Prepubertal Hidradenitis Suppurativa: Two Case Reports and Review of the Literature

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Abstract: Hidradenitis suppurativa (HS) is a chronic suppurative scarring disease of apocrine sweat gland-bearing skin in the axillary, anogenital, and, rarely, the breast and scalp regions. Females are more commonly affected than males and it is usually seen at puberty or later. We report two girls with prepubertal hidradenitis suppurativa whose initial presentation predated any signs of puberty. This early onset is very rare and its etiology remains unknown. Severe disease can be seen in prepubertal children and surgical intervention is effective in these cases.

Hidradenitis suppurativa (HS) is a chronic scarring suppurative disease involving the apocrine gland-bearing regions of the body. Velpeau first described it as a distinct disease in 1839 (1). Early disease is characterized by tender nodules that usually progress to boils and abscesses. With recurrent disease, sinus tracts and fibrosing scars eventually develop. In protracted cases, squamous cell carcinoma has been reported (2). The disease occurs more frequently in females than in males with a ratio reported as high as 4:1 (3). Predisposing factors include obesity, a genetic tendency to follicular occlusion, hormonal factors, and possibly an end-organ hypersensitivity to androgens (4).

HS usually develops in the second or third decade of life after the onset of puberty (5). Our two patients are unique in that they developed HS prior to any clinical signs of puberty and also lacked any clinical or laboratory signs of androgen excess.

CASE REPORT

Patient 1

At age 8 years, patient 1 developed tender red nodules in the suprapubic and groin regions that progressed to boils and abscesses. By age 9, she had similar nodules in both axillae. According to the report of a pediatric endocrinologist, she had extensive disease at age 9 years 8 months while she was at Tanner stage I of sexual development. She had no axillary or pubic hair and no breast development.

On her first visit to our clinic (age 9 years 10 months) she had tender nodules accompanied by hemorrhagic ulcers, draining sinuses, fibrosis, and malodorous pustular drainage in both axillae (Fig. 1). In the anogenital region she had numerous deep-seated nodules and draining sinuses. Extensive comedonal changes were also noted. By this time, early signs of pubic hair were evident (Fig. 2). In the transverse abdominal crease there was a central area of ulceration with deep-seated nodules (Fig. 3). She also had a dark brown, velvety cutaneous thickening on the posterior neck, in the axillae, and on the medial aspects of the thighs consistent with acanthosis nigricans (Fig. 4). No evidence of androgen excess was noted on physical examination.

Her weight was 182 lb (+5 standard deviations above normal) and her height was 148 cm (+2 standard deviations above normal). Personal medical history was sig-
significant for recurrent urinary tract infections and family history was significant for non-insulin-dependent diabetes mellitus, hypothyroidism, and hypertension.

Abnormal laboratory values included the following: serum glucose of 141 mg/dl (normal 60–100), paired with a fasting insulin level of 128 μU/ml (normal 5–25), total protein of 8.4 g/dl (normal 5.5–8.0), triiodothyronine (T3) uptake of 20% (normal 22%–35%), and total cholesterol level of 193 mg/dl (normal <170). Normal laboratory findings included the following: dehydroepiandrosterone sulfate of 0.6 μg/ml (normal for prepubertal age group 0.1–0.6), total testosterone of 16 ng/dl (normal <62), free testosterone of 5 ng/dl (reference range not established), estradiol of <10 pg/dl (normal <20), total thyroxine (T4) of 11.4 μg/dl (normal 4.5–12.5), free thyroxine (T4) index of 2.3 μg/dl (normal 1.4–3.8), and glycosylated hemoglobin of 5.3% (normal <6.5%). In addition, a bone age determination was normal. Cultures taken from the axilla grew coagulase-negative Staphylococcus aureas, Streptococcus species, and diphtheroid species.

