A 15-year-old boy presented with asymptomatic, erythematous papules and plaques with an annular pattern on the legs. The lesions have been present for 6 months and have slowly increased in size. He was in good health and was not taking any medication. There was no family history of similar skin lesions.

Physical examination revealed multiple erythematous, firm, nonscaly papules and annular plaques localized to the extensor surfaces of both legs. Some of the lesions had an annular configuration with a clearer center and slightly elevated and indurated borders composed of small papules. The rest of the physical examination findings were normal.

What’s your diagnosis?
Granuloma annulare is a benign and usually self-limited granulomatous disease of the dermis and subcutaneous tissue. Clinically, the condition is characterized by asymptomatic, firm, flesh-colored or erythematous to brown papules, which classically are arranged in an annular, circinate configuration and which usually involve the extensor surfaces of the distal extremities.

**PREVALENCE**
Although the point prevalence of granuloma annulare in the community is not known, it is estimated that 0.1% to 0.4% of new patients attending dermatologic clinics have granuloma annulare. There is no known predilection for race or ethnicity. Most cases of granuloma annulare occur before the age of 30 years; the condition is especially common in school-aged children. The female to male ratio is approximately 2 to 1.

**ETIOLOGY**
In the majority of cases, the etiology is idiopathic. Occasionally, granuloma annulare has been reported to follow trauma, insect bites, tuberculin skin tests, viral infections (e.g., herpes zoster, Epstein-Barr, hepatitis B, hepatitis C, HIV), vaccinations (e.g., hepatitis B, diphtheria-tetanus, bacillus Calmette-Guérin), medications (e.g., allopurinol, diclofenac, thalidomide, interferon, calcium-channel blockers, ant depressants), diabetes mellitus, autoimmune thyroiditis, rheumatoid arthritis, and malignancy. Familial cases of granuloma annulare, although uncommon, also have been reported. Certain human leukocyte antigen alleles (e.g., HLA-A29, HLA-A31, HLA-B8, HLA-B14, HLA-B15, HLA-B35) occur with increasing frequency in patients with granuloma annulare.

**PATHOGENESIS**
The presence of helper T cells with histiocytes in the inflammatory infiltrate in granuloma annulare suggests that a delayed hypersensitivity and cell-mediated immune response to an antigen contribute to the pathogenesis.

**HISTOPATHOLOGY**
Histologic examination of a classic lesion shows central degeneration of collagen fibers and mucin deposits surrounded peripherally by palisading histiocytes and inflammatory cells. The presence of mucin is a key histologic feature that helps to distinguish granuloma annulare from other noninfectious granulomatous diseases.

**CLINICAL MANIFESTATIONS**
Several distinct subtypes have been recognized, namely localized granuloma annulare, generalized or disseminated granuloma annulare, subcutaneous granuloma annulare, papular granuloma annulare, interstitial or patch granuloma annulare, and perforating granuloma annulare; some of the subtypes have overlapping clinical features.

Localized granuloma annulare is the most common form in children, comprising 75% of cases. The lesion starts as a ring of small, smooth, firm, asymptomatic, erythematous, violaceous, brown or flesh-colored papules. As the condition progresses, some central involution occurs. The ring of papules often becomes coalescent to form an annular plaque. The lesion gradually enlarges to usually less than 5 cm in diameter. Typically, lesions are solitary or few in number. Sites of predilection include the dorsal surfaces of the hands and feet.

Generalized granuloma annulare occurs in approximately 15% of patients with granuloma annulare. The condition manifests as numerous (at least 10) small, asymptomatic, erythematous, violaceous, brown or skin-colored papules. Lesions are symmetrically distributed on the trunk, extremities, and neck. Generalized granuloma annulare has a bimodal peak age of presentation, in the first decade of life and again between the fourth and sixth decades of life. It is more commonly associated with diabetes mellitus.

Subcutaneous granuloma annulare is diagnosed primarily in children and young adults. The lesion usually presents as solitary or multiple painless, flesh-colored, subcutaneous nodule(s) with no inflammatory appearance at the skin surface. Sites of predilection include the preauricular areas, feet, forearms, hands, fingers, scalp, and forehead.

