

## Nodular regenerative hyperplasia of the liver: A review of 14 cases

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### INTRODUCTION

Nodular regenerative hyperplasia (NRH) of the liver is a chronic condition characterized by the development of nodules in the hepatic parenchyma without fibrosis. In this study we report 14 cases of NRH of the liver which were diagnosed during a 5-year period (1992-1997). The diagnosis was based on clinical manifestations, findings of the imaging studies and liver biopsy histology which showed nodules within the hepatic parenchyma without fibrosis. Vascular lesions were not present. The most common clinical manifestations were those of portal hypertension, namely hepatosplenomegaly, ascites and gastrointestinal bleeding due to rupture of esophageal varices. Liver failure and hepatic encephalopathy did not develop. Synthetic liver function, as evidenced by serum albumin, bilirubin and prothrombin time was not impaired.

In 10 (71%) of 14 cases there was cholestasis with elevation of g-glutamyl transpeptidase and alkaline phosphatase. Interestingly, 10 of our 14 patients had associated diseases, 4 myeloproliferative disease, 2 patients had undergone renal transplantation, one heart-lung transplantation and 3 had heart failure, an observation which has been recognized in other studies. The patients were treated mainly for portal hypertension with beta blockers, surgical shunt (mesenteric-caval shunt) and transjugular intrahepatic portal systemic shunt (TIPSS) with satisfactory results.

Patients with NRH of the liver may be predisposed to the

development of hepatoma and should be followed up with regular measurements of alpha-feto-protein and CT scan. Although NRH of the liver is not a common condition, it should be considered in patients with unexplained portal hypertension and cholestatic syndrome. It is distinguished from liver cirrhosis in view of the difference in the natural history, prognosis and management.

Pancreatic cancer is the fourth leading cause of cancer death with poor prognosis. The 5-year survival rate, even after surgical resection remains low. Diagnosis is usually made at a stage when the tumor is inoperable. Diagnosis of early pancreatic cancer is still elusive.

The inability, worldwide, to diagnose early pancreatic cancer stems from the fact that it is difficult to identify high risk groups and apply a screening program in the general population. The only effective form of management at the present is surgical resection which is feasible in 15%-18% of patients, even in centers with rich experience.

### ETIOLOGY

The main etiological factors in carcinoma of the pancreas are as follows:

1. Smoking, is the commonest risk factor which doubles the risk.
2. Diet high in animal fat and protein and low in fresh fruit and vegetable.
3. Genetic factors which cause around 10% of all cases. Abnormality of BR CA 2 is the most important germ cell disorder.
4. Chronic pancreatitis may account for 5% of all cases of pancreatic cancer.
5. Hereditary disorders associated with carcinoma of the pancreas are familial pancreatic cancer, hereditary pancreatitis, hereditary non polyposis colorectal cancer, familial adenomatous polyposis and Gardner's syndrome, and melanoma syndrome.

### MOLECULAR BIOLOGY

The genetic defects which have been characterized in carcinoma of the pancreas are in the order of frequency mutations of the K-ras, p16, p53 and DPC4 genes. Recently K-ras mutations have been identified in the non-invasive form of neoplastic precursor of carcinoma of the pancreas, the "pancreatic intraductal lesion (PIL)".

### DIAGNOSIS AND STAGING

The imaging methods, mainly computed tomography, magnetic resonance [JY] cholangiopancreatography, endoscopic retrograde cholangiopancreatography and endoscopic ultrasound have contributed significantly to the diagnosis and staging for resectability.

The main criteria for resectability are: (1) liver metastases; (2) vascular involvement of superior mesenteric artery, celiac axis or portal vein; (3) extension of tumor to neighboring organs and; and (4) ascites or peritoneal involvement.

Percutaneously guided fine needle aspiration biopsy or core

biopsy have been utilized to confirm the diagnosis preoperatively. The possible seeding of tumor cells has been a concern to the effect that percutaneous biopsy should be reserved for patients who are not considered for surgical resection. Pancreatic biopsies may be also obtained with endoscopic ultrasound guidance.

Tumor markers may be useful in the detection of carcinoma of the pancreas in patients where there is clinical suspicion. CA 19.9 is the most widely used tumor.

