glion of the tibia. The patient was referred to the orthopedic surgery service, where she declined standard surgical excision and instead opted for aspiration with subsequent compression. At the time of writing, she continued to be monitored through the orthopedic surgery service.

**Discussion** | Periosteal ganglia are uncommon single or multiloculated subcutaneous cystic nodules. These lesions are rarely encountered by dermatologists and are usually seen in the orthopedic setting. Although described mainly in men, these lesions also have been reported in children. Periosteal ganglia typically involve the tibia, but reports have also described involvement of the medial malleolus, femur, ilium, radius, and ulna. Duration before presentation varies from several weeks to years. Lesions can be asymptomatic or tender, and a history of trauma is variable.

Mucoid degeneration of the periosteum is the most frequently proposed pathogenesis for the formation of periosteal ganglia. Fibroblasts are thought to form intercellular mucin, which coalesces to form cystic lesions. Accumulation of mucoid material compresses the surrounding tissue, thereby inducing further fibroblast proliferation, collagen production, and ultimately an encapsulating fibrous wall. The central cystic contents are composed of an acellular mucinous or gelatinous fluid. Although communication with the underlying joint space has not been reported, cases have shown varying degrees of underlying cortical erosion with scalloping and spiculated bone reactions. Choi and colleagues described a case with an underlying interosseous component. However, as in our patient, theseysts frequently have no underlying connection to the cortical bone.

Several imaging modalities to evaluate periosteal ganglia have been described. Plain radiographs, although helpful in detecting underlying bony changes, are nonspecific and do not differentiate pretibial ganglion cysts from other surface tumors. Computed tomography is helpful in further discerning characteristics of the soft-tissue mass, but magnetic resonance imaging is the modality of choice. Magnetic resonance imaging demonstrates a homogeneous signal intensity, which appears isointense to muscle on T1-weighted images and has a high signal intensity when compared with fat on T2-weighted images.

Definitive treatment of periosteal ganglia is by surgical excision. Some authors recommend excising an adjacent margin of normal periosteum to prevent recurrence. Although recurrence after surgical excision has been described, this may represent continued mucoid degeneration rather than incomplete excision.

The clinical differential diagnosis for pretibial subcutaneous masses or nodules is broad and includes erythema nodosum, nodular pretibial myxedema, subcutaneous sarcoidosis, periosteal chondroma, parosteal lipoma, subperiosteal hematoma, subperiosteal abscess, periosteal aneurysmal bone cyst, chondromyxoid fibroma, or periosteal osteosarcoma. Although uncommon and rarely encountered by dermatologists, periosteal ganglion cysts remain an important condition to consider in the differential diagnosis of subcutaneous pretibial lesions. This case highlights the need for dermatologists to recognize this uncommon diagnosis to facilitate appropriate workup and referral.

**Letters**

**Acute Generalized Exanthematous Pustulosis Induced by Sorafenib**

Sorafenib (Nexavar; Bayer HealthCare AG) is an oral multitargeted tyrosine kinase inhibitor approved by the US Food and Drug Administration for the treatment of unresectable hepatocellular carcinoma and advanced renal cell carcinoma. It inhibits multiple tyrosine kinases, including C-RAF and B-RAF, vascular endothelial growth factor receptors, and platelet-derived growth factor receptor (PDGFR).

Acute generalized exanthematous pustulosis (AGEP) is a rare skin eruption associated principally with drugs. To our knowledge, only 1 report of sorafenib-induced acute localized exanthematous pustulosis (ALEP) has been published. Herein, we report the first case of AEGP induced by sorafenib.

**Report of a Case** | A woman in her 50s presented with a history of multifocal hepatocarcinoma previously treated unsuccessfully with radiofrequency, arterial embolization, and selective hepatic radioembolization. After the appearance of lung metastases, treatment was begun with sorafenib (400 mg every 12 hours). Two weeks later, the patient developed hand-foot skin reaction (HSFR), so the treatment was suspended with resolution of the lesions. Treatment with the drug was reintroduced at half dose with good results, and full doses were then administered. Ten days later, the HSFR reappeared, and sorafenib treatment was suspended again. After 3 weeks, sorafenib treatment was restarted at half dose.
After 4 weeks, and without any other drug being added to the treatment regimen, the patient developed an abrupt eruption consisting of erythematous and edematous plaques with hundreds of tiny nonfollicular pustules that appeared first in the genital and inguinal areas and subsequently on the legs, abdomen, buttocks, and neck (Figure 1). She had no mucosal lesions, fever, or any other relevant symptoms. The blood neutrophil count was elevated (7.1 × 10⁹/L), as was the eosinophil count (0.44 × 10⁹/L). (To convert neutrophils and eosinophils to number of cells per microliter, divide by 0.001.)

