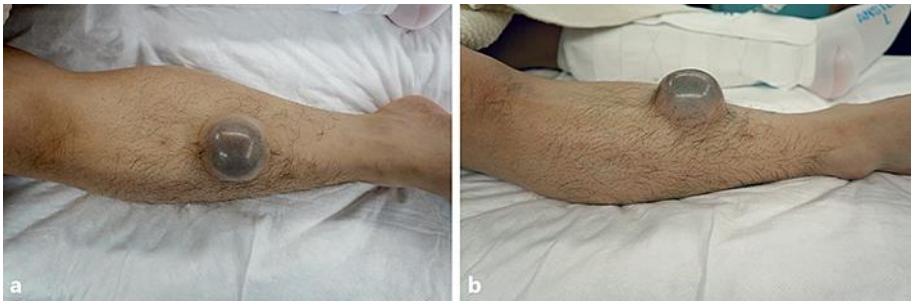

Fig. 1. Anteroposterior (**a**) and lateral clinical appearance (**b**) of the right lower leg. The lesion was hemispheric and firm, measuring 5 × 4 cm. The overlying skin was smooth and not ulcerated.

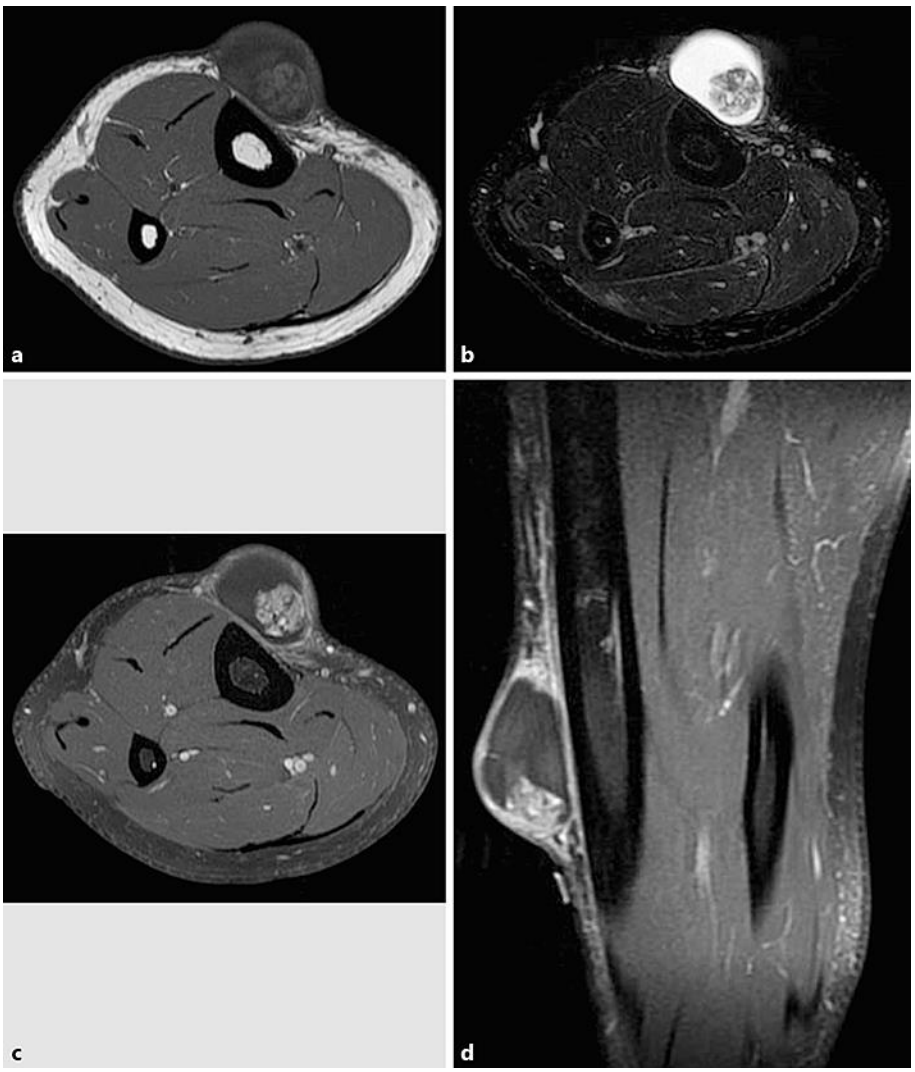

Fig. 2. Preoperative MRI of the right lower leg. **a** Axial T1-weighted image revealed a hypointense lesion with markedly isointense area. **b** On fat saturation T2-weighted image, the lesion was hyperintense to muscle and contained a heterogeneous area, measuring 1.5 × 1.5 cm. **c**, **d** Postcontrast fat saturation T1-weighted image showed a prominent enhancement of the internal mass and the periphery of the lesion.

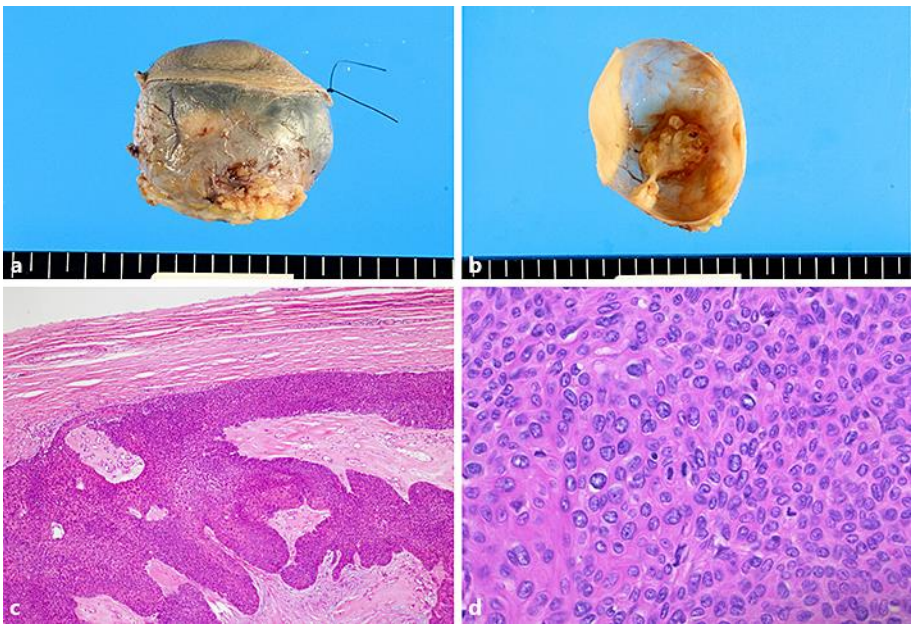

Fig. 3. **a** Resected specimen after marginal resection. The tumor was resected with the overlying skin and underlying fascia. **b** The tumor was predominantly cystic with partial fungiform solid mass. **c**, **d** Microscopic examination of the tumor revealed epithelial cells that were arranged in lobules and sheets with atypia and sporadic mitosis.