Hidradenitis Suppurativa Complicating Epithelial Malignancy in Immunocompromised Patient

Shubhangi Vithal Dhadke1, Milind Bhausaheb Korade2, Shashikala Anant Sangle3, Vithal Narayan Dhadke1

Abstract
Hidradenitis suppurativa complicating epithelial malignancy in people living with HIV is very rare. Hidradenitis suppurativa is very rare seen in only 1% of general population and 4% of young adults.

We report a case of Hidradenitis suppurativa complicating an epithelial malignancy in an immunocompromised (HIV reactive) patient.

Introduction
Hidradenitis suppurativa was first described in 1839 by Velpeau. In 1854, Verneuil associated the supplicative process with the sweat glands, and the condition was given its current name, described as Verneuil disease. Hidradenitis suppurativa was accepted as an acneiform disorder that begins with follicular occlusion rather than an infection of the sweat glands. Hidradenitis suppurativa is a defect of the follicular epithelium; therefore there is a movement towards calling the disease acne inversa instead of hidradenitis suppurativa.

Average age of affected individuals is 23 years. Rarely, Hidradenitis Suppurativa occurs before puberty or after menopause. Onset is insidious. Symptoms of pruritus, erythema, and local hyperhidrosis occur first. Later, first the patients develop painful, asymmetric pauciarticular arthritis to a symmetric polyarthritis. Diagnosis is primarily clinical, and biopsy is rarely required, especially if lesions are well-developed.

Three key elements are required to diagnose Hidradenitis Suppurativa: typical lesions, characteristic distribution and recurrence. Based on these three premises, a set of typical lesions, called primary lesions, was compiled, as described below.

- Painful or tender abscesses
- Inflamed discharging papules or nodules
- Dermal contractures and
- Rope-like elevation of the skin.

Case Report
A middle-aged male was admitted with fever, multiple pustular lesions with pigmentation over chest (Figure 1), neck, shoulder and right cheek region for 10 days with c/o difficulty in swallowing and right eye swelling with purulent discharge. He had been recently diagnosed as HIV-positive. He was a known case of cerebrovascular disease with right sided hemiparesis 4 years ago. On general examination patient was drowsy, responding to verbal commands, febrile with pulse 102 rate/min, regular. BP was 130/90 mm Hg, lymphadenopathy was present bilaterally in axillary, supraclavicular and cervical regions (Figures 2 and 3); nontender, firm, mobile with induration present over swelling. Eye examination revealed bilateral conjunctivitis. There was poor oral hygiene noted. Skin examination showed multiple papulo-pustular lesions over cheek, neck, chest and axilla. On respiratory system examination there were bilateral diffuse crepts. Abdominal, perianal and genital examination was normal. He had a right supranuclear facial palsy, hypertonia in right UL Power gr. 3 in right UL. Plantar was extensor on right side. Multiple papulo-pustular lesions were seen over body with sinus openings with discharge, comedones and hyperpigmentation. Thus he was diagnosed as Hidradenitis Suppurativa with bilateral conjunctivitis with old stroke with HIV/AIDS.

Investigation CBC: TLC 16000/ul, neutrophils 68%, lymphocytes 19%, HB% 14.5 g, platelets 2.4 lac, HIV/ELISA positive, CD-4 unit =503/ul, Na 153, K+ =2.8, creat 2.2 (USG A+P: S/O B/L Medical renal parenchymal disease, RK 8.8 × 3.6, LK 10 × 4). He had normal blood sugar and liver functions.

USG NECK/AXILLA – multiple iso-hypo echoic lesions in b/l axilla 3.3 × 2.2 cm right, 3.1 × 1.4cm left, s/o bil. Axillary, Bil. supraclavicular lymphadenopathy right 1.3 × 1.5 cm, left 1.6 × 0.8 cm with destruction of architecture. FNAC LT axillary lymph node (specimen no.13/646) In a background of lymphocytes, clusters of round to oval cells, having hyperchromatic nuclei and dark eosinophilic cytoplasm, few cells showing eccentric nucleus with clear cytoplasm (signet ring). Positive for epithelial malignancy (Figure 4).

Despite all efforts and treatment offered patient succumbed to his disease due to septicemia with multi organ failure.

