

582 THE HISTOLOGIC FEATURES OF PROLONGED HEPATIC ACETAMINOPHEN TOXICITY

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Background: The classic histologic features of acute acetaminophen toxicity consists of Zone 3 necrosis, which typically occurs 4-6 days after ingestion and either resolves rapidly with restoration of hepatic function and architecture, or results in death or transplantation. We describe 3 rare cases of prolonged hepatic dysfunction (4 weeks) resulting in subacute, subfulminant hepatic failure.

Design: Liver biopsies and one explant from three patients are observed. They presented in acetaminophen-induced liver failure, with a mean hospital course of 37 days. All had significantly elevated liver tests on admission. Biopsies and explantation occurred 4 weeks after admission. One patient was discharged with liver function tests that stabilized near the normal range. One patient underwent orthotopic liver transplant after 29 days. The third died after 38 days. We characterized the histologic features on H and E and on trichrome which were seen in these subacute courses.

Results: All specimens showed extensive central zonal necrosis with parenchymal extinction accompanied by exuberant ductular reaction. Necrotic cells were sparse and replaced by signs of early to late organization evidenced by the presence of edematous stroma and early deposition of fibrous tissue leading to scar formation. The most parenchymal loss was seen in the patient who died.

Conclusion: This subacute hospital course is an unusual result of acetaminophen toxicity. The reparative, organizing process and submassive centrilobular necrosis with prominent ductular reaction is histologically atypical for resolving acetaminophen damage and appears to be the result of on-going hepatocyte destruction and repair. The nature of the ductular reaction is curious because the ductules morphologically appear to contain cells of hepatocyte derivation, suggesting a metaplastic response. The etiology of this persistent hepatic damage with resultant organization is unclear. The coincident finding of other ingested toxins such as cocaine, tricyclic antidepressants, and benzodiazepines could be one explanation for such prolonged damage to the liver. Their presence could have exacerbated the initial damage due to acetaminophen toxicity and interfered with the liver's normal reparative process in the face of an acute insult.

583 MULTIVARIATE ANALYSIS OF NEURAL INVASION IN PANCREATIC CANCER

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Background: To investigate the relationships between neural invasion and the biological behaviors of pancreatic cancer.

Design: Three hundred and thirty eight cases of pancreatic carcinomas were subjected to clinicopathologic examination by observing HE slides. Multivariate analysis including neural invasion of pancreatic carcinomas towards age and gender of patients, size and location of tumours, the amount of interstitial connective tissue, histological types of pancreatic carcinomas, atrophic pancreatitis in surrounding tumours, tumour infiltrating lymphocyte was performed with software SPSS8.0 spearman test and x2 test.

Results: The overall incidence of neural invasion in 338 cases of pancreatic carcinoma was 58.9%. Incidences of neural invasion in pancreatic carcinoma with or without atrophic pancreatitis in surrounding tumour tissue and with or without tumour infiltrating lymphocyte was 65.32% (162/248) or 40.23% (35/87) and 64.01% (153/239) or 46.46% (46/99) & #65292; respectively. Significant differences were showed between pancreatic carcinoma with or without atrophic pancreatitis in surrounding tumour tissue and with or without tumour infiltrating lymphocyte (P<0.01), respectively. Incidences of neural invasion in well, middle and low differential adenocarcinoma and other types of carcinoma in pancreas were 58.73% (37/63), 59.22%(106/179), 70.68%(41/58) and 39.47%(15/38), respectively. There was a significance between rates of middle differential adenocarcinoma, low differential adenocarcinoma and other types of pancreatic carcinoma, respectively (P<0.05 and P<0.01, respectively).

Conclusion: The overall incidence of neural invasion in 338 cases of pancreatic carcinoma was 58.9%. Incidences of neural invasion in pancreatic carcinoma was significantly high in pancreatic carcinoma patients with atrophic pancreatitis in primary cancer surrounding tissues than those without atrophic pancreatitis and high those with TIL than without TIL, respectively, but was not associated with distribution of TIL. Patients who suffered from ductal adenocarcinoma more frequently occurred neural invasion than those who suffered from other types of pancreatic carcinomas. Neural invasion in pancreatic carcinoma was not correlated with age and gender of patients, size and location of primary tumours, the amount of interstitial connective tissue. [Key words] pancreas, carcinoma, neural invasion, lymphocyte.

History of Pathology

584 A HISTORICAL SURVEY OF PATHOLOGICAL ANATOMY IN ITALY UP TO NINETEENTH CENTURY

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Background: Every scientific discovery starts from a question. Medical evolution was based on four questions about the human body. How is it made? How does it work? How does it become ill? How can it be repaired? The answers have been gradually supplied from "specializations" that grew out of the primary discipline of anatomy. In particular, the third question was answered by the medical specialty known as "Pathological Anatomy". Different from the other branches of medicine, the current terminology and significance of pathological anatomy represented a major break from the past.

