Review

Acne inversa

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Acne inversa (synonyms are intertriginous acne, acne triad, acne tetrad, hidradenitis suppurativa, pyodermia fistulans sinifica) is a chronic inflammatory disorder of the sebaceous follicles and terminal hair follicles and is one member of the acne family. It is characterized by acne conglobata in an inverse pattern involving the axillary, inguinal, and perigenital regions, together with perifolliculitis and abscesses on the nape and scalp. The severity of the condition varies from a few suppurating lesions to widespread and disabling disease.

Historical survey

There is a long history of confusion regarding the taxonomy, pathogenesis, and treatment of the disease. Dissecting cellulitis of the scalp, one facet of acne inversa, was first described in 1908 by Hoffmann, but it was not related to acne. In 1951, Kierland wrote a classical paper on this subject, naming the various components “unusual pyoderma (hidrosadenitis suppurativa, acne conglobata, dissecting cellulitis of the scalp).” Unfortunately, the connection with apocrine sweat glands was established. Pillsbury, Shelley, and Kligman, in 1956, brought together acne conglobata, hidradenitis suppurativa, and dissecting cellulitis under the term follicular occlusion triad. The central pathogenetic event in all three disorders was a tendency towards follicular hyperkeratinization, leading to the retention of keratin products with secondary bacterial infection as in acne vulgaris. The only flaw in their concept was the focus on apocrine sweat gland involvement, but did not present a detailed explanation. In 1989, Plewig and Steger suggested acne inversa as an all-inclusive and accurate name for what was previously called the occlusion triad or tetrad.

Incidence

Acne inversa is probably more common than once thought, but the diagnosis is frequently ignored or missed. The condition has been found in all races and in both sexes. Adults, not juveniles as in acne vulgaris, are affected.

Pathogenesis

The understanding of the pathogenesis is very limited. Apocrine duct closure by keratinous plugging with bacterial infection was first suggested as the pathogenetic mechanism, but this theory is now only of historic interest. Pathogenic anaerobes have not been regarded of major importance and are usually not found in early lesions; however, secondary bacterial colonization in warm sweating armpits, anal folds, and groins certainly enhances and intensifies chronic inflammation. The application of chemical depilatory agents, deodorants, and antiperspirants, and the shaving of body hair have been suggested as possible factors in the etiology of the disease, but none of these causes has been proven. Obesity is common, but not a constant feature of acne inversa. A role for smoking habits as a contributing factor seems speculative. Some patients have been found to be diabetic or have impaired glucose tolerance, but the significance of these findings is unclear. Abnormal levels of testosterone, androstenedione, estrogen, and progesterone, together with menstrual irregularities and hirsutism, have sometimes been reported, but
Figure 1 Acne inversa. Tunneled abscesses and dehiscing scars afflict the armpit

Figure 2 Acne inversa. Many abscesses have bridged tunnels from right to left, through fascias and muscles, extending deep into the thighs

the relevance of abnormalities in androgen metabolism is not clear. Hormonal levels are normal in most patients, and systemic and local administration, or the implantation of pellets of androgens and estrogens into axillary skin, has not resulted in the development of acne inversa. Frictional trauma may be an important inciting influence, especially in inguinal and mammary sites where tight-fitting apparel, such as blue jeans, pantyhose, girdles, seamed panties, and brassieres, is worn; however, this cannot explain acne inversa on the nape of the neck and the hairy scalp. Neither primary cellular nor humoral abnormalities in the immune system can be held responsible. Congenital α1-antitrypsin deficiency has been reported to be associated with acne inversa, but this could not be confirmed in other studies. Heredity may be important in acne inversa, but few details are known. The occurrence of the disease in two or more members of the same family has been occasionally reported, indicating an autosomal dominant inheritance with high penetrance. On the other hand, acne conglobata occurs frequently in first-degree relatives. Human leukocyte antigen (HLA) frequencies may distinguish these patients from the remainder of the population. HLA-A1 and HLA-B8 may predispose the patient to more severe disease, but further investigations are necessary to confirm this.

Clinical findings

There is a characteristic discrepancy between the relatively mild acne conglobata on the trunk and the severe intertriginous inflammation lasting for years or decades. Many patients have more than one major site involved. One or both axillae may be affected (Fig. 1), as well as the inguinal region, often with spread to the scrotum, labiae, mons pubis, mammary or perineal region, and buttocks (Fig. 2). Women develop the inguinal form of the disease more commonly, as well as mammary lesions. Confluent infiltrations, 5–30 cm in length, develop, which are firm and tend to merge at many points. In the axilla, there are scars and contractures up to the size of a finger, together with persistent erythema. Mobility is restricted, and the upper arm may not be fully raised above the horizontal. The inguinal–anogenital infiltration is brown–red, with pus, blood, and foul-smelling secretions emerging from the numerous fistula openings. The secretions often contain gram-negative bacteria, an additional curse of this disabling disease. In the upper anal fold or above the coccyx, one finds thickened scars from which terminal hairs emerge, known as pilonidal sinus. On the nape and on the scalp, diffuse scarring occurs with residual grouped hairs (toothbrush sign); keloids also appear (acne keloidalis nuchae, folliculitis sclerosicans nuchae). Without adequate...
treatment, the process may spread from the nape into the entire scalp. Spondylarthropathy occurs sporadically in patients with acne inversa; the findings are similar to those seen in other seronegative spondylarthropathies, except for the lack of association with HLA-B27. It has been suggested that the arthropathy may be reactive to the chronic inflammatory process.

