Neurotoxicity in patients with small-cell lung cancer

tify primary intracranial neoplasms among the population of Rochester, Minnesota, for the period 1935 through 1990. We ascertained 382 cases, 134 males and 248 females. A comparison of the age-specific incidence rates for the periods 1935 to 1977 and 1978 to 1990 showed no change for glioma or meningioma. The overall age-adjusted average annual incidence rate per 100,000 was 15.5 (95% confidence limits 13.4–17.6) for the total, 12.7 (10.5–14.9) for males, and 14.2 (12.7–15.6) for females. The age- and sex-adjusted incidence rates per 100,000 for different types of brain tumors were 4.1 for glioma, 5.0 for meningioma, and 3.9 for pituitary tumors. For gliomas and meningiomas, the age-specific incidence increased progressively with advancing age. The higher incidence of primary brain tumors in females and the excess of meningioma over glioma were attributable to the inclusion of asymptomatic meningiomas diagnosed initially by neuroimaging or at autopsy. Based on 76 live patients, the prevalence of primary brain tumors in the Rochester population on January 1, 1991, was 85 per 100,000. Pituitary tumors increased from 1.9 per 100,000 in 1935 to 1977 to 3.7 per 100,000 in 1978 to 1990; this trend probably resulted from advances in hormonal assays and neuroimaging.

P129. Cerebral Lymphomatoid Granulomatosis

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Lymphomatoid granulomatosis (LG) is an uncommon lymphoproliferative disease characterized by perivascular pleomorphic cellular infiltration and necrosis. The lung is the usual primary site with secondary central nervous system (CNS) involvement in 20% of cases. Primary cerebral LG is a rare but potentially treatable disease with protein manifestations. We will describe 5 cases of cerebral LG, of which 3 had no clinical evidence of disease activity outside the CNS. The neurological manifestations included encephalopathy followed by seizures in 2, mass lesions in 1, and an illness resembling multiple sclerosis in 2. Cerebrospinal fluid (CSF) protein levels were elevated in 4 of 4 patients, and oligoclonal bands were positive in 1 of these. However, only 1 patient had CSF pleocytosis and CSF cytology was unhelpful. Transthoracic lung biopsy was performed in 2 patients (1 of whom had a normal chest x-ray film) and was diagnostic in both, obviating the need for cerebral biopsy. Two received radiotherapy, 2 received chemotherapy, and 1 died without specific treatment. Four patients died 6 months to 2 years (mean 13 mo) following onset of CNS disease, while the fifth remains alive following therapy at 5 years. The clinical features, laboratory investigations, neuroimaging, and pathological findings of cerebral LG will be presented.

P130. Immunological and Pathological Study of a Patient with Anti-Ri–associated Encephalopathy

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A previous report described an autoantibody called anti-Ri found in serum and CSF of some patients with opsoclonus ataxia (Luque et al, Ann Neurol 1991;29:241–251). Most of the patients had breast cancer and the syndrome was thought to be paraneoplastic. Anti-Ri reacts with neuronal nuclear proteins that are also expressed in the patient's tumor. We now report the autopsy findings in 1 of these patients. A 73-year-old woman developed progressive ataxia, nystagmus, upward gaze limitation, and peripheral neuropathy. She died 3 years later of progressive neurological disease. At autopsy, tumor was not grossly evident. The brain contained perivascular and interstitial inflammatory infiltrates, particularly involving tegmentum of pons and mesencephalon. Deposits of immunoglobulin G (IgG) were detected in the cytoplasm (and some nuclei) of neurons. Elution of the IgG revealed a high percentage of anti-Ri IgG. The proportion of anti-Ri IgG in the IgG extract from various areas of the nervous system's serum and CSF was determined by quantitative Western blot analysis. Anti-Ri IgG was ubiquitously expressed in all regions of the brain with particularly strong reactivity in dorsal mesencephalon. The presence of anti-Ri antibody in neurons and of inflammatory infiltrates in the brain (particularly brainstem) supports the hypothesis of an autoimmune basis for the anti-Ri syndrome and suggests that the antibody itself may play a role in pathogenesis.

