A rare presentation of multiple eruptive vellus hair cysts and dystrophic nails in a pediatric patient with Stüve-Wiedemann syndrome

Nouf Almuhanna, MD,[a] Lulwa Alogayell, MD,[a] Sarah Alkhezzi, MD,[a] Salman Al-Malki, MD,[b] Rasha Alhamazani, MD,[a] Fatimah Altassan, MD,[a] Alanoud Alsuhibani, MD,[a] Yazeed Alowairdhi, MD,[a] Khalid Alekrish, MD,[a] and Faris A. Alhomida, MD[a]

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INTRODUCTION

Stüve-Wiedemann syndrome (SWS) is a rare and severe autosomal recessive disorder caused by genetic mutations in the leukemia inhibitory factor receptor gene (LIFR). It is typically characterized by congenital skeletal dysplasia and has been associated with short stature, dysautonomia (including hyperthermia), ocular and neurologic abnormalities, facial dysmorphism, global developmental delay, respiratory distress, and feeding difficulties, which may lead to an increased risk of failure to thrive.[1,2] These constellations of findings may result in a high-mortality rate in the infantile period.[1] The cutaneous manifestations of SWS are rarely reported.[2,3] We hereby present the rare occurrence of multiple eruptive vellus hair cysts (EVHCs) in association with SWS in a pediatric patient.

SWS has been reported worldwide, namely in North and South America, Europe, Africa, and the Middle East. The exact prevalence of SWS, however, remains unknown, but the majority of cases reported are from Europe, followed by the Middle East.[1,4] It is estimated that the prevalence in the United Arab Emirates is 0.52 of 10,000 births; likely secondary to the increased frequency of consanguinity in the population.[4]

Abbreviations used:

EVHC:	Eruptive vellus hair cyst
LIFR:	Leukemia inhibitory factor receptor gene
SWS:	Stüve-Wiedemann syndrome

CASE PRESENTATION

A 5-year-old girl was referred to our tertiary center dermatology clinic for a sudden generalized eruption of multiple skin-colored papules throughout her skin. Her mother reported that it initially began few months after birth before rapidly progressing in number and frequency around the age of 2 years. The mother denied any pruritus, erythema, edema, bleeding, ulceration, or discharge of the lesions. She also denied any changes in color or size of the lesions. Family history was notable for consanguinity and maternal type 2 diabetes mellitus. The patient did not take any medications and had no known drug or food allergies.

The patient has a complicated medical history with a peripartum history notable for cesarean section at full-term, secondary to breech presentation and macrosomia, with a 2-month stay in the neonatal intensive care unit for hypoglycemia. She also had a history of short stature, bilateral clenched fists, gross motor delay with an unsteady gait, dysautonomic hyperthermia, and bilateral corneal opacities. Her history was further notable for radiologically confirmed, skeletal dysplasia with scoliosis, camptomelia (bent limbs), rhizomelia (shortened limbs) of all 4 limbs, and flexion contracture of the fingers with ulnar deviation and brachydactyly (shortened

From the Department of Dermatology, King Fahad Medical City, Riyadh, Saudi Arabia[a]; and Department of Pathology, King Fahad Medical City, Riyadh, Saudi Arabia.[b]

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Correspondence to: Faris A. Alhomida, MD, Department of Dermatology, King Fahad Medical City, Prince Abdulaziz Ibn Musaid Ibn Jalawi St, Riyadh 12231, Saudi Arabia. E-mail: farisalhomida@gmail.com.

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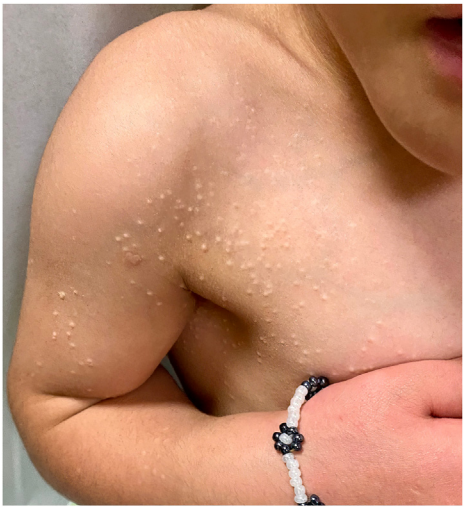

Fig 1. Scattered, multiple skin-colored to whitish papules on the right shoulder, upper portion of the right arm, right forearm, and chest. Hyperpigmented atrophic plaque on the right shoulder from the biopsy site.

Fig 2. Dystrophic nails, with onycholysis, brachyonychia, and ragged cuticles.

digits). Additionally, the patient also had history of failure to thrive secondary to dysphagia with aspirations, requiring gastrostomy tube feeds.

Given the myriad of findings, genetic testing was done by the pediatric team that confirmed a homozygous pathologic frameshift mutation of the LIFR gene on chromosome 5p13.1. Parental segregation analysis was positive for heterozygous LIFR gene mutation in both parents.

