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Intracranial tumors in the elderly

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LEO MATHIAS COONEY, JR.

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INTRACRANIAL TUMORS IN THE ELDERLY

Leo Mathias Cooney, Jr.

A Thesis Presented to the Faculty of the
Yale University School of Medicine in
Candidacy for the Degree of Doctor of
Medicine

Department of Pathology

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Introduction

Neurological disease in an aged population has always presented a difficult diagnostic problem. Intracranial neoplasms in the elderly present an especially difficult problem; this problem is compounded by the impression that such a lesion is rare in this age group. This impression sprang from Harvey Cushing's classic series of brain tumors, in which less than 5% of the lesions occurred in patients 60 years of age and older. This series, with subsequent ones which tended to reinforce the original impression, ²⁵ suffered from the bias of including only diagnosed tumors. These series were all surgical, i.e., they reported only those tumors that had been diagnosed and operated on ante-mortem. In order to determine the actual incidence of brain tumors in all age groups, an autopsy survey was required.

Alerting the clinician of the probability of these lesions in the elderly, however, is just the first step. Not only are the neurological signs and symptoms of a brain tumor similar to other common conditions in this age group (cerebral hemorrhage, cerebral thrombosis, cerebrovascular insufficiency, senility), but the tumors themselves often present differently in this age group than in a younger population. ³⁶ The clinical picture of a brain tumor in an elderly person must be outlined.

The age incidence of brain tumors was determined by an autopsy survey; the clinical picture of these tumors in the elderly was outlined by a review of the clinical records of those older patients with brain tumors.

Materials and Methods

A review was made of the anatomical findings of all autopsies performed at the Yale-New Haven Hospital from 1930 until 1967, a total of 17,000. All patients with brain tumors demonstrated at autopsy were arranged according to tumor type and age group.

An examination of the hospital records of all patients 60 years of age and older with primary intracranial neoplasms was undertaken. The data was transcribed onto McBee Keysort cards. A synopsis of the hospital course was recorded on the cards, while such data as the presence or absence of neurological or neuropsychiatric symptoms, normal or abnormal laboratory examinations, and the clinical impression were coded and punched onto the cards. The cards were then manually sorted and the results tabulated.

Table I

Age Incidence of Primary Intracranial Neoplasms

| | <u>Total</u> | <u>0-9</u> | <u>10-19</u> | <u>20-29</u> | <u>30-39</u> | <u>40-49</u> | <u>50-59</u> | <u>60-69</u> | <u>70-79</u> | <u>80--</u> |
|---------------------------------|--------------|------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|-------------|
| Glioblastoma Multiforme | 161 | 2 | 4 | 8 | 13 | 33 | 57 | 35 | 8 | 1 |
| Meningioma | 57 | 3 | 0 | 2 | 4 | 9 | 18 | 11 | 9 | 1 |
| Meningioma (subsidiary) | 50 | 0 | 0 | 0 | 1 | 2 | 6 | 9 | 21 | 11 |
| Pituitary Adenoma | 60 | 0 | 3 | 2 | 3 | 9 | 10 | 14 | 16 | 3 |
| Hemangioma | 31 | 1 | 1 | 2 | 3 | 3 | 4 | 10 | 3 | 4 |
| Astrocytoma | 41 | 6 | 6 | 4 | 6 | 8 | 7 | 4 | 0 | 0 |
| Medulloblastoma | 20 | 13 | 3 | 1 | 2 | 1 | 0 | 0 | 0 | 0 |
| Cranio- pharyngioma | 16 | 2 | 2 | 3 | 7 | 2 | 0 | 0 | 0 | 0 |
| Cranial Nerve Neuroma | 21 | 1 | 1 | 2 | 1 | 5 | 3 | 6 | 1 | 2 |
| Ependymoma | 15 | 5 | 0 | 2 | 1 | 2 | 2 | 2 | 1 | 0 |
| Oligo- dendroglioma | 7 | 0 | 1 | 2 | 0 | 3 | 0 | 1 | 0 | 0 |
| Glioma | 9 | 4 | 1 | 0 | 1 | 1 | 0 | 2 | 0 | 0 |
| Intracranial Primary Sarcoma | 9 | 2 | 1 | 2 | 1 | 2 | 0 | 1 | 0 | 0 |

