A Collection of Conditions With Dermatologic Manifestations

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Keratosis Follicularis

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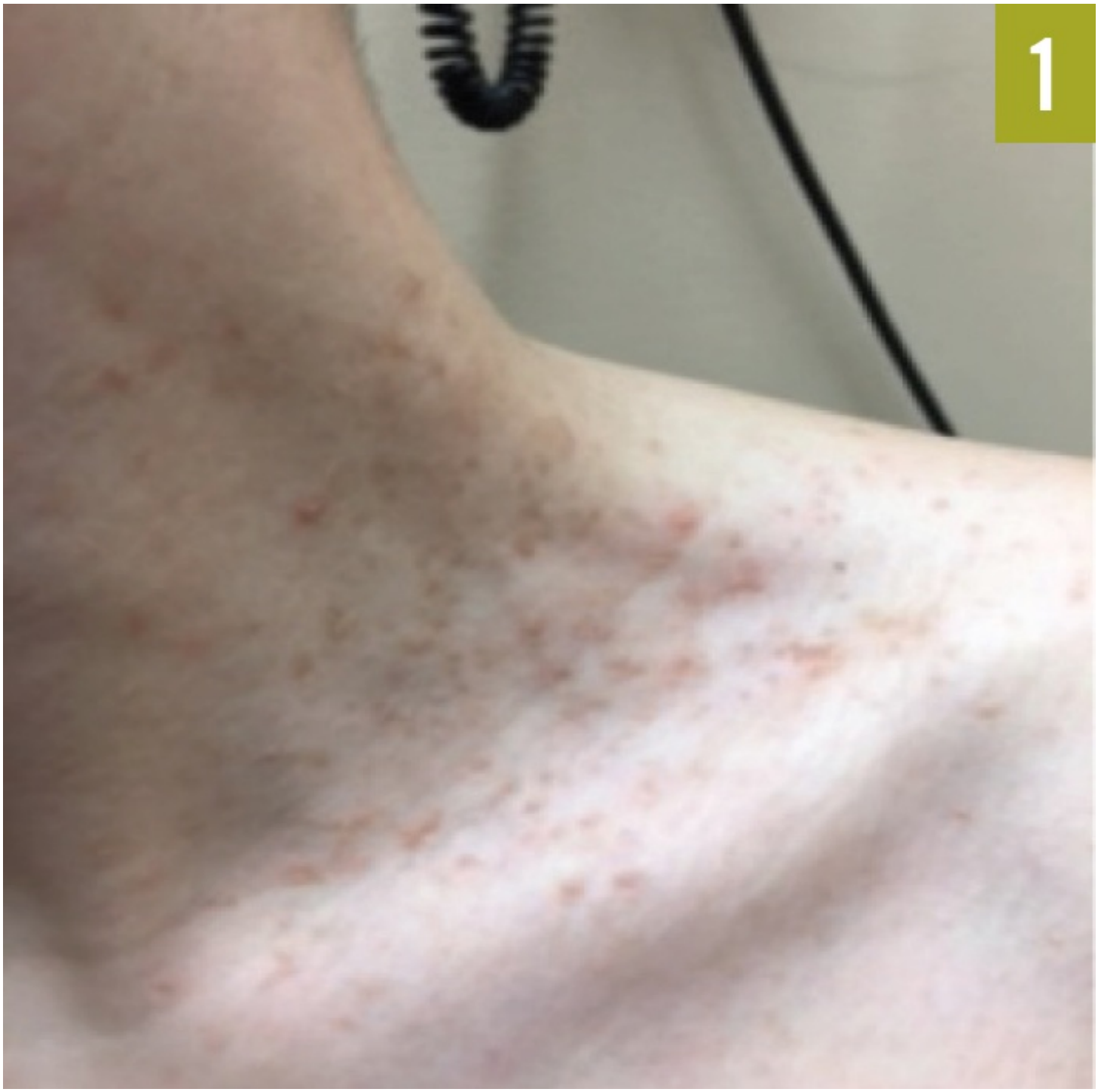
A 14-year-old boy presented with a chronic rash located on his neck and upper back areas. The rash was causing the patient persistent and mild pruritus without exudates.