P131. Intracranial and Other Neoplasms in Ollier's Disease and Maffucci's Syndrome

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Ollier's disease and particularly Maffucci's syndrome are known to be associated with certain malignancies. The oncogenic basis is unknown. Of 93 patients seen at the Mayo Clinic with multiple enchondromatosis from 1984 to 1993, 83 patients were found to have Ollier's disease and 10 patients had Maffucci's syndrome. Primary intracranial neoplasms were found in 7 patients with Ollier's disease. Two patients had gliomas (1 with brainstem glioma, the other with multicentric brainstem and hemispheric Grade II oligodendroglioma); 3 had pituitary adenomas; and 2 had chordomas. Multiple nonskeletal neoplasms were found in patients with Maffucci's syndrome, and also Ollier's disease including neuromas, adenocarcinomas, adenomas, and ovarian tumors. Sarcomatous degeneration of the skeletal chondromas was common. Metastasis of the chondrosarcomas were usually to the skull base, causing cranial nerve palsies and brainstem compression. Identification of patients with Maffucci's syndrome and also Ollier's disease is essential since periodic surveillance for malignancies is warranted. In addition, targeted studies on patients who develop neoplasms will be valuable in the future for determining the mechanisms of oncogenesis in these cases, and possible development of treatment modalities.

P132. Neurotoxicity in Patients with Small-Cell Lung Cancer

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There have been several reports of neuropsychological side effects of the currently used treatment regimen in patients with small-cell lung cancer (SCLC), including systemic chemotherapy with or without locoregional and prophylactic cranial irradiation (PCI). Especially PCI was blamed for its neurotoxicity. Thirty-two consecutive patients with histologically proven SCLC were tested neuropsychologically before (t0), after chemotherapy, and after PCI. They were examined on the 15 Words Test, the Stroop Colour Word Test, and the Trailmaking Test. In the precondition and postcondition, these patients were compared also with a matched control group of normals. The patients were seen at different points in time by a neurologist. A CT scan of the brain was performed before at t0. Patients with brain metastases were ex-

cluded. For statistical analysis, the independent samples t test was used. The pretreatment and posttreatment results were generally worse compared to those of the matched normals ($p < 0.001$). No significant deterioration was found after chemotherapy, nor after PCI ($0.1 < p < 0.8$). We concluded that there was an important effect on cognitive functioning of the cancer and associated somatic condition itself. This effect was independent of the treatment used. It could very well have contributed to the neurotoxic effects of PCI reported in other studies. This study showed no additional chemotherapy or irradiation effects.

P133. Metastatic Pilocytic Astrocytoma: A Case Report

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Pilocytic astrocytomas are typically benign lesions, frequently completely resected and with an excellent prognosis. We report a patient with a hypothalamic pilocytic astrocytoma that recurred in the cerebellum 6 years after initial therapy. The boy was 12 years old when he first presented with 3 months of headache and personality change, and 1 week of vomiting and visual loss. Computed tomographic scan revealed a large hypothalamic/suprasellar mass with obstructive hydrocephalus. A ventriculoperitoneal shunt was placed, followed by subtotal resection of a pilocytic astrocytoma. CSF revealed atypical cells similar to the tumor. He received focal external beam radiation, 5,400 cGy in 28 fractions to left and right lateral fields. He was left with visual loss and panhypopituitarism that required medical replacement. However, he was able to graduate from a regular high school and live independently. He was without new symptoms when on a follow-up magnetic resonance imaging 6 years later a new enhancing left cerebellar mass was noted, outside the radiation field. In retrospect, a very small abnormality at this site may have been present on the original scans. His examination was notable for no stigmata of neurofibromatosis, normal mental status, bilateral optic atrophy, only vision of color and motion, nystagmus, mild left facial weakness, and mild slowing of left fine-finger movements without ataxia. Gross total resection of the well-demarcated mass revealed a pilocytic astrocytoma, similar to the original tumor. This unusual case demonstrates that pilocytic astrocytoma rarely seeds the CSF with the capacity for late and distant recurrence.

POSTER PRESENTATION: NEUROOPHTHALMOLOGY

P134. Association of the 11778 Mitochondrial DNA Mutation and Demyelinating Disease

Kevin M. Flanigan and Donald R. Johns, Baltimore, MD

Leber's hereditary optic neuropathy (LHON), a maternally inherited form of acute visual loss, is most commonly associated with a mitochondrial DNA mutation at nucleotide position 11778. Recently, 6 white women with clinical multiple sclerosis (MS) and 2 white women with demyelinating white matter lesions who had bilateral visual loss and the 11778 mutation were described; no neurological disease was detected in more than 50 men with LHON (Harding, Brain 1992). We present 4 cases (2 white women, 1 black woman, and 1 white man), all of whom had positive oligoclonal bands and MRI abnormalities consistent with demyelinating disease. All had acute visual loss (age at onset ranged from 21–43 yr). Three had other neurological signs and symptoms and were diagnosed with MS. These cases support the possible association of demyelinating disease and the presence of the 11778 mtDNA mutation and suggest that the association is neither gender nor racially limited.

P135. Visual Phenomena Limited to the Hemianopic Field in Lesions of the Central Visual Pathways

Michael Vaphiades, Gastone G. Celesia, and Mitchell Brigell, Chicago, IL

Patients with homonymous hemifield defects due to ischemic infarction of the visual pathways were studied prospectively. Each patient was tested with Goldmann perimetry, complete neuro-ophthalmological examination, and color vision testing. A detailed questionnaire was used to assess the extent of the patient symptoms and awareness of the deficit. Spontaneous visual sensations in the blind hemifield were subdivided into (1) phosphenes characterized by unstructured flashes of light or zig-zag lines; (2) photopsias characterized by regular and often repetitive visual patterns (flowers, geometric figures, etc.); (3) visual hallucinations characterized by complex scenes perceived, at least temporarily, as real. Hemianopic agnosia was defined as unawareness of the hemifield loss; hemiachromatopsia was defined as loss of color vision in the spared areas of the affected hemifield; and palinopsia was defined as the persistence of the visual image after the image has been removed. The prevalence of these phenomena was: hemianopic agnosia 23%; hemiachromatopsia 15%; visual hallucinations 30%; photopsias 38%; phosphenes 23%; and palinopsia 15%. A correlation between visual phenomena and extent and location of magnetic resonance imaging-verified lesions was obtained. The higher occurrence of these visual phenomena in our study is most likely related to the detailed examination of each patient with a visual field defect.

POSTER PRESENTATION: NEUROPHARMACOLOGY

P136. Antidystonic Effects of Novel Sigma Ligands

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The antidystonic effects of two novel sigma ligands were tested in a rat model of torticollis. A role for sigma receptors in the pathophysiology of dystonia was suggested by (1) abnormal sigma binding in a mutant strain of dystonic rats; (2) the tendency of neuroleptics with sigma activity to produce dystonic reactions in humans; and (3) the ability of unilateral intrarubral microinjection of sigma ligands and sigma-active neuroleptics to produce torticollis in rats. Two potent and selective sigma drugs (BD1047 and BD1063) were developed as possible antidystonic agents. In radioligand binding studies, the drugs were found to have a 100-fold or better affinity for sigma sites, as compared to 8 other tested receptors (opiate, PCP, muscarinic, dopamine, alpha-1, alpha-2, 5-HT1, and 5-HT2). For the behavioral studies, chronic indwelling guide cannulae were implanted above the red nucleus. Torticollis was quantified as the angle of deviation of the head after unilateral microinjection. In normal animals, BD1047 or BD1063 had no significant effects on head posture. However, these drugs markedly attenuated pharmaco-