Table II

Signs and Symptoms of Brain Tumors in the Elderly

| | <u>Total</u> | | <u>Glioblastoma</u> | | <u>Meningioma</u> | | <u>Other</u> | |
|---------------------------------|--------------|----------|---------------------|----------|-------------------|----------|--------------|----------|
| | <u>56</u> | <u>%</u> | <u>36</u> | <u>%</u> | <u>13</u> | <u>%</u> | <u>7</u> | <u>%</u> |
| Patients | | | | | | | | |
| Decreased intellectual capacity | 30 | 53% | 23 | 64% | 5 | 38% | 2 | 28% |
| Hemiparesis | 28 | 50% | 21 | 58% | 5 | 38% | 2 | 28% |
| Aphasia or Dysphasia | 25 | 44% | 20 | 55% | 3 | 23% | 2 | 28% |
| Mental Status change | 23 | 41% | 16 | 44% | 6 | 46% | 1 | 14% |
| Headache | 24 | 42% | 17 | 47% | 4 | 30% | 3 | 42% |
| Seizures | 18 | 32% | 11 | 30% | 5 | 38% | 2 | 28% |
| Lethargy or Somnolence | 16 | 28% | 9 | 25% | 4 | 30% | 3 | 42% |
| Coma | 14 | 25% | 12 | 33% | 1 | 8% | 1 | 14% |
| Visual Disturbances | 12 | 21% | 8 | 22% | 2 | 15% | 2 | 28% |
| Emotional Disturbance | 11 | 19% | 8 | 22% | 3 | 23% | 0 | 0% |
| Vertigo or Dizziness | 11 | 19% | 7 | 19% | 2 | 15% | 2 | 28% |
| Personal Carelessness | 10 | 18% | 8 | 22% | 2 | 15% | 0 | 0% |
| Alexia, Acalculia, etc. | 8 | 14% | 6 | 17% | 2 | 15% | 0 | 0% |
| Vomiting | 8 | 14% | 6 | 17% | 1 | 8% | 1 | 14% |
| Numbness and Paresthesias | 7 | 12% | 4 | 12% | 2 | 15% | 1 | 14% |

Duration of Symptoms

| | | | | | | | | |
|----------------------------|----|-----|----|-----|----|-----|---|-----|
| No symptoms elicited | 3 | 5% | 1 | 3% | 2 | 15% | 0 | 0% |
| Catastrophic onset | 4 | 7% | 4 | 12% | 0 | 0% | 0 | 0% |
| 1-4 week onset | 15 | 26% | 14 | 39% | 0 | 0% | 1 | 14% |
| Onset greater than 4 weeks | 34 | 60% | 17 | 47% | 11 | 84% | 6 | 85% |

Table III

Physical Findings in Elderly Patients with Brain Tumors

| | <u>Total</u> | <u>%</u> | <u>Glioblastoma</u> <u>Multiforme</u> | <u>%</u> | <u>Meningioma</u> | <u>%</u> | <u>Other</u> | <u>%</u> |
|------------------------|--------------|----------|--|----------|-------------------|----------|--------------|----------|
| Patients | 56 | | 36 | | 13 | | 7 | |
| Cranial Nerve Deficit | 40 | 71% | 27 | 75% | 7 | 54% | 6 | 85% |
| Hemiparesis | 34 | 61% | 28 | 77% | 5 | 38% | 1 | 14% |
| Abnormal Reflexes | 27 | 48% | 19 | 53% | 5 | 38% | 3 | 42% |
| Papilledema | 17 | 30% | 11 | 30% | 3 | 23% | 3 | 43% |
| Visual Field Deficit | 15 | 27% | 11 | 30% | 1 | 8% | 3 | 42% |
| Cerebellar Dysfunction | 12 | 21% | 7 | 19% | 3 | 23% | 2 | 20% |
| Sensory Deficit | 11 | 19% | 10 | 18% | 1 | 8% | 0 | 0% |
| Nystagmus | 5 | 9% | 2 | 6% | 1 | 8% | 2 | 28% |
| Nuchal Rigidity | 4 | 7% | 4 | 12% | 0 | 0% | 0 | 0% |
| Cogwheeling | 3 | 5% | 3 | 8% | 0 | 0% | 0 | 0% |

Abnormal Laboratory Findings

| | | | | | | | | |
|----------------------|----|-----|----|-----|---|-----|---|-----|
| Lumbar Puncture | 30 | 53% | 20 | 55% | 6 | 46% | 4 | 57% |
| EEG | 28 | 50% | 21 | 58% | 5 | 38% | 2 | 28% |
| Air Contrast Studies | 20 | 36% | 10 | 27% | 5 | 38% | 5 | 71% |
| Skull Film | 16 | 28% | 8 | 22% | 7 | 54% | 1 | 14% |
| Cerebral Arteriogram | 13 | 23% | 9 | 25% | 3 | 23% | 1 | 14% |
| Brain Scan | 4 | 7% | 3 | 8% | 1 | 8% | 0 | 0% |

Clinical Impression

| | | | | | | | | |
|--------------------------|----|-----|----|-----|---|-----|---|-----|
| Brain Tumor | 36 | 64% | 25 | 70% | 6 | 45% | 4 | 57% |
| Cerebrovascular Incident | 14 | 25% | 8 | 22% | 4 | 30% | 2 | 28% |
| Other | 4 | 7% | 2 | 6% | 2 | 15% | 0 | 0% |
| Craniotomy Performed | 27 | 48% | 17 | 47% | 6 | 46% | 4 | 57% |

