Intracranial Aneurysm Causing Panhypopituitarism, Blindness, Seizures, and Dementia

Sid Gilman, m.d., Lewis E. Braverman, m.d., Arnold Starr, m.d., Simon Horenstein, m.d., and Jeremiah G. Tilles, m.d.

Boston, Massachusetts

Intracranial aneurysms of the sellar region which compress the optic nerves, chiasm, or tracts may simulate pituitary tumors by causing

visual field defects (1–3). The presumed rarity of hypopituitarism in association with these aneurysms previously served as one clinical means of distinguishing aneurysm from tumor (4). Paralleling advances in the assessment of pituitary function, however, an increasing number of reports relate pituitary failure to aneurysms of the sellar region (1, 3, 5–17). As the true incidence of hypopituitarism secondary to aneurysm becomes apparent, the value of pituitary failure as a sign of tumor rather than aneurysm diminishes.
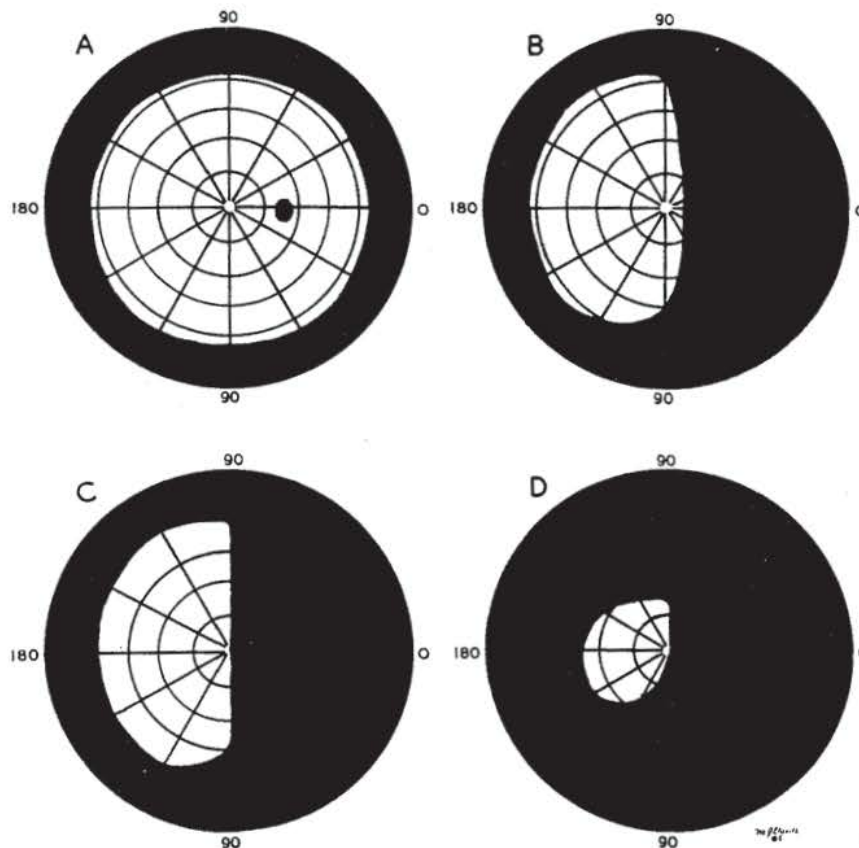

FIGURE 1. Right visual field plotted on tangent screen using a 4 mm white object at 1 m in 1942 (A), 1944 (B), 1953 (C), and 1961 (D).

This report concerns a patient with panhypopituitarism resulting from an aneurysm of the anterior cerebral artery who was followed for over 20 years, providing an opportunity to document the natural progression of this disorder. The aneurysm caused, sequentially, visual loss, a seizure disorder, mild progressive dementia, and, finally, a severe endocrine disturbance. Progressive thrombosis prevented continued growth of the aneurysm and so compromised the lumen that differentiation from tumor would now be difficult by angiographic techniques.

CASE PRESENTATION

T.L.B. visited the outpatient clinic of the Boston City Hospital in June of 1938 at age 35 complaining of left supra-orbital pain of one year's duration. He described an intermittent aching or burning discomfort which also occasionally involved the right supra-orbital or occipital region and often persisted for 2 to 3 weeks. Examination was unremarkable except for a visual acuity of 20/20, right, and 20/40, left. About 6 months later, while aiming a rifle, he found himself almost completely blind in the left eye. Examination in October of 1939 disclosed a visual acuity of 20/30, right, and 4/200, left. The left disc appeared to be pale and waxy.