Design: This study investigated the hypotheses that most pathological alterations had been considered anatomical variants and described as 'Anatomical Anomalies' until the XVIII

century because of the supremacy of the ancient humoral theory of illness, according to which the diseases were considered the consequence of dysfunction of the whole organism and not of the single organs. Although this interpretation did not rule out the importance of the pathological observations, more or less incidental, from the time of Erasistrato (III century B. C.) until early modern Renaissance anatomists, like Antonio Benivieni and Alessandro Benedetti, prompted an association between anatomic alterations and illness.

Results: Our search, based on the Medical School of the University of Padua, begins with the "revolution" carried out by Vesalio, followed by Realdo Colombo, Gabriele Falloppia and Girolamo Fabrici d'Acquapendente. Particular attention focuses on "His Anatomical Majesty" Giovanbattista Morgagni, but also to many Italian anatomists which preceded and followed him, like Gian Filippo Ingrassia, Bartolomeo Eustachi, Marcello Malpighi, Giovanni Maria Lancisi, Antonio Valsalva, Antonio Scarpa, Lazzaro Spallanzani, Giulio Bizzozzero and Camillo Golgi. The survey concludes with Ludovico Brunetti who, in the middle of XIX century, founded the first Institute of Pathological Anatomy in Padua.

Conclusion: The sequential investigations of this series of scientists, present the case that the current discipline of Pathological Anatomy was founded in Italy in the Early Modern period.

HIV/AIDS

585 CORRELATION BETWEEN MR IMAGES AND PATHOLOGY OF CNS INFECTIONS IN AIDS

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Background: The incidence of infectious disease in the central nervous system (CNS) has increased considerably after AIDS and non-invasive methods such as magnetic resonance imaging (MR) have proved a great diagnostic breakthrough. MR is invaluable for accurately defining the size and topography of the lesion and its relation to neighboring structures. Signal features in different sequences, including spectroscopy, may give important insights into the physical features and chemical composition of the diseased tissue.

Design: The aim of this study is to evaluate structural images and MR spectroscopy in three of the most common CNS infections in AIDS (toxoplasmosis, tuberculosis and cryptococcosis), correlating the images with gross and histopathological descriptions from the literature to emphasize that MR may improve on the details of gross morphology. MR exams of 37 HIV+ patients with CNS infection were analyzed: 22 with toxoplasmosis, 8 with tuberculosis and 7 with cryptococcosis. The final diagnosis was based on serological tests performed on blood or cerebrospinal fluid (CSF), finding of the agent in CSF or on response to treatment. The findings were classified into three groups: granulomas (G), meningitis (M) or others (H), these comprising atypical lesions such as pseudotumors, empyemas and dilated Virchow-Robin spaces. Meningeal contrast enhancement defined meningitis. Granulomas were characterized by focal, nodular or dot lesions showing MR signal alteration with contrast enhancement.

Results: The results are shown according to etiology and lesion patterns. Some patients had more than one type of lesion: Toxoplasmosis (16G), (3M), (4H); Tuberculosis (3G), (7M), (1H); Cryptococcosis (3G), (5M), (4H). The signal alteration in granulomas (hyperintensity in T2 weighted images (WI)), was attributed to a higher water content of the central necrotic area, and the peripheral contrast enhancement, to the inflammatory halo, associated to increased vascular permeability of proliferated capillaries. Toxoplasmosis granulomas were found diffusely distributed over the parenchyma, mainly in the subcortical region and basal ganglia. Bleeding areas were hyperintense in T1WI due to subproducts of hemoglobin degradation (methemoglobin). Among the patients with tuberculosis, granulomas were not localized to any particular region, but rough nodular meningeal enhancement preponderated in the base, as observed on tuberculous meningitis specimens. In cryptococcosis, dilated Virchow-Robin spaces, represented by T2WI hyperintense dots, mainly in the basal ganglia, indicated gelatinous masses of fungi. With treatment and recovery of cellular immunity, the hyperintense dots regressed while meningitis and granulomatous reaction appeared. Spectroscopy of granulomas showed elevated choline and lactate and decreased N-acetyl aspartate, indicating high cellular turnover, glycolysis and vasogenic edema. Tuberculous lesions also had lipids, attributable to necrosis.

Conclusion: The cases here analyzed demonstrate that, although basically unspecific, the MR images of inflammatory lesions may acquire patterns more suggestive of one etiological agent. This may be useful for the clinician in the choice of initial treatment and, for the pathologist receiving only small specimens, MR informs precisely the site, size and tissue features of the lesion hinting at the more likely diagnosis and orienting use of special stains and immunohistochemistry.

586 THE IMPACT OF HIV ON MATERNAL MORTALITY IN MOZAMBIQUE: AN AUTOPSY STUDY

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Background: Reduction of maternal mortality is one of the major targets promoted in the Millennium Development Goals set up by the United Nations in 2000 (World Bank Group).