Conservative therapy initiated at 8 years of age had been unsuccessful and included oral erythromycin and tetracycline as well as topical antifungal and antibacterial (clindamycin) medications. At 9 years 2 months, oral isotretinoin was started at a dose of 1 mg/kg/day and was continued for 8 months. Her HS initially showed mild improvement but ultimately worsened due to the development of granulation tissue in the axillary and anogenital regions. By this time her disease was so severe that she was unable to walk or raise her arms and her clothes had to be changed several times a day because of extensive drainage. Ultimately she missed an entire academic year due to the severity of her disease. Her state continu-
ued to worsen despite oral prednisone and intramuscular triamcinolone injections. Isotretinoin was discontinued at 10 years of age because of the extensive development of painful granulation tissue and adverse effects including severe cheilitis, frequent epistaxis, and mild hypertriglyceridemia. Oral prednisone and oral dicloxacillin were started as the isotretinoin was discontinued. After 6 weeks the granulation tissue and drainage had somewhat regressed, but her overall condition had improved relatively little.

At 10 years 1 month, a series of surgical excisions and skin graft placements was started. She had radical excision of both axillae and groin regions. A surgical pathology analysis of tissue excised from the anogenital regions was consistent with HS. A split thickness skin graft measuring 15 cm × 13 cm obtained from the left thigh was placed in the right axilla. A second graft measuring 195 cm² was placed in the left axilla and was obtained from the left and right thigh. Three more skin grafts measuring 288 cm², 152 cm², and 37 cm² were placed in the left groin, right groin, and right thigh, respectively. Multiple debridements were performed to remove granulation tissue and two large open wounds in the medial thigh creases were left to heal by secondary intention.

The patient required a 6-week hospitalization for pain management and because a deep venous thrombosis developed in the right femoral vein. General anesthesia was required for daily dressing changes during the first 2 weeks of hospitalization. She also experienced a 15 lb weight loss.

Four months after surgery she was able to lift her arms above her shoulders and ambulate without assistance. Five months after surgery, a new nodule was noted at the gluteal cleft of the right buttock, but it had spontaneously resolved by the time of her next clinic visit. Nine months after surgery, the axillary grafts and medial thigh grafts were totally healed and the open wounds in the right and left inguinal creases were 50% and 90% healed, respectively (Figs. 5 and 6). By this time she was also able to walk and ride a bicycle. On her last visit (13 months after surgery) she continued to show improvement, as the left inguinal crease open wound had totally healed and the wound in the right inguinal crease was 70% healed. The patient is currently continuing whirlpool and physical therapy. Despite encouragement to lose weight, she has gained 30 lb since her surgery. More intense nutritional counseling is being sought at this time.

**Patient 2**

At 11 years 9 months, patient 2 developed a single tender nodule in the left inguinal groin crease. At age 12 years a diagnosis of HS was made because of the presence of deep-seated nodules with numerous single- and double-headed open comedones in the inguinal region. Mild atrophic scarring was present as well. No pubic or axillary hair was noted and there were no laboratory or physical signs of androgen excess.
Her past medical history was significant for Down syndrome, hypothyroidism, and seborrheic dermatitis. She had no prior history of obesity and her family history was significant for cystic acne in the mother.

Oral tetracycline was initiated at age 12 years and was effective but had to be discontinued because of severe gastrointestinal discomfort. Subsequently minocycline was started at 100 mg twice a day, with improvement noted. The patient has been on this regimen for the past 2.5 years and her disease has been well controlled. Predictably her HS flares when even two doses of medication are withheld. Within the past year, two episodes of mild yellow-colored drainage were noted in the groin area.

On her last visit (age 14 years 6 months), her HS had shown no progression since her initial diagnosis. By this time she was menstruating and had axillary and pubic hair.

DISCUSSION

Prepubertal HS is a very rare condition and very few cases have been reported. To our knowledge, only seven cases in addition to ours have been reported where disease was present in the absence of endocrine abnormalities or androgen excess in prepubertal children (6–8). HS has been reported in one 8-year-old girl with premature adrenarche (9). The disease has an unpredictable course and may be resistant to multiple treatment regimens (as in patient 1) or may be easily controlled with relatively little intervention (as in patient 2). Worsening of the disease has been reported at puberty (8).

