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Case report

Monoclonal anti cytokeratin antibodies reveal bile duct origin of cirrhotic ductular proliferations (dp)

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One of the well known features of liver cirrhosis is the so-called pseudo-tubules consisting of outgrowths of epithelial cells. They can be found in all types of cirrhosis (except the primary biliary form) as well as in certain chronic inflammatory processes of the liver. However, the cellular origin of these proliferations has not yet been established unequivocally. Both bile duct epithelium (Kettler 1958) or dedifferentiated hepatocytes (Cottier 1980) have been suggested as possible cellular sources.

Intermediate filament proteins are new tissue specific markers which can identify epithelial cells (which contain cytokeratins) but which also can discriminate between different epithelial lineages (Moll et al. 1982, Osborn and Weber 1982). Denk et al. have stressed the importance of cytokeratin analysis in liver pathology (Denk et al. 1982; 1984).

We have recently produced monoclonal antibodies against cytokeratins (Karsten et al. 1983, 1985). One of them (A45-B/B3) reacts with all epithelia and mesothelia and therefore seems to recognize a common epitope of many (if not all) cytokeratins. The other (A53-B/A2) seems to be specific for cytokeratin no. 19 of the catalogue of Moll et al. 1982. This particular cytoskeletal protein has been shown to be absent in epidermis and hepatocytes (Kasper et al. 1985). Using both monoclonal antibodies were tried to identify the cellular nature of cirrhotic pseudo-tubules by means of immunohistochemistry. We examined cryostat sections (4 μm thick) from normal liver and different types of liver cirrhosis (6 individuals) using a modified PAP technique (Kupper et al. 1984) and immunofluorescence. Antibody A45-B/B3 stained hepatocytes, bile ducts and pseudo-tubules, thereby confirming the epithelial nature of the latter. A53-B/A2, in contrast, reacted with bile ducts and pseudo-tubules (Fig. 1/2), but not with hepatocytes. We conclude that the pseudo-tubules contain cytokeratin 19 and are therefore more likely to be derivatives of the bile ducts.

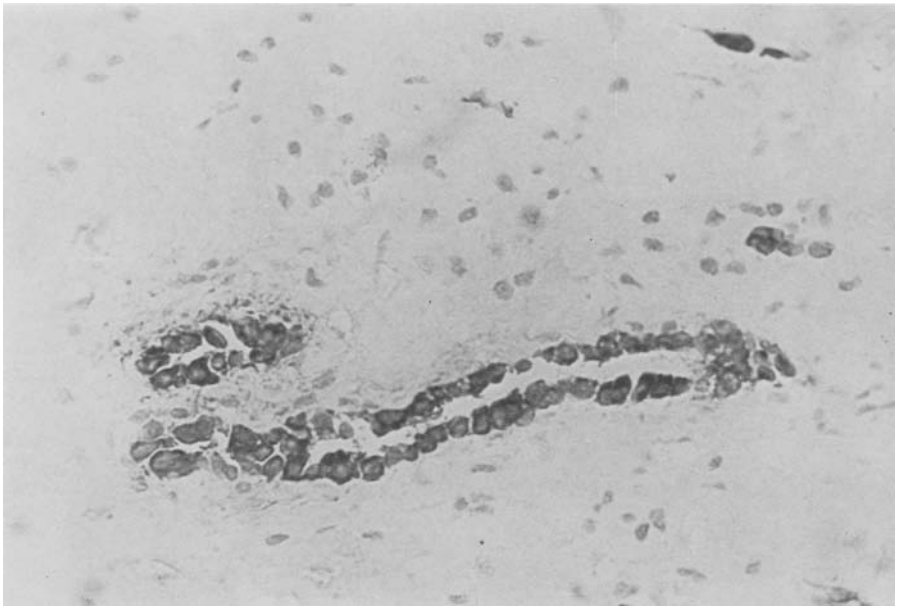

Fig. 1. Reaction of the monoclonal antibody ZIK-A53-B/A2 with normal bile duct epithelium (PAP, × 800)

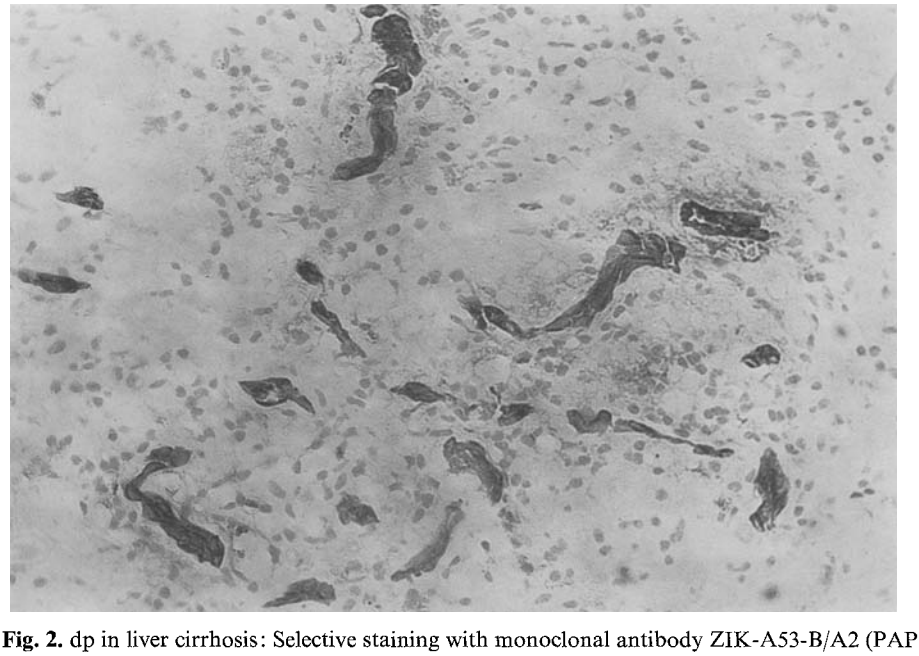

Fig. 2. dp in liver cirrhosis: Selective staining with monoclonal antibody ZIK-A53-B/A2 (PAP, × 800)

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