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Case Report

Pseudoepitheliomatous hyperplasia: A Word of Caution

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Abstract

Pseudoepitheliomatous hyperplasia (PEH) is a benign skin disease associated with reactivity to chronic inflammation. The diagnosis is based upon histologic characteristics and thus requires a formal biopsy. Due to its ambiguity, particularly the range of other conditions in which it is associated, a report of PEH instills much difficultly upon the receiving clinician in deciding further management, especially if malignancy had not been discounted prior to the biopsy. The risk of causing unnecessary iatrogensis by obtaining additional biopsies must be weighed with the potential consequence of anchoring to a diagnosis of PEH that reveals it to have been falsely reassuring. If one finds themselves in such a situation when caring for a patient, due diligence is warranted. Determining whether or not additional studies are appropriate should not be taken lightly with a diagnosis of PEH, as the decision may result in significant consequences.

ABBREVIATIONS

PEH: Pseudoepitheliomatous Hyperplasia; SCC: Squamous Cell Carcinoma; HS: Hidradenitis Suppurativa

INTRODUCTION

Pseudoepitheliomatous hyperplasia (PEH) is a benign skin condition associated with a wide variety of disease processes including cancer and occult infections [1]. PEH is thought to arise as a reactive process secondary to inflammation. The variety of disease in which pathologic inflammation occurs is vast. As such PEH has been associated with many different conditions ranging from infectious to non-infectious, benign to malignant. Occult infections and autoimmune disorders are among the most common pathologies associated with PEH [2-4]. Peculiar reactions to foreign bodies such as tattoo ink have also been reported [5]. Although these diseases are benign, PEH has also been associated with many forms of malignancy including melanoma [6]. The ambiguity that materializes from a report of PEH presents the receiving clinician with a dilemma in regard to deciding next steps in management, especially if the clinical picture had been unclear prior to obtaining the biopsy in question. The predicament lies in deciding whether or not further diagnostic testing is warranted. With a diagnosis of PEH, tenacious clinical judgement and consideration for its many associated conditions is required when deciding on how to proceed with management. We present a case that highlights the diagnostic challenges that may follow a report of PEH along with the potential for poor outcomes when management errs too conservatively.

CASE PRESENTATION

A 56-year-old Caucasian woman presented to the outpatient surgery office with complaints of increasingly severe pain and drainage secondary to a chronic perineal wound of approximately three years' duration. The patient did not have a clear diagnosis despite having received care from several providers since the onset of her wounds. A review of documentation revealed that PEH had been reported consistently from three separate punch biopsies of the wound. Almost a dozen subsequent attempts to reveal an occult infection were all unsuccessful. At the time of her presentation, the patient's wound was affecting her quality of life to such a degree that she requested for it to be excised in totality with subsequent perineal reconstruction. She also reported recently discovering a new "bump" in her vagina and requested management of this lesion as well.

The patient's past medical history was not particularly impressive. She had a history of psoriasis and hypothyroidism. She was up-to-date on her health maintenance screening and had no history of significant environmental exposure. She had no history of immunocompromise nor Crohn's disease. She had no personal history of malignancy and there was no history of cancer in her family. Upon examining the patient in the office, a circumscribed area of in duration and erythema was visualized

just left of the perineum. Due to uncontrolled pain, a pelvic exam was deferred at that time and the patient elected for an exam under anesthesia with the provision of obtaining additional biopsies.

In the operating room a small nodule was palpated in the anterior wall of the vagina. The perineal wound remained unchanged from prior examination. Excisional biopsies of both lesions were obtained and sent to pathology for review. The perineal wound biopsy returned as squamous cell carcinoma (SCC) in a background of hidradenitis suppurativa (HS). The biopsy of the vaginal nodule reported melanoma with lymphovascular invasion. The patient underwent a PET scan shortly thereafter which noted intrathoracic, retroperitoneal, and pelvic lymphadenopathy (Figures 1-3). A subsequent retroperitoneal lymph node biopsy confirmed metastatic melanoma.

DISCUSSION

PEH is a benign skin condition associated with a variety of ongoing inflammatory states such as those seen with chronic infection and autoimmune disorders. PEH has also been associated with several cancers, including melanoma. HS is a chronic inflammatory disease that affects areas of the skin containing apocrine glands such as the groin and axillae. In addition to its deleterious effects on patient self-esteem and quality of life, HS is also associated with SCC [7].

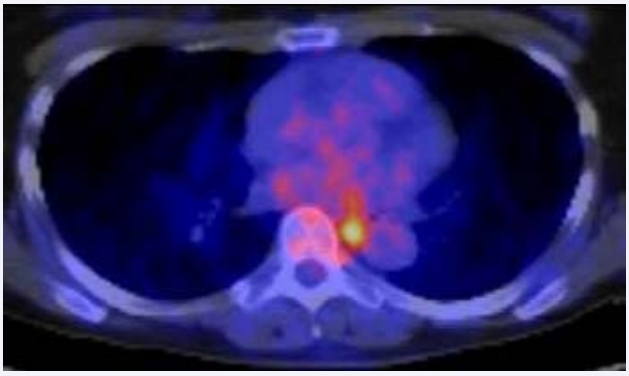

Figure 1 PET imaging of intrathoracic lymphadenopathy.

