11 PATHOLOGY OF THE SPLEEN IN AIDS AUTOPSIES (AA): COMPARING THE PRE- AND POST-ANTI-RETROVIRAL ERAS.

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Background: Pathologic findings attributed to HIV have been described in the spleen in a few existing studies which encompass the pre-multi-drug therapy era. White pulp depletion, amyloid-like protein, hemosiderin, spindle cell proliferations, and concentric vascular cuffing are all previous observations. Infectious and malignant infiltrates have also been described. Our aim is to compare the histopathologic and clinical findings of AA spleens from the pre-multi-drug therapy era with AA spleens since the introduction of protease inhibitors. **Methods:** Histology from 168 cases of AA spleens were reviewed for significant pathologic findings using previously reported descriptions as a guideline. Patient ages ranged from 21 to 71 and all but 12 were male. All patients carried an ante-mortem diagnosis of AIDS and were autopsied at our institution from 1982-2000. Treatment histories, CD4 counts, and viral loads were obtained and histochemical stains examined when available. Morphologic parameters where carefully characterized and systematically recorded. The degree of white pulp depletion was graded semi-quantitatively. **Results:** Rates of AA have markedly declined since their peak in 1993. Although 40% of spleens weighed over 300 grams, clinical enlargement was detected in only ten cases. Rates of CMV and MAI infection decreased markedly after 1993, however, rates of splenic involvement remained constant in infected patients. Malignant infiltrates included multiple cases of lymphoma and Kaposi's sarcoma. Plasma cell infiltrates, deposition of proteinaceous material, blood vessel hyalinization, and white pulp depletion were common findings. White pulp appeared to be preserved in patients who received multi-drug therapy that included protease inhibitors. The graded quantity of white pulp was increased in the post-treatment era (1994-2000) when compared to spleens examined from the pre-protease inhibitor era (1982-1993). **Conclusions:** 1. A significant decrease in the rate of AA is occurring. 2. Protease inhibitors appear to contribute to the preservation of white pulp. 3. Rates of splenic involvement by MAI and CMV in infected patients have remained constant although the overall rates of these opportunistic infections are decreasing.

12 Lymph Node Silicosis And Pulmonary Silicosis: An Autopsy Study

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Background: Lymph node silicosis (LS) may increase the likelihood of parenchymal silicosis (PS). During a pilot study on lung cancer and silicosis, using autopsy tissue and exposure data from German uranium miners, we investigated this hypothesis.
Design: From a large East German autopsy archive, 1957-1992, we selected 302 former uranium miners: 205 cases of presumed lung cancer and 97 cases dying of other causes. Autopsy slides on 292 cases were reviewed by 4 pathologists; 251 were graded for LS and PS by at least two pathologists. Estimates of silica exposure (Si-Exp) were available for all.
Results:

Variable (mean):	None	LS	PS	LS+ mild PS	LS+moderate severe PS
Cumulative Si-Exp (ppcc-yrs)	1067 [a]	1749 [c]	1967 [cb]	2991 [c]	2613 [cb]
Average Si-Exp (ppcc)	100 [a]	155 [b]	156 [b]	200 [ab]	249 [c]
Years Si-Exp	15.3 [ab]	16.1 [ab]	14.8 [ab]	19.0 [a]	12.9 [b]

Across a row, means with the same letter are not significantly different

In a multi-variable logistic analysis model, the presence of lymph node silicosis was highly significant for the outcome of PS with a substantial odds ratio of 7.
Conclusion: In our autopsy cross-sectional analysis study, the majority of PS cases (88%) also had LS. Those cases of LS alone had lower cumulative silica exposures than those cases with a combination of LS and PS. These data support the hypothesis that LS may precede PS.

13 OPTIMAL USE OF POSTMORTEM CYTOGENETICS.

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Background: It has been previously recommended that postmortem cytogenetics (PC) be performed at autopsy on all stillbirths and infants <28 days old with few exceptions. In order to reduce unnecessary testing and autopsy expenses, it is desirable to identify subsets of perinatal autopsies (PA), which uniformly have normal PC. We reviewed our database of PA to determine if more stringent guidelines for performing PC could be established.
Design: All PA from 1/1994-8/2000 with PC were included in the study. Results were correlated with the presence of anomalies and antenatal cytogenetics (AC).
Results: Of 357 PA, PC were sent in 117. No growth occurred in 17, and maternal contamination occurred in 2. Nine PC repeated AC with no growth in one and no discrepancy in the remaining 8. Abnormal PC were noted in 16 cases with anomalies present in 15. In the case without obvious anomalies, fetal evaluation was limited due to mummification. PC were normal in 82 cases of which 43 had anomalies. All cases of isolated genitourinary tract anomalies (13), isolated congenital heart disease (6), isolated CNS malformation (3), and multiple anomalies due to amniotic disruption sequence (4) had normal PC. Of cases with extreme prematurity/chorioamnionitis (16) or placental infarct/abruption (11) and no congenital anomalies, 3 had no growth with normal PC in 24. In cases of intrauterine fetal demise with indeterminate cause of death (11), 6 had normal PC and 5 had no growth.
Conclusions: 32% of PA had PC performed with abnormal PC detected in 14.5%. Repetition of AC or performing PC in cases with isolated genitourinary, cardiac or CNS anomalies may not be necessary. PC may not be required in cases without anomalies if the condition of the fetus allows for adequate evaluation.