Papular granuloma annulare presents as asymptomatic, skin-colored or hypopigmented papules. The papules usually measure 1 to 3 mm in diameter, and the consistency is firm. Papular granuloma annulare most commonly affects children,
predominately on the dorsa of the hands.\textsuperscript{11}

Interstitial granuloma annulare manifests as asymptomatic, erythematous or violaceous patches without scales or papules that may or may not have an annular configuration.\textsuperscript{8} Sites of predilection include the trunk and extremities.\textsuperscript{8}

Perforating granuloma annulare is rare. It presents with papules that are 1 to 5 mm in diameter and occurs more often on the dorsa of the hands and feet.\textsuperscript{9,9} Characteristically, these papules have a yellowish central umbilication or crusts and are well-demarcated.\textsuperscript{8} Perforation occurs in the central portion of the lesion through which mucoid material consisting of degenerated collagen fibers is eliminated.\textsuperscript{6,9} Itching occurs in up to 25\% of cases, especially when there are lesions on palms.\textsuperscript{9}

**LABORATORY INVESTIGATIONS**

Children with granuloma annulare generally are healthy, and laboratory investigations usually are not necessary.\textsuperscript{1} Nevertheless, a recent case-control study shows that adult patients with granuloma annulare are more likely to develop dyslipidemia.\textsuperscript{12} It has been suggested that it is reasonable to test for fasting serum lipid levels in adult patients with granuloma annulare, especially if other risk factors for dyslipidemia are present.\textsuperscript{6} Patients with generalized granuloma annulare should be checked for the presence of diabetes mellitus. As well, there are some reports of autoimmune thyroiditis associated with granuloma annulare. As such, serum thyroid-stimulating hormone, antithyroglobulin antibody, and antithyroid peroxidase antibody should be ordered if autoimmune thyroiditis is suspected.

**DIAGNOSIS**

The diagnosis is mainly clinical and can be aided by dermoscopy, which typically shows peripheral, structureless, orange-reddish borders.\textsuperscript{13} Skin biopsy is warranted for atypical cases or when the diagnosis is unclear, particularly to rule out other granulomatous conditions such as sarcoidosis.

**COMPLICATIONS**

In the adult population, granuloma annulare is associated with diabetes mellitus, dyslipidemia, and, possibly, autoimmune thyroiditis.\textsuperscript{9,12} Rarely, granuloma annulare may be complicated by nerve involvement as a result of granulomatous inflammation surrounding cutaneous nerves and perineural infiltrates of histiocytes in the dermis.\textsuperscript{2} In the pediatric population, an association between granuloma annulare and uveitis has been reported.\textsuperscript{4}

**PROGNOSIS**

Localized granuloma annulare usually resolves without scarring within 1 to 2 years.\textsuperscript{2,7} Other forms may persist for a few years or more.\textsuperscript{3} A shorter duration is associated with younger age and recent onset.\textsuperscript{10} The recurrence rate is approximately 40\%.\textsuperscript{7}

**MANAGEMENT**

Most cases of granuloma annulare are asymptomatic and self-limited. As such, treatment usually is not required other than reassurance.\textsuperscript{7} For patients who insist on treatment for cosmetic or symptomatic reasons, options include potent topical or intralesional corticosteroids, cryotherapy, and pulsed dye laser therapy.\textsuperscript{2,7} Less commonly, topical imiquimod cream or topical calcineurin inhibitors (tacrolimus, pimecrolimus) are employed. Surgical removal is an option for the nodular lesion seen in subcutaneous granuloma annulare.\textsuperscript{2} Systemic therapy may be required for generalized granuloma annulare, which often is resistant to treatment.\textsuperscript{7} Interventions that have been used with varying degrees of success include phototherapy, oral corticosteroids, fumaric acid esters, dapsone, isotretinoin, hydroxychloroquine, methotrexate, cyclosporine, niacinamide, calcitriol, and tumor necrosis factor-α inhibitors (adalimumab, infliximab).\textsuperscript{3,6}

This patient was treated by his dermatologist with potent topical corticosteroids applied nightly, as well as narrowband UVB phototherapy 3 times per week for just over 2 months, which resulted in complete clearance of the lesions and mild postinflammatory hyperpigmentation.

**Alexander K. C. Leung**, MD, is a clinical professor of pediatrics at the University of Calgary and a pediatric consultant at the Alberta Children’s Hospital in Calgary.

**Benjamin Barankin, MD,** is medical director and founder of the Toronto Dermatology Centre.

**REFERENCES**