

Department of Pathology

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General Summary

The research projects of our department focus on the pathogenesis, histogenesis, morphogenesis, and clinical pathology of nonneoplastic and neoplastic human diseases by means of light and electron microscopy, morphometry, immunohistochemistry, and gene analysis.

Research Activities

Pathology of the liver

We continued to study the evolution of fibrosis in nonalcoholic steatohepatitis (NASH). Previous annual reports have found that bridging fibrosis develops between adjacent central veins and that portal tracts tend to be well preserved in the early stage. Because NASH leads to liver cirrhosis, this early stage could be called the non-cirrhotic stage. Furthermore, we used the tissue reconstruction method to examine at autopsy a case of NASH showing conspicuous fibrosis. We found that most bridging fibrosis was central-to-central bridging fibrosis, whereas portal-to-portal bridging fibrosis was rare. As a result, peripheral portal tracts were in the fibrous mesh formed by central-to-central bridging fibrosis. The pattern reminds us of so-called congestive cirrhosis. On the other hand, we found that small arteries developed around the central and hepatic veins. These arteries are apparently derived from preexisting arteries in the portal tracts. The histologic features provide us with useful data for considering the self-assembly of liver tissue in the thermodynamic nonequilibrium system.

We also studied the ballooning degeneration of hepatocytes to clarify the pathogenesis and progression of NASH. Ballooning cells were conspicuous in the centrilobular regions and fibrotic lesions. However, they were neither essential for NASH nor related to the fatty changes of hepatocytes and inflammation.

The relation of the development of hepatocellular carcinoma to the abnormal vasculature of the liver was examined at autopsy in 2 cases. However, a clear conclusion could not be obtained, and further studies are needed.

Renal pathology

The site and pattern of tissue damage were examined in idiopathic and drug-induced interstitial nephritis. Analysis showed that the damage tended to appear in the medullary ray region.

Histologic evaluation of specimens of renal cell carcinoma collected in the department was continued with revised general rules for clinical and pathological studies of renal cell carcinoma. In particular, the stage was reevaluated according to a newly revised rule.

Gastrointestinal pathology

A total of 5,058 colon polyps accumulated in the past 5 years were examined pathologically. Of these polyps, 4,363 (86.2%) were neoplastic and 696 (13.8%) were nonneoplastic. The most numerous nonneoplastic polyps were hyperplastic polyps, followed by juvenile polyps.

Lung pathology

We continued to investigate morphologic changes of lungs with centrilobular emphysema by means of thick histologic sections stained with Elastica-van Gieson. Histologic reconstruction was performed with both thin and thick sections to observe angioarchitectural changes in pulmonary emphysema. In normal lung, the pulmonary arteries gave rise to branches and were regularly distributed. Pulmonary arteries and veins were interdigitated with each other. On the other hand, in advanced lesions in pulmonary emphysema, the density of small pulmonary arteries clearly decreased. In addition, suspended arteries that had lost alveolar attachment appeared in cystic centrilobular lesions. These changes were thought to reflect the destruction of the pulmonary structure beginning from alveolar damage.

Urogenital pathology

The relation of expression of phosphorylated AKT (pAKT) and Ets-related gene (ERG) by cancer cells was investigated in prostate cancer. The expression of pAKT was recognized in 50% of prostate carcinomas from Japanese patients, whereas the expression rate of ERG was 25% in the same specimens. The staining intensities of pAKT and ERG showed a reciprocal relation. This finding suggests that these 2 carcinogenesis pathways are unrelated and independent.

A comparison of the incidence, volume, and patient age was made between cases of prostate cancer in specimens obtained at autopsy in the 1980s and from 2008 through 2011. We found that the incidence and the volume were greater in 2008 through 2011 than in the 1980s.

The TMPRSS2-ERG fusion gene is reportedly involved in the development of prostate cancer in American and European patients. The presence or absence of the fusion gene was examined in Japanese patients with prostate cancer.

Gynecological pathology

Clinicopathologic examinations were performed of 50 atypical polypoid adenomyomas (APAMs). The APAMs showed various histologic features. For example, in 1 case the tumor progressed into the myometrium, and in another case of APAM that had developed in an adenomyoma. In 15 cases APAMs were associated with adenocarcinomas that had a good prognosis. Curettage specimens often made diagnosis difficult. Sometimes,

APAM was misdiagnosed as endometrioid adenocarcinoma. Hysterectomy is the first choice for treatment.

Breast pathology

A total of 191 cases of breast cancer of borderline malignancy were collected and studied with immunohistochemical staining for actin, p63, and CD10. When cells positive for these antibodies are present inside an intraductal proliferative lesion, the lesion is thought to be a benign tumor, papilloma. However, differentiating benign and malignant lesions is difficult when the positive cells are present along the luminal margin of the duct and are not found inside an intraductal proliferative lesion.

Oncology

Expression of the protein prominin 1 (PROM1) was examined in hepatocellular carcinoma. Expression of PROM1 is significantly down-regulated in primary lesions compared with the corresponding nonneoplastic regions. No difference was found in PROM1 protein expression between primary tumor lesions and metastatic lesions. These results suggest that PROM1 is involved in the carcinogenesis of hepatocellular carcinoma.

Others

Clinicopathological studies were performed of a case of rectal goblet cell carcinoid associated with ganglion neuroma, a case of benign mesenchymal tumor of the stomach, and a case of primitive neuroectodermal tumor of the prostate.

Publications

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