History
Acne inversa begins in the sebaceous follicles, which are rare in the intertriginous regions, or, more commonly, in the terminal hair follicles. Histologically, the fundamental change is the same as in acne vulgaris, namely hyperkeratosis of the infundibulum, giving rise to comedo-like horny impactions. It is not a primary disease of the apocrine or eccrine sweat glands. These are secondarily involved in the giant abscesses of the confluent inflammation. The earliest inflammatory event is the circumscribed rupture of the follicular canal, spilling foreign-body material, such as corneocytes, bacteria, sebaceous matter, and hairs, into the connective tissue. The cause of the rupture is not known, although friction in intertriginous locations may be a contributing factor. The dumping of the foreign product excites first an infiltrate of granulocytes, followed by mononuclear cells, becoming a foreign-body granuloma. Epithelial strands are sent out in vain attempts to encapsulate the abscess. Secondary comedones are a typical feature. The disease speeds up enormously, and the tissue reaction is complicated by extensive inflammation, as well as enhanced by secondary bacterial colonization. In chronic lesions, bacteria can be demonstrated in and around the glands and local lymphatics. Far-flung abscesses dissect through the dermis, reaching the subcutaneous fat, and causing lobular and sepal panniculitis.

Laboratory findings
Patients with acute lesions of acne inversa are ill, with elevated erythrocyte sedimentation rate (ESR), leukocytosis to 15,000/mm³ or more, low serum iron, and serum protein abnormalities on electrophoresis. One can isolate from the sinuses almost every microorganism known to bacteriologists, including streptococci, gram-positive and gram-negative rods, and the full range of fecal bacteria. The microbiological flora is not constant and changes unpredictably.

Differential diagnosis
Acne inversa is to be suspected in any adolescent or adult patient with a history of acne conglobata who demonstrates one or more tender abscess-like swellings in the intertriginous sites, especially in the axillary, inguinal, or perigenital regions. Differential diagnosis includes lymphogranuloma inguinale, regional ileitis (Crohn's disease), furuncles, vegetating pyoderma, actinomycosis, and tuberculosis subcutanea et fistulosa.

Complications
Acne inversa is an extremely chronic disabling disorder characterized by abscesses, with communicating epithelial lined channels and draining sinuses in unusual locations, burrowing deeply into the skin, relentlessly progressing and leading to keloids and contractures, if the diagnosis is not established and surgical intervention missed. The soiling of underwear, bed linen and other clothing, and an offending smell, turn the patients into outcasts, and social contacts become impossible. Swellings of elephantiasis nostras following streptococcal complications may be superimposed on acne inversa lesions, leading to monstrous enlargement and distortion of external genitalia. Squamous cell carcinoma with metastases arising from the background of the chronic inflammation (Marjolin ulcer) has been described. Bacterial meningitis, bronchitis and pneumonia, and systemic amyloidosis are rare, but serious and sometimes fatal complications.

Treatment
Many attempts have been made with a variety of treatment modalities to stop the progression of this terrible disease, including X-ray irradiation, epilation or depilation, scalping, hormones such as estrogens, progesterone, and cyproterone acetate, vaccines, systemic or local antibiotics, and corticosteroids, but none of these has been effective. Acne inversa calls for surgical treatment, which we recommend for all intertriginous lesions at the earliest recognized stage. Simple incision of individual lesions offers only a short period of relief from pain, is associated with a high recurrence rate, and is therefore of little value in the long term. Wide excision, well beyond the clinical borders of activity, is mandatory, regardless of the localization of acne inversa. In the axillae, all affected areas are excised for the fatty tissue and repaired by plastic surgery. As far as possible, excision and rotation flaps or free transplants are used for the inguinal–genital region. Fistulas extending from the anal fold via the buttocks to the hips may be treated surgically in the same way. Sometimes, the best functional results are obtained with secondary wound granulation, perhaps in combination with free skin grafts. In some cases, the technique of CO₂ laser treatment combined with healing by secondary intention may provide an alternative method for the management of acne inversa. The CO₂ laser stripping–secondary intention
technique allows the simple treatment of early lesions which would otherwise have been treated using less effective, local conservative remedies. Post-surgery results are satisfactory, both cosmetically and with regard to the quality of life. The drug of choice for pretreatment is isotretinoin (13-cis-retinoic acid) a few months prior to the surgical procedures. This is given at a dose of 0.5–1.0 mg/kg daily to reduce the inflammatory components. Isotretinoin is by itself, with rare exceptions, insufficient to stop the disease.

**Prognosis**

In most patients, early surgical intervention is sufficient to stop the disease. Too often, precious time is lost with inadequate treatment, with the consequence that many patients drift away from society. Unemployment, depression, alcoholism, obesity, and divorce may be the sequela. Recurrence usually results from inadequate excision. Many patients develop new lesions at a site not affected at the time of their initial surgery.

**References**


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