Perianal malignant nodular hidradenoma in HIV infected pregnant patient

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Malignant nodular hidradenoma (MNH) is a rare invasive tumour arising from eccrine sweat glands, with significant risk for local recurrence and distant metastases. Hidradenoma papilliferum is reported in pregnancy. To our knowledge this is the first MNH in a human immunodeficiency virus (HIV) infected pregnant woman. The patient presented with a painless perianal growth. Wide local excision was performed and the wound left to heal by secondary intension. The pathology report confirmed MNH. The patient has been followed for 14 months without evidence of recurrence. MNH should be considered in the differential diagnosis of similar lesions in HIV infected patients. Treatment for such HIV infected patients with MNH may be similar to that in immune-competent patients; they may benefit from a longer follow-up period.
Key words: Malignant Nodular Hidradenoma, HIV infection, Pregnancy.

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Introduction

Malignant nodular hidradenoma (MNH), first described as clear cell eccrine carcinoma by Keasbey and Hadley in 1954[1-3] is an uncommon, highly malignant, primary skin tumor derived from eccrine sweat glands[1-6] accounting for approximately 6% of malignant eccrine tumors.[1,4] MNH has been described in the literature using various nomenclature, including clear cell hidradenocarcinoma, malignant clear cell myoepithelioma, malignant clear cell hidradenoma, clear cell eccrine carcinoma, and malignant clear cell acrospiroma.[1,2,4,5] MNH is usually found on the face, scalp, or anterior surface of the trunk,[3-6] typically arising de novo, but on occasion transforming from the benign variant.[1-6] Local recurrence after excision has been described in up to 50% of cases, and metastases in up to 60% of cases.[1-6] These metastases tend to affect the regional lymph nodes but can also involve the lung, bone, brain, liver, viscera, and skin.[3,5,6] Most tumors occur in elderly individuals,[1,4] with no obvious gender predominance.[1,3-6] Only one author specifically addressed the issue of HIV infection: Souvatzidis et al. reported that none of their seven patients were HIV positive.[1]

MNH typically presents as a solitary, firm, painless intradermal mass, measuring 1 to 5 cm, and is covered by intact or occasionally ulcerated pink, purple or blue-colored skin.[1,3,4,6] It is characterised by slow growth for many years, but may undergo a sudden rapid increase in size.[1-3] Its aggressive behavior is more apparent after each local relapse with faster growth and more aggressive invasion of the surrounding tissues.[1-5]

Histologically, MNH has nodular or lobulated architecture with two main cell subpopulations: one type consists of polygonal cells with round nuclei and vacuolated cytoplasm as a result of abundant glycogen, while the second type of cells is characterised by oval nuclei and dark basophilic cytoplasm with infiltrative or invasive growth patterns into the dermis and surrounding tissues.[1-3,5]

Immunohistochemical analysis is strongly positive for Ki 67 and p53, positive for keratin AE1/3 and cytokeratin 5/6, and negative for CEA, S-100 protein, GCDFP-15, EMA, blc-1 and blc-2.[1,2,5] Moreover MNH, like other skin tumours with eccrine differentiation, may express positive immunohistochemical staining for oestrogen and progesterone receptors.[1]

Complete surgical excision with 3–5 cm margins is the current treatment of choice.[1-5] Because the diagnosis is rarely known prior to the initial excision, a second, wider resection with extended surgical margins is nearly always necessary.[1,3]Lymph node metastases have been described up to 3 years after the initial excision.[1] The mean time to local recurrence was 16 months in six out of seven cases (85.7%) after initial excision.[1] Because of the aggressive nature of MNH and its propensity to spread through regional lymphatics,[1-6] many authors advocate prophylactic lymph node dissection, especially for large, recurrent or anaplastic tumors.[1-5]

The effect of adjuvant chemotherapy or radiotherapy is still controversial with no proven benefit in local control or survival. The few case reports describing potential benefit also advocate for further study.[1-5] Oestrogen receptor analysis may also provide avenues for adjuvant therapy: those patients who are oestrogen receptor positive would then be offered hormonal therapy.[1]

Patient information

A 31-year-old woman presented with an enlarging, painless perianal growth over the four months prior to presentation. Coincidentally, she was 4 months pregnant. She was known to be HIV infected with a CD4 count of 793. On examination the uterus was 18 weeks gestational size. There was a nodular growth of 5 x 5 cm, with areas of ulceration and serous discharge to the right side of the anus. It was intradermal, firm, non-tender and did not feel attached to the underlying structures (Figure 1). There was no inguinal lymphadenopathy. Differential diagnoses of lymphoma, fibroma and sarcoma (including Kaposi in an HIV patient) were considered.

Since the nature of the tumour was not known prior to operation, local excision with a 1 cm margin of healthy tissue was performed, and the wound left open to heal by secondary intension (Figure 2). The pathology report described a tumour measuring 7 x 5 x 4 cm. It was located in the dermis and extended to the subcutaneous fat with lack of circumscription, an infiltrative growth pattern, and deep extension (Figure 3). Nuclear pleomorphism, marked cytologic atypia including squamous and clear cell differentiation, and increased mitotic figures more than 4 mitoses per 10 HPFs were described (Figure 4). Immunohistochemistry demonstrated positive Ki 67 and AE1/AE3, but negative for S100 Protein.

