Infantile anogenital digitate keratoses: A case series of a novel entity

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INTRODUCTION

Digitate keratoses (DK) are a heterogenous group of inherited or acquired disorders of keratinization.[1,2] These rare entities are characterized by digitate spiked keratotic papules that can be both follicular and non-follicular in origin.[1-3] DK have multiple clinical presentations, resulting in confusion and debate in the literature. Caccetta et al[3] suggested a classification and diagnosis algorithm dividing DK into localized and generalized forms.

The localized forms include[3]:

1. Palmoplantar DK (spiny keratoderma, arsenical keratoses, and multiple filiform verrucae).
2. Postirradiation DK.
3. Facial DK (digitate keratoses, trichodysplasia spinulosa, and hyperkeratotic spicules).

This classification does not include a distinct localized variant in the anogenital region of infants.

Infantile anogenital digitate keratoses (IADK) is a novel, separate subtype of localized DK. IADK is characterized by digitate, rigid, rough, and spiked keratotic projections with yellowish-white-pink color that appear in the anogenital area of infants. IADK is not commonly known to dermatologists and pediatricians, and may be incorrectly diagnosed.

Abbreviations used:

DK:	digitate keratoses
IADK:	infantile anogenital digitate keratoses
MMDH:	multiple minute digitate hyperkeratoses

MATERIALS AND METHODS

A multicenter case series that presents 7 cases of IADK, discussing the epidemiology, clinical symptoms, dermoscopic and histologic features, treatment strategy, and the course of this novel entity. The study was approved by the local institution review board.

The cases were collected from the following institutes:

1. Pediatric Dermatology Unit, Sheba Medical Center, Israel - 2 cases.
2. Pediatric Dermatology Service, Hadassah Medical Center, Israel - 2 cases.
3. Pediatric Dermatology Department, Heim Pál National Children's Institute, Hungary - 1 case.
4. Pediatric Dermatology Unit, Tel Aviv Sourasky Medical Center, Israel - 1 case.

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IRB approval status: The study was approved by the local institution review board.

Patient consent: All patients gave consent for their photographs and medical information to be published in print and online and with the understanding that this information may be publicly available.

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Table I. Patients characteristics and clinical manifestations

Patient number	Sex	Age at onset of rash (months)	Age at resolution (months)	Duration of skin lesions (months)	Location	Background
1	F	1	5	4	Genital and perianal areas	Erythematous
2	M	4	13	9	Perianal	Erythematous
3	M	1	5	4	Perianal	Erythematous
4	M	1	3	2	Perianal	Erythematous
5	M	0.5	4	3.5	Perianal	Erythematous
6	M	15	16	1	Perianal	Hyperpigmented
7	M	2.5	3.5	1	Perianal	Erythematous
8[4]	M	1	15	14	Genital and perianal areas	Erythematous

F, Female; *M*, male.

5. Dermatology Unit, Edith Wolfson Medical Center, Israel - 1 case.

CASE PRESENTATIONS

A summary of the 7 presented cases and 1 previously published case,[4] are shown in Table I.

Case 1

A 3-month-old healthy female infant with an unremarkable medical history presented 1 month after birth with perianal and genital mild erythema and small white rigid spiked keratotic papules. Initial treatment included topical therapy, specifically emollients, antibacterial, and antifungal treatments. The erythema improved, but the hyperkeratotic papules remained (Fig 1, *A*). Termination of treatment was recommended, and observation ensued. Spontaneous resolution occurred at 5 months of age (Fig 1, *B*).

Case 2

A 7-month-old healthy boy, following a normal pregnancy and delivery, presented to the dermatological clinic with perianal skin lesions. His past medical history included an infantile hemangioma of the lip treated with an oral beta-blocker (Atenolol). At 4 months of age, asymptomatic perianal lesions emerged composed of yellowish-white tiny rigid, rough, and spiked papules on a mildly erythematous background (Fig 2, *A*). Fungal culture was negative. He was treated with a topical corticosteroid and antifungal cream for 2 weeks in combination with a thick, zinc-based diaper ointment, without resolution. At 7 months of age, skin biopsy from a small follicular keratotic lesion was performed. The findings were nonspecific and demonstrated a polyp-like structure without parakeratosis (Fig 2, *B*). The skin lesions resolved without treatment at 9 months of age and did not recur.