Table IV

Diagnostic Acumen of Special Procedures

| | <u>L.P.</u> | <u>EEG</u> | <u>Skull Film</u> | <u>Air Contrast Study</u> | <u>Cerebral Angiogram</u> | <u>Brain Scan</u> |
|---------------------|-------------|------------|-------------------|---------------------------|---------------------------|-------------------|
| <u>TOTAL CASES</u> | | | | | | |
| Total Tests | 37 | 29 | 35 | 23 | 15 | 4 |
| Abnormal Tests | 30 | 28 | 16 | 20 | 14 | 4 |
| % Abnormal | 80% | 96% | 46% | 87% | 93% | 100% |
| <u>GLIOBLASTOMA</u> | | | | | | |
| <u>MULTIFORME</u> | | | | | | |
| Total Tests | 25 | 21 | 24 | 12 | 10 | 3 |
| Abnormal Tests | 20 | 21 | 8 | 10 | 9 | 3 |
| % Abnormal | 80% | 100% | 33% | 83% | 90% | 100% |
| <u>MENINGIOMA</u> | | | | | | |
| Total Tests | 8 | 5 | 8 | 5 | 4 | 1 |
| Abnormal Tests | 6 | 5 | 7 | 5 | 4 | 1 |
| % Abnormal | 75% | 100% | 87% | 100% | 100% | 100% |
| <u>OTHER</u> | | | | | | |
| Total Tests | 4 | 3 | 3 | 6 | 1 | 0 |
| Abnormal Tests | 4 | 2 | 1 | 5 | 1 | 0 |
| % Abnormal | 100% | 67% | 33% | 83% | 100% | |

Results

In a series of 17,000 autopsies, 497 primary intracranial neoplasms were discovered. The patients are arranged according to tumor type and age in Table I.

The table shows that 176 of the 497 tumors (35%) occurred in patients 60 years of age or older. Eighty-two percent of the meningiomas termed subsidiary at autopsy, 56% of pituitary adenomas, 43% of cranial nerve neuromas, 37% of major meningiomas, 27% of glioblastomas multiforme, 20% of ependymomas, 14% of oligodendrogliomas, 11% of primary intracranial sarcomas, and 9% of astrocytomas occurred in this age group.

Hospital charts of 113 of the 176 elderly patients were available for review. In 56 of these 113 cases (50%), the tumor was considered clinically significant and a primary cause of death. Thirty-six of the 56 were glioblastoma multiforme, 13 were meningiomas, and the seven remaining were classified as "Other", including three acoustic nerve neuromas, two ependymomas, one oligodendroglioma, and one astrocytoma.

The incidence of signs and symptoms referable to these tumors is listed in Table II. This table shows that the vague complaints of aging and senility, i.e., decreased intellectual capacity and mental status changes evidenced by memory loss, confusion, and disorientation, were the most common symptoms presented. Nearly 50% of the patients, however, presented with the clearly neurological symptoms of aphasia or hemiparesis. The "classic" findings of headache and seizures were found in 42% and 32% of the cases, respectively, while only 8% of patients presented with vomiting.

The distinction between the more "irritative" lesions (meningiomas) and the "destructive" lesions (glioblastomas) was not apparent. Although the meningiomas generally were less symptomatic than the glioblastomas, there was no clear preponderance of one type of symptom complex in either lesion.

The onset of symptoms was generally a gradual one; only four per cent of the tumors presented with an abrupt onset and over 60% of the patients entered the hospital with at least a four week history of symptoms. The rate of onset of symptoms did provide a clear differentiation between the slower growing meningioma and the more rapidly progressing glioblastoma; while 51% of the glioblastomas had histories of less than four weeks, none of the meningiomas had so short a clinical course.

The neurological examination of these patients produced rewarding results. Seventy-one per cent of patients were discovered to have cranial nerve deficits, 61% hemiparesis, and 48% abnormal reflexes, while only 30% demonstrated the more diagnostic papilledema. Again, no striking differentiation was evident between meningiomas and tumors of the brain substance itself, save for the generally lower percentage of positive findings in the meningiomas. The findings of visual field and sensory deficits showed the greatest discrepancy between the two lesions; visual field and sensory losses were noted in 30% and 28% of glioblastomas, respectively, while only eight per cent of the meningiomas demonstrated these findings.

The diagnostic accuracy of special procedures employed as diagnostic aids was of particular interest. The time period of this series precluded the use of the newest aid, the brain scan, in more than four of the cases. In all of these cases, (three glioblastomas and a meningioma), however, this technique demonstrated the lesion. The electroencephalogram was also diagnostically accurate, disclosing an abnormality in 96% of the cases in which it was used. Only 20 of the 28 "abnormal" EEG's (71%), however, were interpreted as consistent with the lesion found at autopsy. The remaining eight EEG's were either diffusely abnormal without a localizing focus or with an inaccurate focus.