Once the histologic diagnosis of MNH was confirmed, the patient was counselled on re-excision of the area which, given its location, may involve abdominoperineal resection. The patient did not want to consider a more extensive resection. The oncologists therefore discussed the potential role of chemotherapy or radiotherapy. Once again, the patient declined, and opted for close follow-up.

The patient has been followed for the last 14 months. The wound is healing well, and there is no clinical sign of local recurrence Figure 5. There is also no clinical evidence of metastatic disease. We would have considered lymphoscintigraphy, but it was not possible in our setup. She is scheduled for close follow-up.

Discussion

It is difficult to estimate the true incidence of MNH. The literature consists of case reports and reviews.[1,2,4,5] MNH is a rare, aggressive tumor with significant risk of local recurrence and metastases.[1-6] Prognosis is usually poor, and 5-year disease-free survival is less than 30%.[1,3] Most cases occur in the sixth and seventh decades of life with no gender predominance.[1-3] Our patient's young age may be related to her HIV positive state. The most common sites for MNH are the head, the trunk and the extremities. These tumors typically occur as solitary nodules measuring 1–5 cm, with or without central ulceration. Although most MNH arise *de novo*, they may arise in a pre-existing hidroadenoma.[1-6]

Definitive diagnosis requires histological examination.[1-6] Differential diagnoses includes haemangioma, lymphangioma, squamous cell carcinoma, basal cell carcinoma, dermofibrosarcoma protuberans, pyogenic granuloma, blue nevus, malignant melanoma, and metastatic lesions of the skin.[1,3]

An inverse relationship exists between tumor size and survival.[2] Metastases seems to affect regional lymph nodes initially, then may spread to distant sites including bones, vertebrae, ribs, pelvis, viscera and pleura.[1,3,5]

Surgical excision is the current therapeutic modality of choice. While current recommendations are for 3–5 cm-wide margins,[1-5] this was not possible in our patient without an abdominoperineal resection. She was not willing to entertain such a radical procedure.

Elective regional lymphadenectomy after lymphoscintigraphy should also be considered.[1-5] This was not possible in our setting. Sentinel lymph node biopsy remains controversial.[1-5] Locoregional recurrence even after wide surgical excision has been reported. [1,4] Close follow-up is advocated in all cases.

Adjuvant chemotherapy and radiotherapy do not appear to have a significant impact in local control or survival.[1-5] Receptor status may dictate a potential role for hormonal therapy.[1,5]

Conclusion

To our knowledge this is the first case of malignant nodular hidradenoma (MNH) in an HIV infected pregnant patient. The possibility of MNH should be considered in the differential diagnosis of such lesions in young HIV infected patients. The outcome of operative treatment for HIV infected patients may be similar to that in immune-competent patients. Our early experience, albeit only with one patient, brings in to question the necessity for 3–5 cm wide surgical margins.

Competing Interest

The authors declare no conflict of interest.

Authors' Contributions

AGB conceived the idea, performed the operation, searched literature and drafted the manuscript, ABE reviewed the manuscript, histologic slides and did pathologic literature review, AG reviewed the manuscript. The three authors read and approved the case report for submission.

Figure 1. Preoperative appearance of perianal lesion.

Figure 2. Postoperative appearance after wide excision.

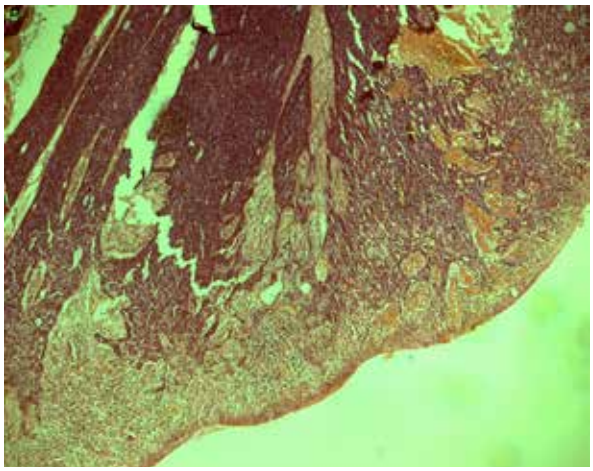

Figure 3. 4 x objectives Ulceration of the overlying skin and infiltrative growth pattern.

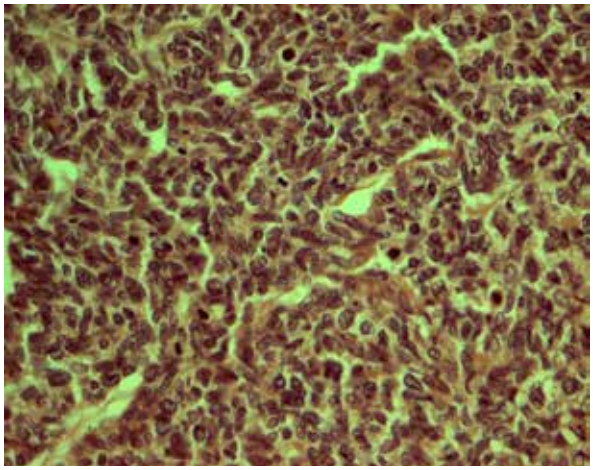

Figure 4. 40 x Showing marked cellular pleomorphism

Figure 5. 14-month postoperation.

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