History. The patient had a past psychiatric history of unspecified psychosis with prodromal symptoms, which are prominent in patients who receive a schizophrenia diagnosis later in life. During the initial evaluation, the patient also reported having commanding auditory hallucinations and delusions. The delusions were numerous but mainly were of the paranoid and grandiose type. Furthermore, the boy's grandmother disclosed a positive family history of mental illness in both of the patient's parents; because of the debilitating nature of the parents' mental disorder, the patient had been raised by his grandmother.

Physical examination. Vital signs were as follows: body mass index, 25.4 kg/m^2; pulse, 63 beats/min and regular; respiration rate, 16 breaths/min; temperature, 37°C; and blood pressure, 110/65 mm Hg. His neck was supple, with a normal thyroid and no jugular distention. The lungs were clear to auscultation. Cardiac and abdominal examination findings were normal.

Dermatologic examination revealed a rash of yellow-brown papules with a warty and greasy texture on the neck and upper back (**Figures 1 and 2**). The lesions had mild to moderate pruritus and were negative for erythema and exudates. No blisters were noted, and the lesions were nontender.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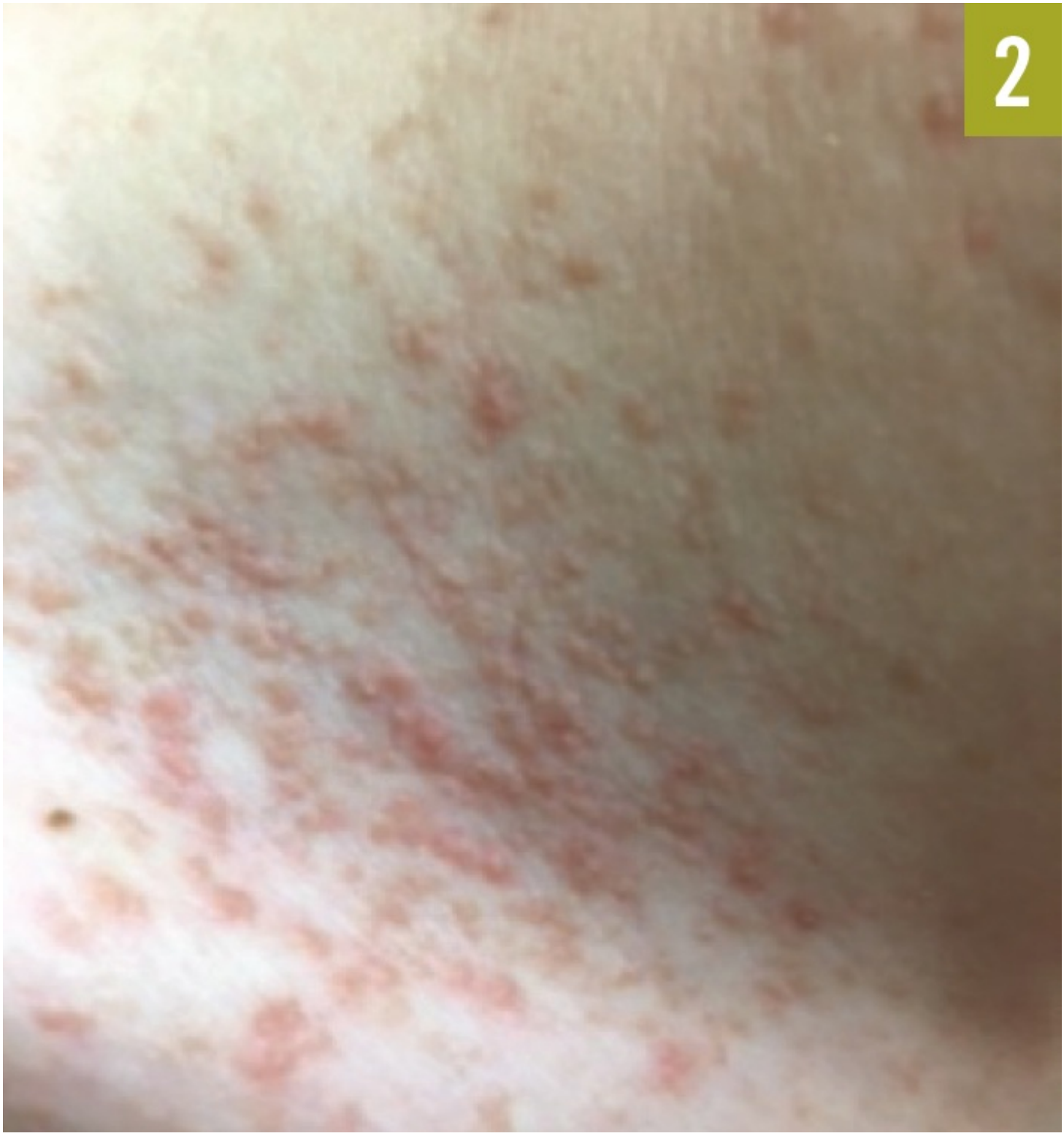
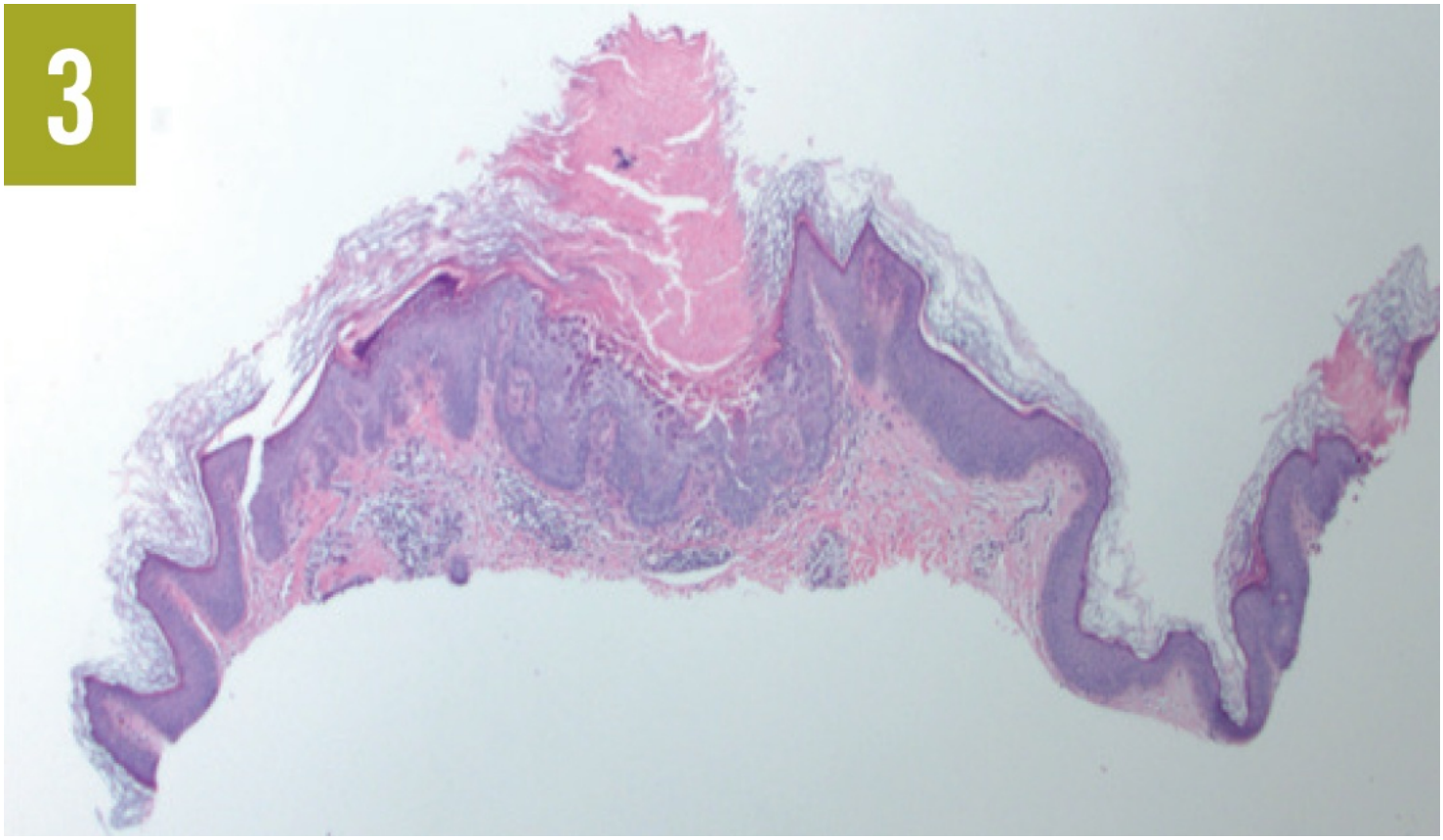


On mental examination, the patient was cooperative but with suspicious behavior. He was poorly groomed and had fair hygiene, with a dysthymic mood and a constricted affect. His thought process was tangential, and flights of ideas were present, as well. He revealed paranoid and grandiose delusions as part of the thought content, along with perception disturbances noteworthy for auditory hallucinations of the commanding type, of which patient stated, “They tell me to harm others.” He denied any suicidal or homicidal ideation. Cognition was intact, alert, and oriented to person, place, and time.