The more complicated and potentially dangerous procedures, the cerebral arteriogram and the air contrast study, were positive in 93% and 87% of the cases, respectively, in which they were performed. The lumbar puncture, the most widely used procedure (66% of cases) produced an abnormal finding (elevated pressure or elevated total protein) in 80% of the occasions in which it was employed. The skull film, another common diagnostic aid (62% of cases) was positive in only 46% of cases; 87% of the films taken of patients with meningiomas, however, produced positive findings, while only 33% of the glioblastomas showed up on the skull x-ray.

Sixty-four per cent of these patients were correctly diagnosed as having brain tumors. Seventy per cent of glioblastomas and 46% of meningiomas were diagnosed ante-mortem. Twenty-five per cent of the patients were thought

to have either cerebrovascular thrombosis, hemorrhage, or "cerebrovascular insufficiency." Forty-eight per cent of the patients underwent craniotomies.

In order to obtain a more complete picture of the clinical presentation of these patients, the following representative cases histories are presented:

Case #1

M.W., a 65 year old white female, entered the Grace New Haven Hospital on 6/8/53 with a chief complaint of progressive loss of speech over 6 weeks. Six weeks prior to admission, her private physician noted "difficulty in speaking which seemed related to stuttering." To this time she had been in excellent mental status. Three weeks PTA, she had a grand mal seizure with turning of her head to the right. Her speech progressively deteriorated during the six weeks before admission.

Physical examination on admission revealed an aphasic, well preserved white female with a blood pressure of 140/90, pulse of 88 and respirations of 18. The patient was able to give an occasional jargon reply, but usually answered with a yes or no. The gait was normal, cerebellar sense intact, and reflexes within normal limits. Cranial nerves were intact save for a right facial weakness. The right grasp was weaker than the left.

Lumbar puncture revealed an opening pressure of 170 mm water, closing pressure of 60 mm, no cells, and a total protein of 84 mg%. Skull x-ray revealed a calcified pineal gland in a posterior position. EEG was abnormal with a well localized slow wave focus in the left frontal region. Ventriculogram revealed a left frontal mass resulting in displacement of the ventricular system to the right.

Left frontal craniotomy on 6/11/53 revealed a large cyst in the left frontal lobe lined by three mural tumor nodules. The cyst was evacuated and the tumor nodules were removed and were reported as glioblastoma multiforme.

The patient deteriorated progressively post-operatively and died on 8/28/53.

Autopsy revealed a 6 cm in diameter glioblastoma multiforme in the left frontal lobe.

Case #2

T.F., a 65 year old white male, entered the Grace New Haven Hospital on 4/22/57 with a chief complaint that "my powers of concentration aren't what they used to be." Four months prior to admission he had a sudden attack of dizziness and walked with a "list to the left." He "became unconscious," his face reddened, speech became thickened, and he ran a fever of 102-103 degrees for four days. He stayed home from work for two weeks. Two months prior to admission he couldn't concentrate, gave up his job, repeated himself as often as 10x/15 minutes, became confused easily and suffered occasional dizzy spells. He suffered a 20 pound weight loss during these four months.

Physical examination revealed an agitated white male who had difficulty following directions and had a blood pressure of 190/100, pulse of 88, and respirations of 20. He was oriented to person and place but not time. Cerebellar sense, sensation, and muscle strength were all intact and equal bilaterally. Cranial nerves appeared grossly intact, but there was some visual inattention on the right. Reflexes were within normal limits with no abnormal reflexes.

During his hospital course, the patient became progressively more confused, developed apraxia of the right hand, cerebellar dysfunction, a right homonymous hemianopia, agraphia, and acalculia.

The patient was treated with oral anti-coagulants and experienced a partial remission of his symptoms for three to four weeks followed by a return to his confused, apraxic state. He later developed a severe mid frontal headache and slurred speech. He was discharged on 7/31/57 with a diagnosis of middle cerebral thrombosis on the left and retained on oral anti-coagulants.

The patient was readmitted on 10/22/57 with a "convulsion," with no further history. Physical examination revealed a cachectic, semicomatose white male, responsive only with movement. Blood pressure was 195/115, pulse 88. The head was turned to the left and the right side was spastic. Deep tendon reflexes were hyperactive but symmetrical, and there was a positive Babinski on the right. The patient died on 10/23/57 with a clinical impression of middle cerebral thrombosis.

Autopsy revealed a glioblastoma multiforme in the left cerebral hemisphere, extending from the anterior parietal region to the left occipital lobe, with considerable necrosis and cerebral edema.

It is noteworthy that the diagnosis of intracranial neoplasm was never entertained, although the patient was on the neurosurgical service. No lumbar puncture, skull x-ray, or EEG was ever done on this patient.

Case #5

H.F., a 65 year old white male, entered the Grace New Haven Hospital on 5/26/56 with a chief complaint of "unconsciousness." Evidently well with no history of headache, weakness, convulsions, or trauma, the patient suddenly collapsed in his garden several hours before admission. He was reported to have had a convulsion at Milford Hospital.