Discussion
Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic follicular occlusive skin disorder characterized by recurrent abscesses, draining sinuses, and scarring, with a multifactorial pathogenesis. The answer to the question whether HS may be considered a systemic disease relies on the presence of accompanying systemic manifestations.1

1 Associate Professor in Medicine, 2 Assistant Professor in Medicine, 3 Professor and Head in Medicine, Dr. Vaishampayan Memorial Government Medical College, Solapur, Maharashtra
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Chemokines play a paramount role in the tumor progression. Chronic inflammation promotes tumor formation. Both tumor cells and stromal cells elaborate chemokines and cytokines. These act either by autocrine or paracrine mechanisms to sustain tumor cell growth, induce angiogenesis and facilitate evasion of immune surveillance through immunoediting. The chemokine receptor CXCR2 and its ligands promote tumor angiogenesis and leukocyte infiltration into the tumor microenvironment. In harsh acidic and hypoxic microenvironmental conditions tumor cells up-regulate their expression of CXCR4, which equips them to migrate up a gradient of CXCL12 elaborated by carcinoma-associated fibroblasts (CAFs) to a normoxic microenvironment. The CXCL12–CXCR4 axis facilitates metastasis to distant organs the CCL21–CCR7 chemokine ligand–receptor pair favors metastasis to lymph nodes.

These two chemokines ligand–receptor systems are common key mediators of tumor cell metastasis for several malignancies and as such provide key targets for chemotherapy. In this paper, the role of specific chemokines/chemokine receptor interactions in tumor progression, growth and metastasis as related to angiogenesis, metastasis, and immune response to the tumor are reviewed.²

Kurokawa I, et al studied cytokeratin (CK) expression in two cases of well-differentiated and poorly differentiated squamous cell carcinoma (SCC) arising from hidradenitis suppurativa (HS). In both cases, type A (infundibular-like keratinized) epithelia were observed. In type A epithelia, CK 1 and 10 expressions were decreased, and CK 14 and 17 were detectable in the whole layers. In tumor nests of well-differentiated SCC, CK 1 and 10 expressions were downregulated, and CK 14 expression was upregulated. In tumor nests of poorly differentiated SCC, CK 1 and 10 were not expressed, but simple epithelial keratins (CK 8, 18 and 19) were expressed. These changes of CK expression are related to malignant transformation from the sinus tract (type A epithelium) in HS to SCC.³

The risks for HPV-associated high-grade intra-epithelial neoplasia (IN) and cancer are also increased. The prevalence of oral, anal, and cervical HPV infection in HIV-positive individuals compared with HIV-negative individuals increases with progressively lower CD4+ levels, as does incident high-grade IN. In contrast to IN, development of cancer is not related to lower CD4+ level. With increasing grades of IN and cancer, the proportion of tissues with copy-number abnormalities (CNA) increases. This suggests a link between CNA and increased HPV-induced chromosomal instability mediated through de-repressed E6 and E7 expression consequent to loss of functional E2 protein. There are few data to suggest a direct role for HIV in the pathogenesis of HPV-associated neoplasia, but HIV-associated attenuation of HPV-specific immune responses may allow for persistence of high-grade IN and sufficient time for accumulation of genetic changes that are important in progression to cancer.⁴

Hidradenitis suppurativa (acne inversa, Pyoderma fistulans signica, and Verneuil’s disease) is a chronic suppurating infection that affects the apocrine glands of the axilla, groin, and the perineum. The disease begins with the obstruction of the apocrine gland duct, resulting in the infection of the retained secretions. Following gland obstruction, there is rupture of the gland with spread of infection into the dermis leading to abscess formation and involvement of other apocrine glands. There is the formation of multiple intradermal abscesses, which lead to the development of multiple sinuses, fistulae, and scarring of the skin. Occasionally, the disease extends beyond the dermis into the subcutaneous fat, fascia, and muscle. The lesions present in the form of nodules, discharging sinuses, and comedones predominantly over axillae, anogenital region. Atypical sites were involved in this patient such as face, thighs which could be due to HIV-related immunosuppression. Etiology may also have an endocrinal component, and HIV-associated endocrinopathies may alter the course of the disease. Oral retinoids (isotretinoin) have a proven value in unresponsive cases. However, because of financial constraints it could not be used in our patient. Use of isotretinoin for HS in HIV-positive patients on ART needs regular monitoring due to adverse effects such as raised triglycerides and effect on liver transaminases. Other therapeutic options include use of antibiotics such as flucloxacinil or prolonged courses of tetracycline or
metronidazole (minimum 3 months) for their anti-inflammatory action. Combination of clindamycin and rifampicin may be effective. Surgical management like incision and drainage of abscesses and excision of scars need to be individualized.  

Association of HIV/AIDS with chronic skin conditions like HS can be a therapeutic challenge.

References