Case 3

A 4-month-old healthy boy, following a normal pregnancy and delivery, presented 1 month after birth with asymptomatic perianal lesions. The skin lesions were composed of yellowish, follicular, spiked protruding firm papules on an erythematous background, undetachable upon rubbing (Fig 3, *A*). Dermoscopy revealed white-yellowish follicular keratotic papules (Fig 3, *B*).The skin lesions resolved after 1 month, at 5 months of age, without any treatment.

Case 4

A 5-month-old healthy boy, with an unremarkable medical history, presented with a perianal skin lesion composed of hyperkeratotic white, rigid, 1 to 2 mm spiked papules overlying a slightly erythematous base. (Fig 4, *A*). The eruption appeared 1 month after birth and was asymptomatic. The skin lesions did not require any treatment or intervention. The clinical manifestation disappeared completely after a couple of months and did not recur.

Case 5

A 2-week-old healthy male neonate, following a normal pregnancy and delivery, presented with perianal white 1 to 2 mm rough and rigid follicular papules overlying an erythematous base (Fig 4, *B*). He was treated with topical combination therapy including an antifungal, antibacterial, and medium potency steroid cream, and avoidance of baby wipes (wet cloth only). No improvement was seen. Treatment was discontinued, the skin lesions resolved gradually, was absent by 3 and a half months of age, and did not recur.

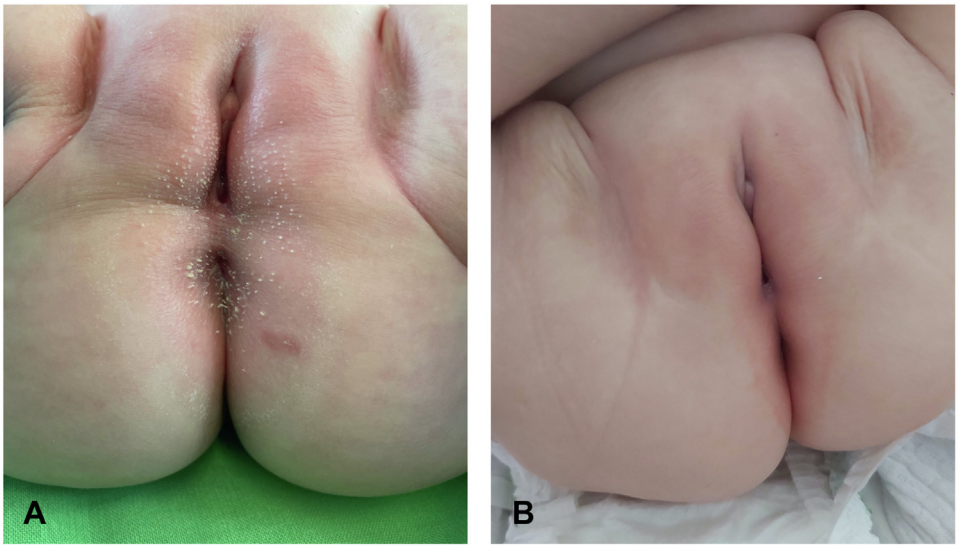

Fig 1. Infantile anogenital digitate keratoses (DK) in a 3-month-old girl. **A,** *Yellowish-white* spiked rigid keratotic papules on a mildly erythematous background. **B,** Spontaneous resolution occurred after 4 months.

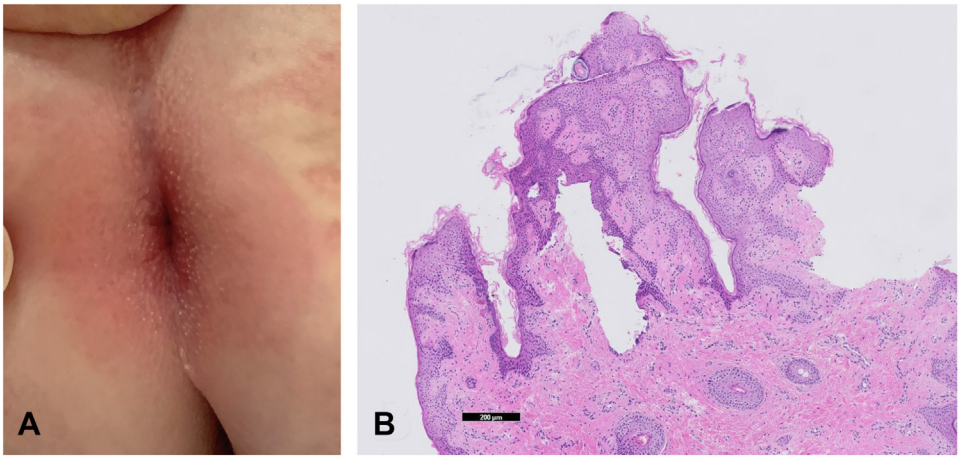

Fig 2. Infantile anogenital DK in a 7-month-old boy. **A,** *Yellowish-white* tiny rigid, rough, and spiked papules on a mildly erythematous background. **B,** Histology: X200 μm, H & E staining demonstrating polyp-like structure without parakeratosis.