As illustrated by patient 1, HS can occur in the prepubertal age group and can be very severe and debilitating. In such instances, surgical intervention may be the most effective form of therapy. Patient 1 has shown dramatic, steady improvement since her surgery after unsuccessful conservative therapy. However, this was a major surgical intervention with a prolonged recovery period.

The etiology of HS remains largely unknown and even less is known about prepubertal HS. Traditionally it has been viewed as an inflammatory disease of apocrine gland-bearing skin. However, recent studies suggest that follicular occlusion in apocrine gland-bearing skin may be the primary event, followed by secondary inflammation and suppuration of the apocrine glands (10,11). It is also viewed by some as an androgen-based end-organ disorder because of its usual postpubertal onset, female preponderance, and association with obesity. This aspect of the disease has been further highlighted by recent studies (12–14). Others have also proposed that HS may represent an abnormal end-organ response to normal circulating levels of androgens (15). It seems likely that the etiology of HS is multifactorial in nature and cannot be solely explained by any one of these factors.

HS is a challenging disease to manage because of its chronicity and potential for multiple complications. Early HS is often treated with antistaphylococcal antibiotics for axillary disease and broad-spectrum antibiotics for perineal disease. In addition, topical antiseptics with warm compresses are used to provide localized relief. Because the condition resembles nodulocystic acne, oral isotretinoin is commonly used but has been variably successful, especially in long-standing and severe disease. For severe HS, surgical intervention remains the most effective treatment option. Although recurrences may arise in adjacent skin, studies have shown that patient satisfaction is highest with this form of therapy (16).

Recent studies have shown etretinate and its derivative acitretin to be effective in treating severe HS (17–20). At least four of the patients reported had prior unsuccessful trials of isotretinoin, thus the aromatic retinoids (acitretin and etretinate) may be more effective treatment options in severe and long-standing HS than isotretinoin. Other studies have shown favorable responses with antiandrogens, gonadotropin-releasing hormone agonists, and oral contraceptives (14,21–23). These may represent other effective options in the treatment of HS and require further investigation.

Our experience with patient 1 made us question the efficacy of isotretinoin in severe HS because it was associated with worsening of the disorder. Cases have been reported where isotretinoin was effective in controlling long-standing HS (24). Cases have also been reported where isotretinoin was ineffective in controlling the disease (8,25,26). Shalita et al. (27) suggest that isotretinoin has a limited role in long-standing and severe HS but may be an effective treatment regimen in early disease as an adjunct to other standard medications.

Of interest was the concurrent finding of acanthosis nigricans and HS in patient 1. Could the acanthosis ni-
grians, which is characterized by hyperkeratosis in the intertriginous zones, have predisposed patient 1 to develop HS at such an early age? Two instances have been reported where HS developed in obese adult men with long-standing acanthosis nigricans (28). Five additional cases have also been reported where acanthosis nigricans and HS were found in adult women with hyperandrogenism (29). None were in the prepubertal age group. HS has been reported in other disorders of keratinization such as pityriasis rubra pilaris and Fox–Fordyce disease (29–32). However, we believe that the concurrent findings of acanthosis nigricans and HS in patient 1 were both due to her obesity and were coincidental.

In summary, prepubertal HS is a very rare condition. It appears to have the same clinical course as HS with onset at puberty or later. When the disease is severe, surgical intervention is effective and appears to be the best treatment option.

ACKNOWLEDGMENTS
We acknowledge the referral of patient 1 by M. Morales, M.D., and N. Superfon, D.O., and of patient 2 by W. Van Arsdel, M.D., and P. Mahalingam, M.D. This article was presented at the Society for Pediatric Dermatology annual meeting, Cambridge, Massachusetts, July 24, 1998.

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