Diagnostic tests. Laboratory tests disclosed the following: white blood cell count, 5200/μL; hemoglobin, 12.6 g/dL; hematocrit, 37.4%; aspartate aminotransferase, 16 U/L; alanine aminotransferase, 12 U/L; urea nitrogen, 11 mg/dL;

creatinine, 0.56 mg/dL; glucose, 84 mg/dL; total cholesterol, 139 mg/dL; low-density lipoprotein cholesterol, 80 mg/dL; high-density lipoprotein cholesterol, 43 mg/dL; triglycerides, 79 mg/dL; platelet count, 225 × 10^3/μL; and total bilirubin, 0.6 mg/dL.

Skin histopathology results showed the epidermis to contain a focus of acantholysis and dyskeratosis. There was a mixed inflammatory infiltrate in the dermis beneath (**Figure 3**). Periodic acid–Schiff stain results were negative for pathogenic fungi.



Discussion. This patient's rash is most consistent with keratosis follicularis (also known as Darier disease or Darier-White disease). Patients with keratosis follicularis typically have a family history of this autosomal dominant inherited condition. However, a number of cases have been reported with no clear family history of keratosis follicularis.[1] Such cases are likely due to sporadic mutations or from a family member with an unrecognized mild case of keratosis follicularis.

Patients with keratosis follicularis exhibit greasy, hyperkeratotic papules with histopathologic evidence of acantholysis and dyskeratosis in seborrheic regions, and nail and mucous membrane changes.[1] The lesions are located primarily in seborrheic areas such as the forehead, scalp, hairline, nasolabial folds, ears, chest, and back.[2] Approximately 80% of patients have mild involvement of the flexure surfaces, including the groin, axillae, or breast creases in women. Approximately 95% of patients have skin changes on the palms.[3]

Keratosis follicularis is estimated to affect approximately 1 to 4 people per 100,000 worldwide, typically between the ages of 6 and 20 years, and is evenly distributed between the sexes. It is a chronic condition with exacerbations that fluctuate with triggers over time. It is caused by mutations of *ATP2A2*.[4] This gene is responsible for encoding the sarcoplasmic/endoplasmic reticulum Ca^{2+}-ATPase isoform 2 protein known as SERCA2, which transfers calcium from the cell into the lumen of the endoplasmic reticulum. It is not known exactly how the molecular mechanisms of *ATP2A2* mutations alter the function of SERCA2.[4] However, the mutations cause acantholysis and dyskeratosis of the skin via defects in protein expression, ATP hydrolysis, calcium transport, calcium binding and kinetics, and

abnormal cytokeratin expression.[4] Mutations in *ATP2A2*, in addition to causing keratosis follicularis, have been associated with neuropsychiatric conditions including epilepsy, schizophrenia, mood disorders, and learning disabilities.[2,3,5]

The appearance and odor of the lesions can contribute to major morbidity through psychosocial consequences.[5]

Differential diagnoses include seborrheic dermatitis, acrokeratosis verruciformis, benign familiar pemphigus (Hailey-Hailey disease), and transient acantholytic dermatosis (Grover disease). Histopathologic findings of acantholysis and dyskeratosis are the main features of keratosis follicularis. It most often includes a large keratin plug that usually shows focal parakeratosis overlying each lesion. Histopathologic testing can confirm the diagnosis, supported by gene sequencing to observe the mutation in *ATP2A2* on chromosome 12.[6]

No specific treatment or cure exists for keratosis follicularis, and treatment is aimed at its symptoms. It is important to take measures to prevent flares, such as keeping the skin moisturized with keratolytics, using antiseptics to prevent infections, and minimizing perspiration. Other treatments include topical corticosteroids and topical and oral retinoids.

Surgical techniques such as dermabrasion, laser ablation, surgical excision, and photodynamic therapy have also been used, but recurrence is common.[7]

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