Case 6

A 15-month-old healthy boy, following a normal pregnancy and delivery, suffered from constipation and was treated with stool softeners and oral antihelminthic treatment, as well as topical barrier diaper cream and petroleum jelly with improvement. It was also noticed that he had perianal white verrucous-like, rigid and spiked follicular keratotic papules, some more elongated and protruding, with a hyperpigmented base (Fig 4, *C*). The skin lesions and accompanying symptoms raised suspicion of the pediatrician for child abuse, namely Human papillomavirus or molluscum infection, which was revoked by the dermatologist. For 2 weeks, he was treated with a combination cream consisting of an antifungal, antibacterial, and medium potency steroid. Resolution of the skin lesions occurred at 16 months of age without recurrence.

Case 7

A 13-week-old healthy boy, following a normal pregnancy and delivery, presented with bilateral perianal diffuse 1 mm yellow, follicular rigid papules on an erythematous background, which appeared at the age of 10 weeks (Fig 4, *D*). Family history was significant for seborrheic dermatitis (father) and

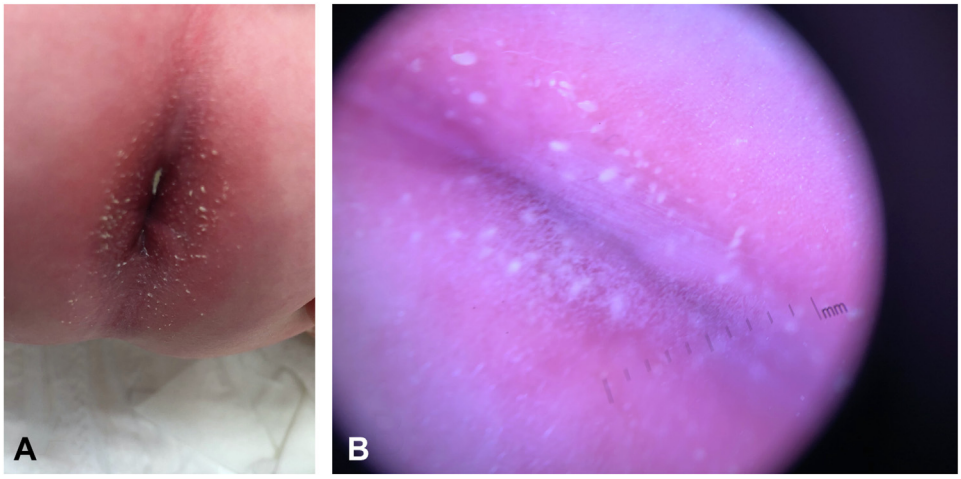

Fig 3. Infantile anogenital DK in a 4-month-old boy. **A,** *Yellowish* follicular spiked protruding firm papules overlying an erythematous background. **B,** Dermoscopy showing *yellowish-white* follicular keratotic papules.

rosacea (mother). The patient was treated with hydrocortisone 1% and clotrimazole cream with a fast resolution of the skin lesions within 1 week, without recurrence.

DISCUSSION

IADK is an idiopathic, benign entity that probably affects male infants more commonly than female infants (7:1 in this case series). It usually appears in the first months of life (average age of onset is 3.2 months), although a later onset at 15 months was also documented. IADK is an asymptomatic self-remitting condition. The infants appear well without any discomfort. This condition was previously described only once in the literature in 2016, in a case report by Santiago et al.[4] In our case series and the case report previously cited, there was no history of diarrhea, diaper rash, usage of irritative creams, or any dermatosis in the affected area. All cases occurred in healthy and well-developing infants, without similar family history. All patients presented due to parental concern.

IADK is characterized by approximately 1 to 2 mm follicular, spiked, rigid, not detachable yellowish-white or pink keratotic lesions, which appear in the perianal area of infants. The genital region can also be involved, especially in female infants, but no other skin regions are affected.