Skin biopsy revealed formation of subcorneal pustules containing neutrophil aggregates with spongiotic change in the epidermis, edema of the papillary dermis, and superficial perivascular neutrophil and lymphocyte infiltration with red blood cell extravasation in the dermis (Figure 2).

A diagnosis of AGEP was made. Sorafenib treatment was discontinued promptly. The patient's skin lesions subsided spontaneously, and desquamation occurred a week later. Results of epicutaneous tests with sorafenib were negative at 48, 96, and 168 hours.

Discussion | The most frequent adverse effects of sorafenib are those affecting the skin (up to 60% patients), although interestingly, some reports suggest that patients taking sorafenib for hepatocellular carcinoma who develop skin toxic effects show a longer survival. The pathogenic mechanism remains unclear. These adverse effects include HFSR, callosities on areas of high pressure, exanthema, itching, subungual splinter hemorrhages, alopecia, keratoacanthoma, squamous cell carcinoma, seborrheic dermatitis-like eruption, and erythema multiforme.

We describe herein a case of a patient who was taking sorafenib who developed AGEP, which is a rare skin eruption characterized by an abrupt onset of edematous erythema with numerous small pustules associated principally with drugs. We know of only 1 case in the literature of the localized form of the drug eruption ALEP induced by sorafenib. We have found no cases of AGEP induced by this new drug. However, several cases of AGEP have been reported in patients receiving imatinib, which shares with sorafenib the inhibition pathway of PDGFR.

The principal differential diagnosis of AGEP consists of pustular psoriasis. The absence of clinical history of psoriasis, the more acute course, and rapid spontaneous resolution after discontinuation of drug treatment make the diagnosis of AGEP more likely. A negative result from the patch tests does not rule out the diagnosis (only 50% of cases of AGEP show a positive result with the drug involved). Despite the lack of fever, considered a typical clinical feature, our case was classified as definite according to the EuroSCAR scoring system.

Recognizing cutaneous adverse effects early and administering appropriate treatment will likely increase medica-
tion compliance and minimize dose reductions and discontinuation of the drug treatment.

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Systemic Sarcoidosis With Unique Vulvar Involvement

Sarcoidosis is a complex, multisystem disease with an unclear cause.1 Research suggests that the pathogenetic mechanism of sarcoidosis is dysregulation of the immune system in individuals with a genetic predisposition who are subsequently exposed to inciting environmental agents.2

Cutaneous sarcoidosis is often one of the earliest clinical signs of the disease and can be divided into 2 subclasses: specific and nonspecific lesions. Specific lesions are characterized by granulomas identified histologically and include macules, papules, plaques, annular lesions, lupus pernio, infiltration of scars, and subcutaneous nodules.3 Alternatively, nonspecific sarcoid lesions, including erythema nodosum, prurigo, or calcifications, are reactive inflammatory processes.4

Report of a Case | A woman in her 40s presented with erythematous papules with perinasal and periorificial distribution involving both the upper and lower eyelids and an atrophic plaque on the dorsal surface of her neck. The patient complained of vaginal changes including itching, burning, tearing, pain with intercourse, and a painful lesion in the perianal area. Examination revealed an erythematous scaly plaque on the mons pubis with atrophic, white, discolored patches in the vaginal area without evidence of tearing (Figure 1).

The patient presented with a 5-week history of productive cough with exertional dyspnea, and her chest radiograph revealed upper-lobe calcified granulomas but no bilateral hilar lymphadenopathy. The patient’s pulmonary function tests revealed no airflow limitations, normal lung volume, and a mild reduction in the diffusing capacity of the lungs for carbon monoxide. The results of blood tests, including complete blood cell count, comprehensive metabolic panel, angiotensin-converting enzyme level, and erythrocyte sedimentation rate, were within normal limits.

Biopsies of the vulva and mons pubis revealed pauci inflammatory nodular granulomas consistent with sarcoidosis. On examination of the epidermis, vaguely psoriasiform epidermal acanthosis with hyperkeratosis was found. Within the dermis, tissue biopsy specimens demonstrated numerous, well-circumscribed nodular granulomas with multinucleated giant cells and lacking significant numbers of neutrophils (Figure 2A). Most of the granulomas were pauci inflammatory, but some had a cuff of lymphoplasmacytic inflammation. Finally, in areas of the epidermis there was transepidermal elimination (TEE) of the granulomas, a unique finding in the vulvar area of a patient with sarcoidosis.

Figure 1. The Vaginal Area of the Patient With Cutaneous Sarcoidosis

White, discolored patches are apparent in the posterior fourchette, which is the site from which the second biopsy specimen was taken (arrowhead).