## MANAGEMENT

Surgical resection is the mainstay of treatment which offers a better prognosis with a 5-year survival rate ranging between 15%-20% and a perioperative mortality of 5%.

Clinical trials using adjuvant postoperative chemotherapy in resectable tumors to prolong survival are in progress. The surgical procedures are the classical Whipple operation (partial pancreateo-duodenectomy), the pylorus-preserving pan createo-duodenectomy and distal resection.

Non-operative management developments in carcinoma of the pancreas have been slow. In chemotherapy, the agent gemcitabine may contribute to break the barrier of chemoresistance which has characterized chemotherapy and has been an obstacle to tumor response and prolong life expectancy.

Matrix metalloproteinases inhibitors (MMPI) have been used in advanced carcinoma of the pancreas with encouraging results. Matrix metalloproteinases (MMP) are proteolytic enzymes which have a role in tumor invasion and metastases. Inhibition of MMP may be used in adjuvant and palliative management.

Specific immunotherapy as vaccine against mucin-associated antigens and antibody mediated therapy targeted for antigens 17-1A and TAG-72 are currently evaluated in clinical trials.

Gene therapy may have a potential in the treatment of carcinoma of the pancreas, which aims to the restoration of tumor suppression genes *p53* and *p16* and the suppression of oncogenes *K-ras* and *Bcl-2* with antisense nucleotides *Bcl-2* is responsible for

the resistance to chemotherapy.

## FUTURE PERSPECTIVES FOR CARCINOMA OF THE PANCREAS

Prognosis of pancreatic carcinoma will improve if the diagnosis can be made in the early stages I or II. In order to achieve this goal, high risk groups should be identified and screening programs should apply with tumor markers and endoscopic ultrasound examination.

Gene therapy may be useful at an early stage in those individuals with family history and positive *K-ras*. A better understanding of the molecular and biochemical aspects of carcinoma of the pancreas will provide new clues which will lead to effective modes of treatment.

## REFERENCES

- 1 Arvanitakis C, Nikopoulos A, Giannoulis E, Karamouzis M, Semoglou C, Theoharidis A, Tourkantonis A. Evaluation of the tumor marker CA 19.9 in the diagnosis of cancer of the pancreas. In: Klapdor R, ed. Tumor associated antigens. *Verlag* 1992: 16-19
- 2 Flanders TY, Foulkes WD. Pancreatic adenocarcinoma: epidemiology and genetics. *J Med Genet* 1996; **33**: 889-898 [PMID: 8950667 DOI: 10.1136/jmg.33.11.889]
- 3 Friess H, Uhl W, Beger HG, Buchler MW. Surgical treatment of pancreatic cancer. *Digestion* 1994; **11**: 378-386 [DOI: 10.1159/000172289]
- 4 Griffin CA, Hruban RH, Morsberger LA, Ellingham T, Long PP, Jaffee EM, Hauda KM, Bohlander SK, Yeo CJ. Consistent chromosome abnormalities in adenocarcinoma of the pancreas. *Cancer Res* 1995; **55**: 2394-2399 [PMID: 7757992 DOI: 10.1016/0165-4608(96)85235-6]
- 5 Hahn SA, Kern SE. Molecular genetics of exocrine pancreatic neoplasms. *Surg Clin North Am* 1995; **75**: 857-869 [PMID: 7660250]
- 6 Neoptolemos JP, Lemoine NR. Pancreatic cancer: Molecular and clinical advances. Blackwell Science, 1998
- 7 Reber HA. Pancreatic cancer. Humana Press, 1998 [DOI: 10.1007/978-1-4612-1810-4]
- 8 Reznick RH, Stephens DH. The staging of pancreatic adenocarcinoma. *Clin Radiol* 1993; **47**: 373-381 [PMID: 8519142 DOI: 10.1016/S0009-9260(05)81056-6]
- 9 Rösch T. Staging of pancreatic cancer. Analysis of literature results. *Gastrointest Endosc Clin N Am* 1995; **5**: 735-739 [PMID: 8535621]
- 10 Warshaw AL, Fernández-del Castillo C. Pancreatic carcinoma. *N Engl J Med* 1992; **326**: 455-465 [PMID: 1732772 DOI: 10.1056/NEJM199202133260706]

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