An erythematous background appeared in all but one patient, in different severities. The exception was in 1 infant who had a hyperpigmented background (case 6), and thus an erythematous background could not be discerned. The erythema improved and in some patients even resolved after treatment with a weak topical corticosteroid therapy, suggesting local irritation. Notably, the follicular DK remained constant and did not respond to any topical treatment in almost all cases. Only in 1 infant (case 7) a fast resolution was noticed 1 week after the usage of topical therapy. The duration of IADK until complete clearness varied from 1 to 14 months (average duration was 4.8 months). All patients experienced complete resolution without recurrence; the average age at resolution was 8 months, with 16 months being the oldest age recorded until complete resolution occurred. Dermoscopy revealed yellowish-white follicular keratotic papules, demonstrating that this tool can aid in making the diagnosis of IADK. The histological features were non-specific.

The previous known case reported by Santiago et al[4] described a healthy 4-month-old boy with multiple small, rough, spiny, non-follicular, yellowish white (1-3 mm) papules in the anogenital area. Histologic examination revealed marked hyperkeratosis with parakeratosis and associated epidermal invagination. The infant was diagnosed with a subtype of multiple minute digitate hyperkeratoses (MMDH) in the anogenital region. A wait-and-see strategy was utilized with complete resolution.[4]

MMDH was first described by Norman Goldstein in 1967.[5] It is a rare disorder of keratinization with an unknown origin.[3,6,7] Lately, it was suggested to be a generalized non-follicular variant of digitate keratoses.[3,7] MMDH appears between the ages of 15 and 81 years,[3] and its typical lesions are similar in appearance to IADK,[3,6,7] however, in the former, numerous keratoses are noted with a propensity for the trunk and extremities, while the anogenital area is typically spared.[3,6-8] Histologic features of MMDH include focal columns of hyperorthokeratosis with a