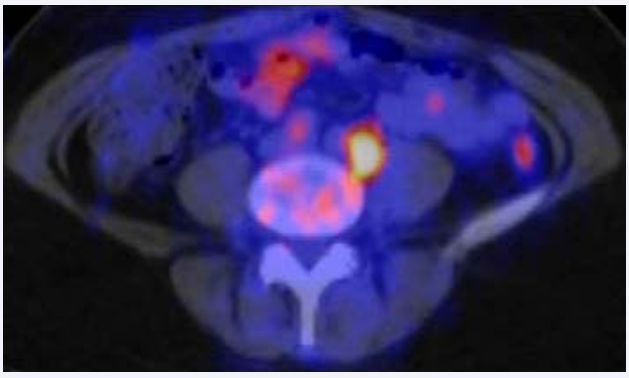

Figure 2 PET imaging of retroperitoneal lymphadenopathy.

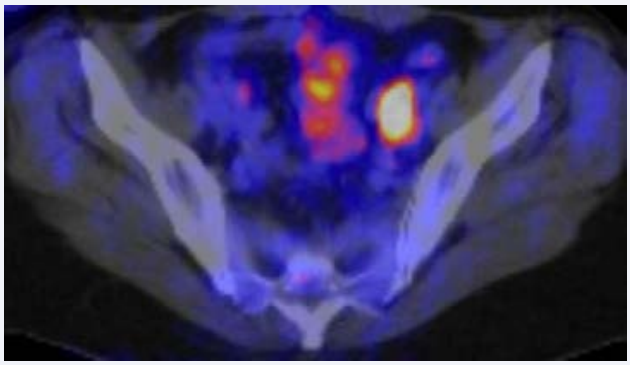

Figure 3 PET imaging of pelvic lymphadenopathy.

It is well known that SCC can arise with chronic inflammation, also known as a Marjolin's ulcer [8]. Thus the association between SCC and a chronic inflammatory condition such as HS is not unexpected. However, the association between PEH and melanoma may be less well known.

Moreover, to our knowledge there have been no reports of these two processes occurring simultaneously in the same patient. Given the potential for poor outcomes following false negative biopsies, clinicians must exhibit proper judgement when faced with a report of PEH to ensure that no underlying malignancy is present.

Although PEH remains a benign condition in and of itself, some authors believe it takes place on a spectrum of transformation from benign to malignant [9]. Even still, others warn of potential iatrogenesis that may occur as a result of unnecessary attempts at differentiating PEH from true oncologic processes [10]. An apparent concern is the opportunity for false positives given that differentiating PEH from SCC appears to be rather difficult. The pressure of making the right clinical decision becomes obvious when the difficultly in differentiating between these two diagnoses is considered with the disparity of their prognoses. In order to rule out malignant potential, factors such as membrane invasion should be evaluated [11]. In practice this is easier said than done, as obtaining biopsies to assess for such characteristics may result in significant scaring or prove difficult to obtain by standard measures. In addition to scarring, there is a clear risk of obtaining invasive biopsies only to discover that they were unnecessary given the absence of malignant disease. Thus the true difficultly in differentiating PEH from cancer exist not only in making the decision to attempt additional biopsies but also in deciding how they can be obtained appropriately with adequate yield.

To our knowledge, this is the first case of SCC and vaginal melanoma occurring simultaneously with associated PEH in the same patient. In addition to this rare occurrence, this case highlights the diagnostic difficulty manifest by PEH. The importance of aggressive management in PEH when appropriate is exemplified. Despite having been managed for three years, there was a poor outcome of this case in terms of the patient's prognosis. The 5-year survival of patients diagnosed with a Marjolin's ulcer is reportedly between 40% to 69% [8]. For vaginal melanoma, the 5-year survival rate is noted at 15%

[12]. Survival rates with both cancers occurring simultaneously are not available though they are likely to be destitute. Several opportunities to obtain biopsies with adequate sampling were missed during this patient's management. Though we cannot comment as to the reasoning for continued punch biopsies, we suspect it was related to hesitation given that PEH is a benign entity. In hindsight the better choice would have been to obtain biopsies through more invasive techniques able to provide adequate tissue samples.

However, the decision would not have been so easy at the time given the ambiguity of PEH and significant morbidity of an invasive biopsy.

When a patient presents with a skin lesion of unknown etiology, physicians are trained to have a low-threshold for obtaining initial minimally invasive biopsies. Though this decision is rather straight forward, many well-trained physicians would reasonably feel uncomfortable taking additional biopsies after receiving a report of PEH. However, before discounting PEH as a benign entity, clinicians should remain mindful of its associated conditions. The potential for an underlying malignancy exists. At the same time conservative management should not be abandoned instinctively, as chasing after benign disease will only result in unnecessary morbidity from invasive biopsies. The outcome of this case favors escalating the diagnostic ladder if a lesion remains and secondary biopsies continue to report PEH without an explanation for its presence. Obtaining imaging and/or additional biopsies appear appropriate in such a situation. If additional biopsies are indeed warranted, techniques able to obtain an adequate sample should be considered. In certain scenarios, the diagnostic yield of more invasive techniques may outweigh the apparent morbidity. Recommending more invasive options to patients is surely difficult, especially if a benign condition such as PEH has been the only finding. Nonetheless, such consideration is surely warranted in the right clinical scenario.

Sparing a patient of immediate morbidity from an invasive biopsy is not a good reason to subject them to the potential for mortality at a later time should an underlying malignancy reveal itself.

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