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IMMUNOHISTOCHEMICAL CHARACTERIZATION OF CARBOXYPEPTIDASES D, E, and Z IN HUMAN PITUITARY ADENOMAS

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Background: Carboxypeptidases are thought to play an important role in prohormone processing among different subsets of the anterior pituitary cells. Altered or insufficient prohormone processing has been demonstrated in some human pituitary adenomas. Our recent studies have shown immunoreactivity of carboxypeptidase E (CPE), carboxypeptidase D (CPD) and carboxypeptidase Z (CPZ) in the majority of anterior pituitary cells with highly selective expression of CPD in corticotrophs. In this study, we characterized expression of CPE, CPD and CPZ immunohistochemically in human pituitary adenomas.
Design: Formalin-fixed, paraffin-embedded archival tissue from 60 pituitary adenomas including ACTH-, PRL-, GH- and LH/FSH-secreting adenomas and null cell adenomas was immunostained with polyclonal antibodies against CPE, CPD and CPZ. Positivity was scored quantitatively by 2 observers using a three tiered scale.
Results: Diffuse intracytoplasmic immunoreactivity for CPE and CPZ was detected in all types of adenomas with some heterogeneity. Low or minimal levels of 3 CPs were observed in the majority of null cell adenomas. Five out of 11 corticotroph adenomas displayed weak CPD immunostaining with the remaining 6 cases exhibited intense immunoreactivity similar to normal corticotrophs. A juxtanuclear dot-like CPD staining was consistently observed in all somatotroph adenomas (12/12) with a diffuse intra-cytoplasmic staining pattern detected in the remaining types of adenomas.
Conclusions: Reduced CPD expression in some corticotroph adenomas probably represents a subset of the corticotroph adenomas and may be related to the pathogenesis of the adenoma. The persistent juxtanuclear dot-like CPD staining in GH-secreting adenomas suggests that CPD may be used as an additional sensitive marker for the diagnosis of GH-secreting adenomas immunohistochemically. Minimal levels of CPs in most null cell adenomas probably reflect a low functional status of prohormone processing in these tumors.

15 TUMOR BURDEN AT AUTOPSY IN PATIENTS UNDERGOING CURATIVE SURGERY FOR LUNG CANCER

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Background: Prior to the introduction of computerized tomography (CT) as a staging tool for lung cancer, 24% of patients who underwent curative resection of their lung tumor and died within 30 days were reported to have unrecognized metastatic disease at autopsy, and 12% residual lung cancer. A similar study has not been performed since the introduction of CT.
Design: Clinical data, surgical slides and autopsy slides from patients who underwent curative resection for non-small cell carcinoma, at the Mayo Clinic, between 1985 and 1999, and who underwent autopsy within 30 days of surgery, were reviewed for the presence of residual or metastatic disease and other primary tumors.
Results: The study group consisted of 32 men and 11 women with a mean age of 68. Preoperative staging was stage Ia in 8 (19%) patients, stage Ib in 7 (16%), stage IIa in 1 (2%), stage IIb in 9 (21%), stage IIIa in 10 (23%), and stage IIIb in 8 (19%). Lung tumors were comprised of 26 squamous cell carcinomas, 15 adenocarcinomas, 1 large cell carcinoma, and 1 spindle cell carcinoma. Lung cancer was unresectable at time of surgery in 2 (5%) patients. One (2%) patient had residual disease following curative surgery. Previously undetected metastases were found in 6 (14%) patients, 1 of which had multiple site involvement. Sites included liver (2), different pulmonary lobe (2), epicardium, adrenal and kidney. The average size was 1.6 cm. Two of the patients with abdominal metastases did not have abdominal imaging. A second primary neoplasm was identified in 6 (14%) patients, and included second lung primary cancer (3), prostate carcinoma, pancreatic intraductal mucinous tumor, and spinal cord astrocytoma.
Conclusion: Despite the advent of CT as a staging tool, a substantial number of patients have unrecognized malignancy, in the form of advanced lung cancer or different primary, at the time of surgery.

16 SEVERE SYSTEMIC ILLNESS IN HEROIN USERS FOLLOWING INJECTION SITE INFLAMMATION: AUTOPSY FINDINGS IN AN OUTBREAK

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Background: An epidemic of unexplained illness among injecting drug users characterised by injection site inflammation and severe systemic toxicity occurred in Ireland and the UK in April-June 2000. 104 became ill and 35 died. In Dublin 8 of 23 patients died; all were epidemiologically linked to a source of heroin. Most had local lesions for 1-2 weeks before developing a systemic illness of 1-3 days before death.
Design: Study of autopsy material and findings from the 8 fatal cases.
Results: There were 6 males and 2 females, mean age 34 years (range 22-47). Extensive injection site inflammation involved the buttock (in 4), leg, groin, arm and a portacath site. All had pulmonary oedema, mean bilateral lung weight 2000 g (range 1650-1800 g). There were pleural effusions in 7, mean 900 mL (range 200-4000 mL) of whom 2 had pericardial effusions (100 and 250 mL). 5 had prominent left ventricular subendocardial hemorrhages. 5 had splenomegaly (mean 570 g). Microscopy revealed pulmonary oedema and a granulocytic reaction mainly in spleen, marrow and myocardium. Extensive microbiological and toxicological studies were unhelpful other than growth of Cl Novyi and Cl Chauvoei, each in 1 case.
Conclusion: Autopsy excluded conventional infectious and toxic causes. An effect of clostridial toxin from injected heroin, contaminated by the fastidious anaerobe, Cl Novyi, has been tentatively suggested but international multi-disciplinary investigations continue. Autopsy findings may suggest this syndrome in non-epidemic situations.

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