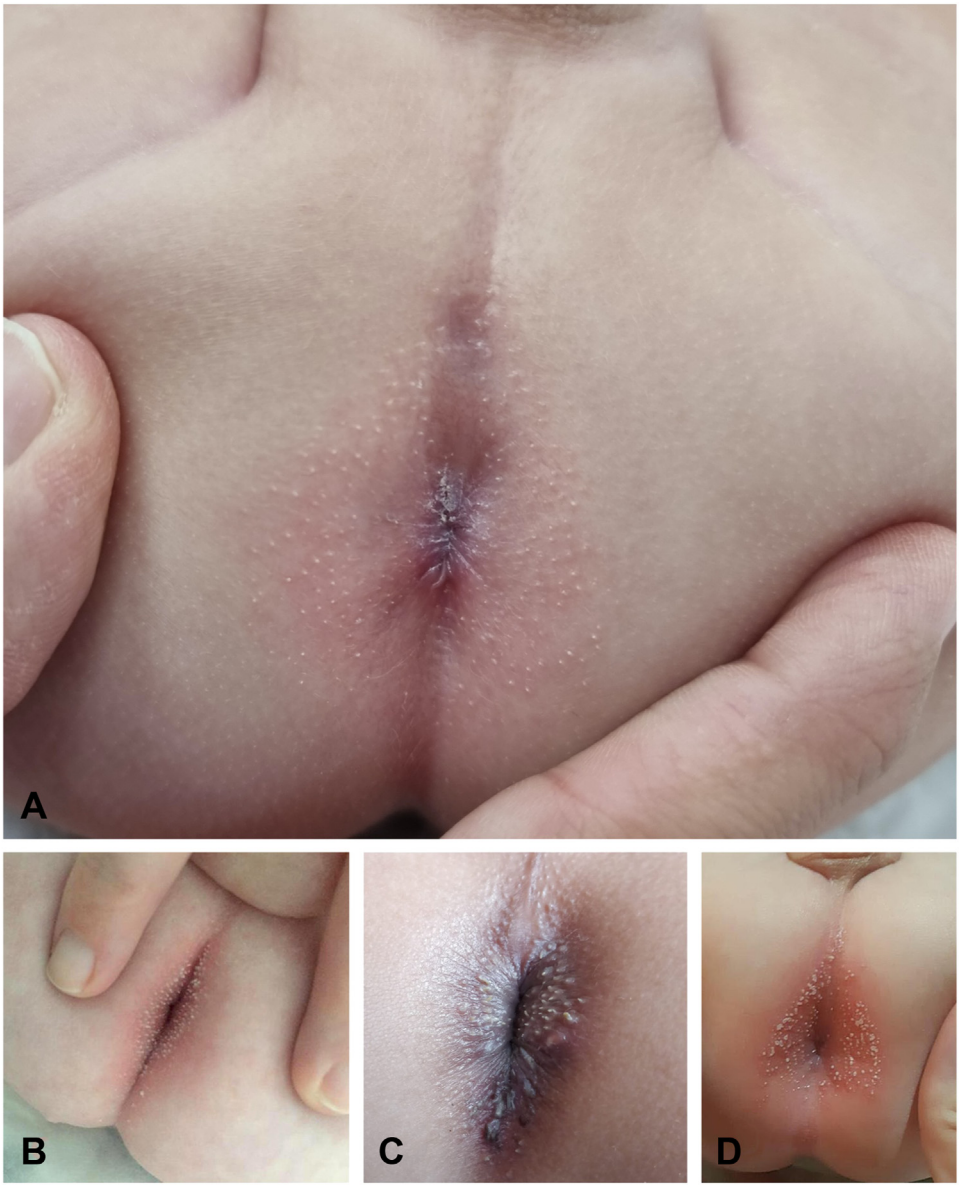

Fig 4. Infantile anogenital DK in 4 infants. **A,** Hyperkeratotic *white* rigid tiny spiked papules on a slightly erythematous base. **B,** White rough and rigid tiny follicular papules overlying an erythematous base. **C,** Verrucous-like, rigid and spiked *white* keratotic papules on a hyperpigmented base. **D,** *Yellow* follicular rigid papules overlying an erythematous background.

compact stratum corneum arising from tented epidermis. Parakeratotic cells are typically not seen. The stratum granulosum is preserved and usually prominent.[6,7] Treatment of MMDH is challenging, as MMDH does not respond to therapy in most cases and spontaneous regression is considered exceptional.[3,6,8]

Santiago et al[4] considered their case of DK in the perianal region of an infant as a subtype of MMDH. However, due to the different histology, the follicular vs non-follicular tendency, distribution, age of onset, and transient character, we argue that IADK is not a subtype of MMDH, but rather a different subtype of DK. We suggest adding this entity to the classification of localized DK.

The pathogenesis of both entities is unknown. Additional analyses such as immunohistochemical keratin staining and molecular genetic studies are warranted to determine the pathogenesis, and the relation of different entities within the classification of DK.

IADK is a rare follicular, self-regressing, easily diagnosed clinical condition, but the lack of knowledge of this entity leads to misdiagnosis,

maltreatment, and in some cases even unnecessary procedures such as skin biopsy. The differential diagnosis includes infections (staphylococcal folliculitis, candidiasis, and less likely human papillomavirus condylomas or molluscum), irritant contact dermatitis, and epidermal nevus.[9-14] A papular anogenital eruption "papular acantholytic dyskeratosis" was described in adults, including a vulvar subtype in girls, but these cases had different presentation and age range.[15] Pseudoverrucous papules are considered to be a result of encopresis or urinary incontinence and are also a part of the differential diagnosis of IADK. However, the appearance is quite different as the pseudoverrucous lesions may be papules or nodules and their typical size of 2 to 8 mm differ from IADK. In addition, pseudoverrucous papules are not similar to the keratotic lesions but the lesions are rounded, smooth, and flat topped. The color is also different and is described to be red and not yellowish-white-pink, such as IADK.[16] Finally, suspicion of sexual abuse can also arise and might lead to devastating consequences and parental distress.[10,15]

IADK is expected to regress spontaneously within several months. It does not require any treatment or intervention, other than daily routine care and application of barrier creams. In cases of irritation and an erythematous background, the application of soothing creams or weak topical corticosteroids may be helpful. We believe that if an infant presents with a typical case of IADK, a skin biopsy is unnecessary and can be problematic in the delicate genital area with concerns of pain, secondary infection, and scarring. We recommend follow-up until resolution, combined with parental reassurance as an appropriate treatment strategy.

This studies main limitation is its small sample size. Larger prospective studies are necessary to further characterize the exact epidemiology and course of the disease. Additional studies with immunohistochemical keratin staining and molecular genetic studies may also shed light on the pathogenesis of this disorder.

CONCLUSION

IADK is an idiopathic, benign, self-regressing novel condition. Increasing awareness of this entity is important to avoid unnecessary investigations and treatments. We recommend parental reassurance and follow-up as appropriate management.

Conflicts of interest

None disclosed.

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