The best diagnosis is:

a. granular cell tumor  
b. lepromatous leprosy  
c. mastocytoma  
d. reticulohistiocytoma  
e. xanthelasma
Granular Cell Tumor

Granular cell tumors (GCTs) tend to present as solitary nodules, not uncommonly affecting the dorsum of the tongue but also involving the skin, breasts, and internal organs. Cutaneous GCTs typically present as 0.5- to 3-cm firm nodules with a verrucous or eroded surface. They most commonly present in dark-skinned, middle-aged women but have been reported in all age groups and in both sexes. Multiple GCTs are reported in up to 25% of cases, rarely in association with LEOPARD syndrome (consisting of lentigines, electrocardiographic abnormalities, ocular hypertelorism, pulmonary stenosis, abnormalities of genitalia, retardation of growth, and deafness). Granular cell tumors generally are benign with a metastatic rate of approximately 3%.

Granular cell tumors are histopathologically characterized by sheets of large polygonal cells with small, round, central nuclei; cytoplasm that is eosinophilic, coarse, and granular, as well as periodic acid–Schiff positive and diastase resistant; and distinct cyttoplasmic membranes (Figure 1). Pustulo-ovoid bodies of Milian often generally appear as larger eosinophilic granules surrounded by a clear halo (Figure 2). Increased mitotic activity, a high nuclear-cytoplasmic ratio, pleomorphism, and necrosis suggest malignancy. Pseudoepitheliomatous hyperplasia may be found and may lead to a misdiagnosis of squamous cell carcinoma if the biopsy is taken too superficially. Granular cell tumors are thought to be Schwann cell derived, which is supported by expression of the S-100 protein and neuron-specific enolase.

Lepromatous leprosy is characterized by sheets of histiocytes with vacuolated cytoplasm, some with clumped amphophilic bacilli known as globi (Figure 3). Mastocytoma can be distinguished from GCTs by the “fried egg” appearance of the mast cells (Figure 4). Although mast cells have a pale granular cytoplasm, they are smaller and lack pustulo-ovoid bodies and the polygonal shape of GCT cells. Reticulohistiocytoma, mastocytoma, and granular cell tumors can be differentiated by histologic features and immunohistochemistry. The presence of S-100 protein and neuron-specific enolase is characteristic of granular cell tumors, whereas mastocytoma is positive for mast cell tryptase and CD117 and leprosy is positive for lepromin and lymphohistiocytic infiltrate.

Figure 1. Pseudoepitheliomatous hyperplasia and sheets of polygonal cells with light pink cytoplasm of a granular cell tumor (H&E, original magnification ×40).

Figure 2. Sheets of large polygonal cells with central nuclei; coarse, eosinophilic, granular cytoplasm; and large eosinophilic cytoplasmic pustulo-ovoid bodies of Milian characterize a granular cell tumor (H&E, original magnification ×600).

Figure 3. Lymphohistiocytic infiltrate with amphophilic collections of mycobacteria (globi) in lepromatous leprosy (H&E, original magnification ×600).

Figure 4. Cells with an ovoid, hyperplastic nucleus and a peripheral rim of eosinophilic cytoplasm, characteristic of mastocytoma (H&E, original magnification ×600).
on the other hand, has two-toned dusty rose ground glass histiocytes (Figure 5), and xanthelasma can be distinguished histologically from GCT by the presence of a foamy rather than granular cytoplasm (Figure 6).

REFERENCES