Physical examination revealed an unconscious male, moving all extremities well, with a blood pressure of 130/70, pulse of 80, respirations of 20, and temperature of 99 degrees. Within 6-8 hours, he became responsive, answered questions, moved all extremities, denied symptoms before his collapse, but had no memory of his collapse. His pupils were equal, round, reactive to light and accommodation, fundi were benign with flat discs; cranial nerve examination showed a tongue deviating to the left, no gag reflex, and a left sided seventh nerve paralysis. Deep tendon reflexes were hyperactive but symmetrical with a positive Babinski on the right. Sensory, motor, and cerebellar functions were all intact.

Later that day the patient was found on the floor conscious but unable to speak or swallow. He recovered fully. Lumbar puncture showed an opening pressure of 85mm water, closing pressure of 65mm, no cell, and a total protein of 20 mg%. He was discharged in an alert state, without aphasia, with a diagnosis of thrombosis of posterior inferior cerebellar artery.

The patient was readmitted on 12/4/56 with a chief complaint of aphasia, hemiplegia, and disorientation. Six weeks prior to admission he suffered a "repeat CVA," with left hemiplegia and aphasia. He had had a fever, progressive cough, and had "gone downhill" for the past two weeks. The family related that the patient became gradually obtunded and that the hemiplegia came on gradually over a period of weeks.

Physical examination revealed an awake but aphasic cachectic white male poorly responsive to commands. The pupils were equal and reactive, but miotic and the fundi were not visualized. The head was turned to the right, the face was flattened bilaterally and a sucking reflex was present on the right. There was a left flaccid hemiplegia, left Babinski, and rigid right side. He was observed performing pill-rolling activities with his right hand. Lumbar puncture revealed an opening pressure of 240 mm water, closing pressure of 140 mm, 750 fresh red blood cells/ cubic mm, and a total protein of 33 mg%. The patient died suddenly on 12/10/56.

Autopsy revealed multiple tumor nodules (glioblastoma multiforme) in the right frontal and parietal lobes.

Case #4

E.F., a 62 year old white female, entered the Grace New Haven Hospital on 8/6/49 with a chief complaint of "episodes of faintness." Five months prior to admission she began to become incontinent of urine. She was first disturbed, then apathetic about this. Four months before admission she fell to the floor without loss of consciousness, but was unable to arise for one half hour. She has since had three more of these episodes accompanied by tremor of her left hand and then whole left side, lasting about one hour and followed by confusion and disorientation. She has become extremely forgetful and has a marked weakness of her left hand.

Physical examination on admission revealed an oriented but apathetic white female unable to stand. Pupils were equal, round and reactive to light and accommodation. The left fundus was benign, while the right fundus showed a blurred temporal margin with obliteration of the cup. The deep tendon reflexes were more active on the left side, but there were no pathological reflexes. There was a spastic weakness of the left arm and weakness of the left leg. Cranial nerves were intact save for a weakness (central) of the left seventh. There was astereogenesis of the left hand. Impression was right fronto-parietal malignancy.

Lumbar puncture revealed an opening pressure of 70 mm water, with a closing pressure of 40 mm. There were no cells and the total protein was 118 mg%. Skull film showed hyperostosis of the inner table of the frontal bone on the left side with localized calcified deposit near the dural surface on the inner table, consistent with a meningioma. The EEG was abnormal with a right sided parieto-occipital and temporal slow wave focus. A ventriculogram showed depression of the right ventricle with a shift to the left. A right carotid arteriogram displayed a right frontal parasagittal meningioma.

On 8/13 a craniotomy was performed and a 7 by 10 cm. meningioma of the convexity of the right frontal lobe with extension to the parasagittal position was removed. On 8/15, the patient suffered a sudden respiratory arrest and died.

Autopsy revealed diffuse cerebral edema without evidence of residual tumor.

51 of the remaining 57 intracranial tumors in this series were termed "incidental" or "subsidiary findings" at autopsy. The remaining six tumors were pituitary adenomas which presented with characteristic findings (headache, visual disturbances, symptoms of altered pituitary function, enlarged sella on skull film) and presented no diagnostic difficulties. In the group of incidental tumors, 6 were pituitary adenomas, 12 were hemangiomas, 2 were acoustic neuromas, 1 an olfactory neuroma, and 30 were "subsidiary" meningiomas. In this group, only three of the meningiomas displayed any symptoms which might be referred to the tumors.

All three of these patients suffered from "fainting spells" of 1, 14, and 15 years' duration. The "spells" in the latter two patients are clearly described as seizures, while no description is available of the spells of the patient with a one year history. One of these cases is described:

G.P., a 70 year old white male, entered the Yale-New Haven Hospital on 4/14/62 with a chief complaint of "seizures." He had a 15 year history of episodes of staring out into space, occasionally beating his fist and smacking his lips. He had been maintained on Mysoline, Phenobarbital, and Dilantin. Two months prior to admission he had a seizure of a "different sort" (not described) and was found to be in complete heart block.