At presentation in our dermatology clinic, she stood at 0.85 m (<3rd percentile) with a weight 16.1 kg (<3rd percentile) and a body mass index of 22.3 kg/m^2 (>97th percentile) and was vitally stable.[5] A full body skin examination was conducted that revealed, multiple, scattered, <10 mm, skin-colored to whitish papules throughout the face, back, chest, abdomen, bilateral axilla, and bilateral upper and lower extremities. (Fig 1) Approximately, >100 lesions were identified. Some of which were also hyperpigmented. Furthermore, scattered, pin-point, yellow papules consistent with milia were noted throughout. Examination was also notable for dystrophic nails with ragged cuticles and features of onycholysis and brachyonychia (Fig 2) and camptomelia (bent limbs) and rhizomelia (shortened limbs) of the lower extremities (Fig 3).

Fig 3. Camptomelia (bent limb) and rhizomelia (shortened limb) of the right lower extremity.

A punch biopsy of one of the lesions of the right shoulder demonstrated, a middermal cyst lined with a stratified squamous epithelium and within the cystic lumen were multiple vellus hair shafts and laminated keratinaceous material (Fig 4). Thus, confirming the diagnosis of an EVHC. Reassurance and education of possible treatment options and clinical course was given to the parents. They elected for conservative management with observation.

She was given follow up for regular once-yearly skin checks and to return sooner if warranted. She continues to follow up with general pediatrics, pediatric neurology, ophthalmology, neurology, endocrinology, orthopedics, general surgery, and the nutrition team.

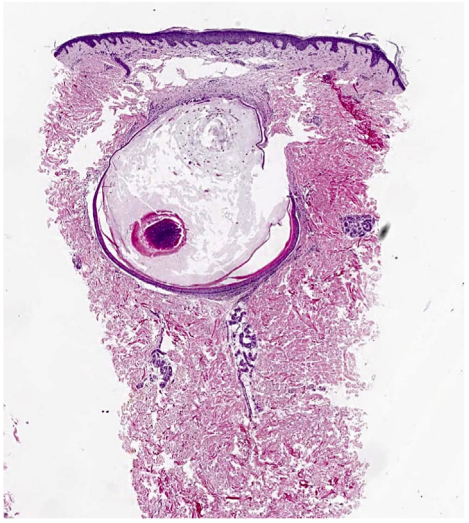

Fig 4. Histopathologic result of the biopsy of a vellus hair cyst in a child with SWS. A middermal cyst lined with a stratified squamous epithelium and within the cystic lumen are multiple vellus hair shafts and laminated keratinaceous material. (hematoxylin-eosin stain; original magnification: ×40.)

DISCUSSION

SWS is a rare entity with characteristic features that were initially thought to be lethal with a previously reported mortality rate of 42% in infancy. The mortality rate has been reported to decrease after the age of 2 years.[1] To our knowledge, reports of the cutaneous manifestation of SWS are scant.[2,3] Previous reports have suggested that SWS may present with sparse hair, thin, wrinkled skin, and milia.[2] Our case corroborates findings previously reported by Lobato-Berezo et al[3] that described multiple EVHC in a pediatric patient with SWS.[3] Furthermore, to our knowledge, there are no cases of multiple EVHC with dystrophic nails in association with SWS reported in the literature to date. This may suggest a novel finding of EVHC and dystrophic nails in association with SWS but data are limited and more research is needed to confirm this association

EVHC is thought to occur because of a follicular developmental anomaly, leading to follicular occlusion of vellus hairs. The exact etiology, however, is unknown.[6] EVHC has been reported to be associated with other syndromes, namely, pachyonychia congenita, anhidrotic ectodermal dysplasia, Lowe syndrome, and cardiofaciocutaneous syndrome.[3] Although benign, this entity is considered difficult to treat given the large number of lesions that tend to be present. Currently, there is no agreed consensus on the standard treatment for EVHC. Reports have suggested some improvement however, with dermabrasions, ablative lasers, and topical retinoids.[6]

To conclude, consider genetic testing, a multidisciplinary approach, patient education and regular skin checks in a patient who presents with a collection of findings in association with an eruption of multiple vellus hair cysts.

Conflicts of interest

None disclosed.

REFERENCES

1. Warnier H, Barrea C, Bethlen S, Schrouff I, Harvengt J. Clinical overview and outcome of the Stuve-Wiedemann syndrome: a systematic review. *Orphanet J Rare Dis*. 2022;17(1):174. https://doi.org/10.1186/s13023-022-02323-8
2. Yeşil G, Lebre AS, Santos SD, et al. Stuve-Wiedemann syndrome: is it underrecognized? *Am J Med Genet A*. 2014;164A(9):2200-2205. https://doi.org/10.1002/ajmg.a.36626
3. Lobato-Berezo A, Tormo-Mainar S, Pujol RM. Stüve-Wiedemann syndrome with multiple eruptive vellus hair cysts and clefted tongue. *Pediatr Dermatol*. 2020;37(2):381-382. https://doi.org/10.1111/pde.14088
4. Romeo Bertola D, Honjo RS, Baratela WA. Stüve-Wiedemann syndrome: update on clinical and genetic aspects. *Mol Syndromol*. 2016;7(1):12-18. https://doi.org/10.1159/000444729
5. Centers for Disease Control and Prevention, National Center for Health Statistics. Accessed March 18, 2023. https://www.cdc.gov/nchs/data/series/sr_11/sr11_246.pdf
6. Anand P, Sarin N, Misri R, Khurana VK. Eruptive vellus hair cyst: an uncommon and underdiagnosed entity. *Int J Trichology*. 2018;10(1):31-33. https://doi.org/10.4103/ijt.ijt_61_17