A 52-year-old white woman presented with an asymptomatic solitary nodule on the right breast. The lesion was first noted 5 months prior as a small papule and evolved to its current size over a period of 2 months. There was no history of trauma to the site. The patient was otherwise healthy. She was a non-smoker and not on any medications. There was a family history of skin cancer.

**PHYSICAL EXAMINATION**

On examination, the nodule was dome-shaped and had a central keratinous crater. There was no regional or systemic lymphadenopathy.

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**What’s Your Diagnosis?**

- A. Basal cell carcinoma
- B. Squamous cell carcinoma
- C. Keratoacanthoma
- D. Pyogenic granuloma
Keratoacanthoma is an epithelial neoplasm characterized by a sharply demarcated nodule with a central keratin-filled crater, rapid growth in the proliferative phase, variable period of lesion stability, and potential for spontaneous involution. It was first described by Hutchinson in 1889.

EPIDEMIOLOGY
Individuals in their 40s to 60s are most commonly affected. The male to female ratio is 2:1. The condition is most common in fair-skinned individuals.

ETIOPATHOGENESIS
It is believed that keratoacanthoma derives from the infundibulum of the hair follicle. Changes in the expression of genes involved in epidermal cell proliferation, cell adhesion, and cell survival may play a pivotal role in the development of keratoacanthoma. In this regard, mutations of the tumor suppressor gene p53 and the apoptosis regulatory protein gene bcl-2/Bak are implicated in the pathogenesis. Moreover, mutations in the transforming growth factor beta receptor and the apoptosis suppressor gene p53 are illustrated in the present case.6 Sites of predilections include sun-exposed areas such as the face, neck, and hands as well as areas of previous trauma. Solar-induced freckles, solar lentigines, and actinic keratoses may be found in the surrounding areas. The lesion is characterized by rapid growth and achieves an average size of 1-2 cm in the first few weeks. The lesion then stabilizes and may regress spontaneously over several months.

CLINICAL MANIFESTATIONS
According to the number, size, and distribution, several clinical variants of keratoacanthoma have been described—namely, solitary keratoacanthoma, giant keratoacanthoma, subungual keratoacanthoma, mucosal keratoacanthoma, keratoacanthoma centrifugum marginatum, MSSE, generalized eruptive keratoacanthomas of Grzybowski, and multiple keratoacanthomas of Witten and Zak. Solitary keratoacanthoma is the most common variant. Typically, solitary keratoacanthoma presents as an asymptomatic, firm, solitary, pink or skin-colored, dome-shaped nodule with a central keratin-filled crater, as is illustrated in the present case. Sites of predilections include sun-exposed areas such as the face, neck, and hands as well as areas of previous trauma. Solar-induced freckles, solar lentigines, and actinic keratoses may be found in the surrounding areas. The lesion is characterized by rapid growth and achieves an average size of 1-2 cm in the first few weeks. The lesion then stabilizes and may regress spontaneously over several months.

Histological findings include epidermal hyperplasia, overhanging epithelial lips, central keratin-filled crater, keratinocytes with glassy eosinophilic cytoplasm, sharp demarcation between tumor nests and surrounding stroma, and mixed inflammatory infiltrate in the dermis. The tumor does not extend into the dermis to a depth below the eccrine glands.

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In addition, keratoacanthomas may be part of Muir-Torre syndrome and xeroderma pigmentosum.1,2

DIAGNOSIS
The diagnosis is usually clinical, based on its distinctive clinical history. Dermoscopy of the lesion reveals keratin crust/scale, central keratin mass, white keratin pearls, white circles, white structureless zones, hemorrhage centrally and in areas of keratinization, glomerular vessels, linear irregular vessels, atypical vessels, and hairpin vessels.1,12 Unfortunately, these features may also be present in squamous cell carcinoma.1,12 Because of a lack of clinical features that can reliably distinguishing keratoacanthoma from squamous cell carcinoma, a biopsy with a sample of sufficient depth should be considered.

DIFFERENTIAL DIAGNOSIS
Differential diagnosis includes squamous cell carcinoma, basal cell carcinoma, Merkel cell carcinoma, hypertrophic actinic keratosis, seborrheic keratosis, verruca vulgaris, pyogenic granuloma, prurigo nodularis, giant keratosis, verruca vulgaris, pyogenic granuloma, prurigo nodularis, giant keratosis, verruca vulgaris, pyogenic hypertrophic actinic keratosis, seborrheic carcinoma, and a biopsy with a sample of keratoacanthoma from squamous cell carcinoma.11,12 Because of a lack of clinical features that present in squamous cell carcinoma.11,12 Unfortunately, these features may also be in fact turn out to be a squamous cell carcinoma on histopathology.2 The choice of the treatment method should be individualized depending on the physician’s comfort level with the various treatment options, the type of keratoacanthoma, the location, number and size of lesions, and the preference of the patient.

Surgical excision is the treatment of choice for a solitary keratoacanthoma. Other treatment options include electrodessication and curettage, cryosurgery, intralesional 5-fluorouracil or methotrexate, topical imiquimod or 5-FU, and laser therapy; some therapies are used in combination.3,4 For a large keratoacanthoma in a sensitive location not amenable to surgery, intralesional 5-fluorouracil or methotrexate should be considered.4,14 For multiple keratoacanthomas, treatment options include oral retinoids, oral cyclophosphamide, and superficial radiotherapy.4,15

Avoidance of sun exposure especially during hours of peak ultraviolet intensity (11 am to 4 pm), regular use of broad-spectrum sunscreens, avoiding tanning salons, and wearing of protective hats and clothes when outdoors should be emphasized to reduce scarring and prevent recurrence.

MANAGEMENT
Some suggest watchful observation of the lesions and to await spontaneous resolution. Should a patient elect to defer treatment, regular close follow-up with serial photography of the lesion is recommended. Most others believe that keratoacanthoma is a variant of squamous cell carcinoma or within the same spectrum and it is wise to treat keratoacanthoma rather than to monitor for its spontaneous resolution since a clinically presumed keratoacanthoma may in fact turn out to be a squamous cell carcinoma on histopathology. The choice of the treatment method should be individualized depending on the physician’s comfort level with the various treatment options, the type of keratoacanthoma, the location, number and size of lesions, and the preference of the patient.

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

REFERENCES:
14. Patel NP, Cervino AL. Treatment of keratoacanthoma: is