Physical examination on admission revealed a semi-comatose patient in complete heart block with no localizing neurological signs. On 4/22/62 a radio frequency pacemaker was inserted into his heart. An EEG at this time was mildly abnormal in a generalized non-specific fashion without signs of a focus or of a distinct seizure disorder. The patient was discharged without incident.

The patient was readmitted on 11/15/65 because of confusion and disorientation with incontinence of urine. Neurological examination was negative save for a blind right eye and involuntary movements of all four extremities. Skull film and ECHO were negative and the impression was cerebrovascular insufficiency.

The patient was readmitted on 1/10/64 with severe progressive personality change with inappropriate behavior and severe dementia. Physical examination revealed a completely disoriented, argumentative, and combative elderly male without localizing neurological signs. Lumbar puncture revealed an opening pressure of 250 mm water (struggling), closing pressure of 110 mm, no cells, and a total protein of 52 mg%. The impression was progressive dementia due to cerebrovascular insufficiency.

Mr. P. was discharged to Middletown State Mental Hospital where he was disoriented, violent, and would not eat. He died on 3/18/64 of unknown causes.

Autopsy revealed a recent myocardial infarction and acute necrotizing pneumonia. Examination of the brain revealed a 1 cm. in diameter firm meningioma on the greater wing of the sphenoid bone which produced a corresponding depression in the left temporal lobe. A minimal degree of cerebral arteriosclerosis and a moderate amount of cortical atrophy was present. No focal lesions were present within the substance of the cerebrum.

It is impossible to establish a definite cause - effect relationship in these three cases. The high incidence of seizures in patients with major meningiomas, however, coupled with the 10% incidence of seizures in this group, heighten the plausibility of this relationship.

Review of Literature

Several autopsy studies supplement the findings of the above survey, i.e., a significant number of intracranial tumors are found in the aged population (see Table V). Aronson and Aronson ² found 36% of gliomas and 82% of meningiomas occurring after the age of 55; Sinha ³⁴ found 29% of glioblastomas and 22% of meningiomas occurring after 60; while Van der Drift ³⁶ found 19% of astrocytomas, 22% of meningiomas, and 30% of glioblastomas in the age group beyond 60 years. These figures are in sharp contrast to the neurosurgical survey of Harvey Cushing, ¹⁰ in which only 3% of gliomas and less than 5% of intracranial tumors were found in the population over 60.

No complete listing of the incidence of signs and symptoms of intracranial neoplasms in an elderly population could be found in the literature. Moensch ²⁵ points out the relative infrequency of headache and papilledema in this age group, while stating that mental symptoms (dullness, confusion, and stupor) are the most common presenting symptoms.

Van der Drift ³⁶ divides brain tumors into two groups: 1) irritative or compensated lesions, including meningiomas, slowly growing gliomas, and glioblastomas and metastatic lesions in the early stages; and 2) destructive lesions, which include glioblastomas and metastases in a more advanced stage.

The authors used pathological data to help develop their concept of the dual presentations of cerebral neoplasms. Their data demonstrated that: 1) there is less peripheral edema surrounding the lesions in the older age group than in younger subjects; 2) the cerebral atrophy of the older subjects allowed more room for the expansion of the mass lesion; 3) the rate of growth of a specific type of tumor is usually slower in older persons, but there are relatively more tumors of the faster growing types (glioblastomas and metastases) in the older age groups; and 4) ischemic foci often develop alongside the irritative type of lesions in older subjects.

These authors found that the clinical course of an irritative lesion is apt to be longer in an older person: the lesion presents earlier because of frequent concomitant ischemic lesions, and the course is protracted by the slower growth of the tumor in the older individual.

The Van der Drift paper concludes that the irritative type of lesion presents many similarities with an ischemic lesion, not only in the clinical course but also in the electroencephalography results. The destructive lesion, however, presents in a more classic manner and shares many characteristics with the clinical course of a tumor in a younger person.

Sencer³³ outlines the difficulties of neurological diagnosis in the aged by presenting a series of case histories

of patients over 70 who entered Mt. Sinai Hospital with neurological complaints. These cases lead Sencer to conclude that: 1) the "classic" gradual onset of tumor is frequently absent, as 9 of 27 tumors presented with the acute onset of a "stroke;" 2) skull x-rays were rarely helpful; 3) EEG's were frequently non-specific; 4) CSF pressure was frequently normal and while total protein in CSF was usually elevated, false positives were frequent; and 5) cerebral arteriograms and air contrast studies have a significant morbidity and mortality in this age group and are at times normal in the early stage of the lesion. The author stresses, however, that the manner of onset of symptoms often indicates the presence or absence of an organic lesion. Noting that the progressive mental deterioration associated with aging has a gradual onset stretching into years, he concludes that patients with recent (week to few months) alteration in mental function deserve a complete neurological evaluation.