When admitted to the Neurological Unit of the Boston City Hospital on April 9, 1942, acuity was 20/50, right, and only light perception in the left eye. The right optic fundus appeared to be normal, and the visual field was full (Figure 1, A). The left pupil, equal in size to the right, reacted sluggishly to direct illumination but briskly to consensual stimulation. Lumbar puncture yielded
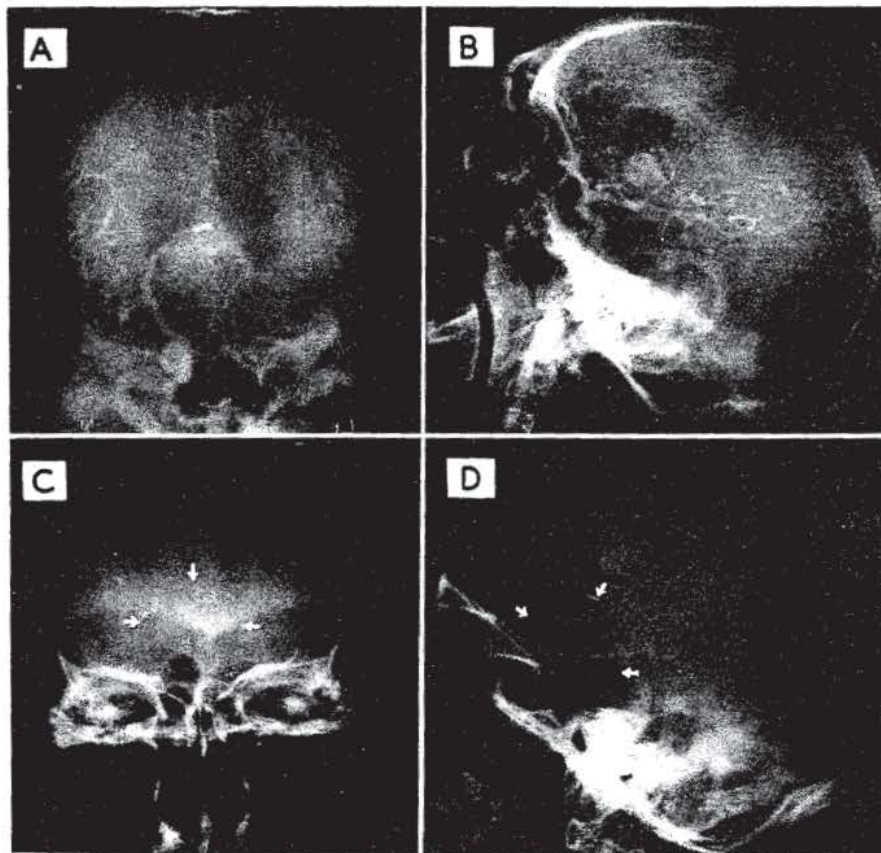

FIGURE 2. Right carotid arteriogram in anteroposterior (A) and lateral (B) projections, performed in 1953 and showing a pedunculated aneurysm arising from the right anterior cerebral artery. The anterior cerebral artery shows a curved displacement with the convexity directed both laterally and posteriorly. Skull X rays taken in 1961, in anteroposterior (C) and lateral (D) projections, show a round linear calcification in the suprasellar region outlined by arrows, with erosion of posterior clinoids and thinning of sella turcica.

clear, xanthochromic fluid under normal pressure containing 6 lymphocytes and a total protein of 104 mg/100 ml. Blood and spinal fluid serologies were negative. The posterior clinoid processes appeared to be slightly thinned in skull films. By July 1944 blindness of the left eye was complete, and the right visual field showed a temporal defect with macular sparing (Figure 1, B).

In 1950 the patient developed recurrent generalized tonicoclonic seizures, which occurred one to 3 times weekly, with associated tongue biting and occasional incontinence. In addition, he had lapses of consciousness which were heralded by wetting and smacking of lips, characterized by staring and unresponsiveness, and terminated by a characteristic cough. An episode persisted for less than one minute and never caused abnormal movements of extremities or loss of postural tone.

By 1953 the patient's family became aware of alterations in his intellect and personality. He had difficulty remembering names, could not think or act quickly, and became increasingly careless about dress and personal hygiene. