Granular cell tumors have been described at various sites along the gastrointestinal tract, most notably in the esophagus, but also in the duodenum, stomach, and colon. The case reported by Patel and Jakate serves to remind physicians that these tumors can also be seen occasionally in the hepatobiliary system. Their case report includes a very helpful, up-to-date summary of the world literature of such lesions in the biliary tree. These lesions are most commonly seen around the extrahepatic common bile duct, though some are described (including 1 from our own center) at the hilum of the liver and in the pancreas. To our knowledge, intrahepatic granular cell tumors have not hitherto been described.

The case report by Patel and Jakate aims to place this lesion into context. Since the first description in the biliary tree in 1952, there have been fewer than 80 such cases reported in the world literature. Granular cell tumors remain, therefore, quite low on the list of differential diagnoses in patients with obstructive lesions in the extrahepatic biliary system. Nevertheless, this lesion does have a peculiar epidemiologic characteristic, in that it is a tumor principally seen in young female African-American patients (with more than three quarters of patients under 40 years of age). Most of these tumors clinically manifest with obstructive jaundice, which is caused by compression of the common bile duct (or, less commonly, the ducts at the hilum) by the mass effect of the surrounding granular cell tumor. Although reactive change may occur in the biliary epithelium overlying a peribiliary granular cell tumor, exuberant pseudoepitheliomatous change does not appear to be a feature and likely does not contribute significantly to the biliary obstruction. Treatment is usually surgical excision with hepticojejunostomy.

In the case reported by Patel and Jakate, the lesion gave rise to chronic cholestasis and a secondary biliary fibrosis leading to hepatic failure with synthetic dysfunction necessitating orthotopic liver transplantation. This case highlights several of the difficulties of establishing a preoperative diagnosis of granular cell tumor involving the biliary system, largely due to the difficulty of access because of anatomical reasons (which was further complicated by consent issues regarding a biopsy before the transplant). Hoda and associates discussed the diagnosis of biliary granular cell tumor via endoscopic brush cytology in 2 cases. In only 1 of these cases, however, was a firm preoperative diagnosis made using this approach; given the predominantly subepithelial nature of this lesion, the sensitivity of such a diagnostic modality is likely to be low.

The histogenesis of granular cell tumors remains of interest. Although the lesion was originally coined “granular cell myoblastoma,” there is no evidence of muscle differentiation. Ultrastructurally, the cells exhibit...
features of Schwann cells and, accordingly, are S-100 antigen-positive. These lesions are commonly seen at sites of abundant nerves, and some exhibit a complex hybrid appearance with concomitant features of a perineurialoma.23 Other neural antigens are also present in granular cell tumors, including calretinin, a calcium-binding protein structurally related to S-100 protein, as well as nestin, p75/NGFR, and PGP 9.5.20-23 Recent immunohistochemical studies, however, have shown that there are also non-neural antigens present. CD 68 immunoreactivity likely reflects the high lysosomal content, rather than any indication of monocyte/macrophage derivation. Of particular note was the demonstration by Murakata and Ishak21 of inhibin alpha immunoreactivity in all 17 of the hepatobiliary granular cell tumors in their series. This protein is classically expressed in sex cord stromal tumors, placental/gestational trophoblastic lesions, and adrenocortical neoplasms. Several researchers have suggested that granular cell tumors represent a non-neoplastic process reflecting a degenerative change in cells of neural origin as a reactive phenomenon; expression of inhibin alpha makes this unlikely. Although granular cell tumors show some morphologic resemblance to so-called PEComas (tumors showing perivascular epithelioid cell differentiation), the former lack the close association with blood vessels, exhibit less diverse microscopic features, and do not express HMB45 or Melan A.

Irrespective of its origin, granular cell tumor can involve the hepatobiliary system. It remains an uncommon lesion but one that, as Patel and Jakate10 and others5 have demonstrated, lead to significant biliary obstruction and hepatic failure.

References