24

McLaurin and Helmer studied the hospital records of 34 patients in whom unsuspected intracranial tumors were found. Twelve were asymptomatic, the remaining 22, with an average age of 53, presented the following symptoms:

| | <u>Meningioma(8)</u> | <u>Glioblastoma(9)</u> | <u>Astrocytoma(5)</u> |
|---------------------|----------------------|------------------------|-----------------------|
| Sudden hemiparesis | 5 | 2 | 1 |
| Gradual hemiparesis | 2 | 5 | 1 |
| Vertigo | 1 | 2 | 1 |
| Dysphasia | 1 | 3 | 2 |
| Headache | 2 | 3 | 3 |
| Confusion | 3 | 1 | 1 |
| Seizures | 5 | 3 | 2 |
| Aphasia | 1 | 2 | 0 |
| Lethargy | 0 | 4 | 1 |
| Personality change | 2 | 2 | 1 |
| Coma | 2 | 1 | 1 |
| Vomiting | 1 | 0 | 2 |

Eleven of the 26 tumor patients were diagnosed as either cerebrovascular thrombosis or insufficiency. The authors make the following diagnostic points: 1) consistent elevation of CSF pressure points towards tumor; 2) a rapidly growing glioblastoma may present with a "stuttering" onset; 3) seizure history indicates tumor; and 4) tumor must be considered in the differential diagnosis of a subarachnoid hemorrhage.

The diagnostic significance of seizures is reinforced by Moore.²⁶ He states that only 12% of CVA patients have seizures, while the figure approaches 50% for cerebral neoplasms (41% of meningiomas, 31% of glioblastomas, and 55% of astrocytomas).

Sinha³⁴ actually documented the frequency of signs and symptoms occurring in a series of patients with glioblastomas. It is of interest to compare the incidence of symptoms in his series of all age groups with the present series of aged patients:

| | <u>Sinha (all ages)</u> | <u>Cooney (60 and over)</u> |
|----------------------|-------------------------|-----------------------------|
| Headache | 58% | 47% |
| Epileptic fits | 29% | 30% |
| Vomiting | 26% | 17% |
| Change in Behavior | 16% | 18% |
| Visual disturbance | 16% | 21% |
| Difficulty in speech | 13% | 55% |
| Blackouts | 13% | 30% |
| Incontinence | 13% | 19% |
| Hallucinations | 5% | 0% |
| Papilledema | 66% | 30% |
| Hemiparesis | 58% | 75% |
| Drowsiness | 26% | 28% |
| Hemianopia | 24% | 30% |
| Confusion | 18% | 44% |

These two series again point out the higher incidence of signs of increased intracranial pressure (headache, vomiting, papilledema) in the younger age group, while mental status changes (confusion) were far more prominent in the older patients. Also of interest is the strikingly higher incidence of speech difficulties (55% vs. 18%) in the older patients.

The clinical findings associated with incidental meningiomas were not discussed in the literature. ¹¹Daly, however, studied the intermittent course of symptoms in 17 patients with meningiomas. These 17 patients, ranging in age from 26-61 years, were found in a series of 210 patients with meningiomas. 13 of the patients experienced transient motor and sensory deficits, three a transient aphasia, two blindness, and two olfactory hallucinations. The author ascribes the intermittent nature of these symptoms to the physical effect of these tumors in compromising the cerebral blood supply.

The danger of overzealous attempts at diagnosis was dramatically brought out by Bruetman. ⁸This author examined 1100 patients with the diagnosis of cerebrovascular insufficiency by means of cerebral arteriography. Eight intracranial lesions were found, of which only four were tumors. Three patients, however, died from complications of the procedure!

Table V

Age Incidence of Intracranial Neoplasms; Comparative Series

Aronson and Aronson²

Sinha³⁴

| <u>Gliomas</u> | | <u>Meningiomas</u> | | <u>Glioblastomas</u> | | <u>Meningiomas</u> |
|----------------|-----|--------------------|-----|----------------------|-----|--------------------|
| 0-15 | 19% | 0-35 | 0% | 31-40 | 18% | 0% |
| 16-25 | 8% | 36-55 | 19% | 41-50 | 24% | 33% |
| 26-35 | 8% | 56-75 | 64% | 51-60 | 29% | 44% |
| 36-45 | 9% | 76-95 | 18% | 61-70 | 26% | 22% |
| 46-55 | 20% | | | 71-80 | 3% | 0% |
| 56-65 | 20% | | | | | |
| 66-75 | 9% | | | | | |
| 76-85 | 4% | | | | | |
| 86-95 | 3% | | | | | |

Van der Drift³⁶

| | <u>Meningioma</u> | <u>Ependymoma</u> | <u>Oligodendroglioma</u> | <u>Astrocytoma</u> | <u>Glioblastoma</u> |
|-------|-------------------|-------------------|--------------------------|--------------------|---------------------|
| 0-20 | 3% | 100% | 6% | 7% | 2% |
| 21-35 | 19% | | 38% | 28% | 11% |
| 26-50 | 30% | | 38% | 27% | 17% |
| 51-60 | 26% | | 12% | 19% | 40% |
| 61-70 | 19% | | 6% | 14% | 22% |
| 70- | 3% | | | 5% | 8% |

Cooney

| | <u>Meningioma</u> | <u>Ependymoma</u> | <u>Oligodendroglioma</u> | <u>Astrocytoma</u> | <u>Glioblastoma</u> |
|-------|-------------------|-------------------|--------------------------|--------------------|---------------------|
| 0-9 | 5% | 33% | 0% | 15% | 1% |
| 10-19 | 0% | 0% | 14% | 15% | 3% |
| 20-29 | 4% | 13% | 28% | 10% | 5% |
| 30-39 | 7% | 7% | 0% | 15% | 8% |
| 40-49 | 16% | 13% | 43% | 20% | 20% |
| 50-59 | 31% | 13% | 0% | 17% | 35% |
| 60-69 | 20% | 13% | 14% | 10% | 21% |
| 70-79 | 16% | 7% | 0% | 7% | 5% |
| 80- | 2% | 0% | 0% | 0% | 1% |

Cushing¹⁰

| <u>Intracranial Tumors</u> | | | | <u>Gliomas</u> | |
|----------------------------|------|-------|-----|----------------|------|
| 0-5 | 2.5% | 41-45 | 13% | 0-15 | 25% |
| 6-10 | 5% | 46-50 | 11% | 16-30 | 22% |
| 11-15 | 6.5% | 51-55 | 8% | 31-45 | 30% |
| 16-20 | 5.5% | 56-60 | 6% | 46-60 | 19% |
| 21-25 | 9% | 61-65 | 3% | 61-75 | 3.5% |
| 26-30 | 9% | 66-70 | 1% | | |
| 31-35 | 10% | 70- | 1% | | |
| 36-40 | 10% | | | | |

Discussion

The data from the above series, with the series of Aronson, Sinha, and Van der Drift, clearly establishes the significant number of primary intracranial neoplasms that occur among the elderly. There is, however, a bias inherent in any autopsy survey. The age distribution of incidental tumors found at autopsy is influenced greatly by the age distribution of the autopsy population. This may account for the high number (82%) of incidental meningiomas occurring in the above patients 60 and over. This survey does not disclose whether the tumors occur at an older age or whether they are indolently present for a long period of time.

The age distribution of those tumors that are clinically apparent and contribute to death is less subject to such bias. The patients with such tumors are not a random component of the autopsy population and subject to its age distribution bias; these patients form a separate subgroup whose age distribution is independent of the autopsy population.

This study was undertaken to present a clearer clinical picture of primary intracranial tumors in elderly persons. That picture, as it evolves, is complicated, variable, and rather blurred. Certain points, however, that are helpful in the differential diagnosis of neurological disease in the elderly have become clear from the study.

The frequency of confusion, disorientation, and loss of intellectual function as presenting symptoms brings confusion with the senility of the aging process. Sencer points out, however, that these symptoms develop over years if they are part of the aging process, while the onset ranges from several weeks to several months in tumor patients. Furthermore, a large percentage of patients with tumors (c. 80%) demonstrate positive findings on neurological examination, which could not be accounted for by senility alone. Finally, the high percentage of tumor patients that demonstrate abnormalities on diagnostic procedures, especially the more benign tests (lumbar puncture, EEG, brain scan), allows one to easily demonstrate the presence of an organic lesion.

The differentiation between tumor and cerebrovascular lesion is more difficult. The frequent presentation of the tumor patients with hemiparesis and aphasia immediately brings cerebrovascular dysfunction to mind. Furthermore, the most common findings on neurological examination (cranial nerve deficit, hemiparesis, and abnormal reflexes) are also characteristic of vascular disease. Even the electroencephalogram findings often point towards an ischemic lesion. Finally, the lower incidence of evidence of increased intracranial pressure in the older patients further complicates the diagnosis.

The differentiation between ischemic and space-occupying intracranial disease is best made by a careful clinical history. Although the mode of onset of the tumor is occasionally intermittent or even abrupt (7% of the above series), the onset is more often a gradual, progressive one. The presence of headache, seizures, or papilledema are also helpful differentiating points. Diagnostic tests which are useful for this differential diagnosis are: the presence of red blood cells in spinal fluid, increased spinal fluid pressure, increased total protein in spinal fluid, the presence of a localized focus on EEG, positive brain scans, and positive skull films, especially in meningiomas.

The essential element in the correct diagnosis, however, is a high index of suspicion. Most of the tumors in the above series were missed because no one bothered to check for papilledema, do a lumbar puncture, or take a careful history of the illness. The age old axioms of clinical acumen are thus upheld by this study.

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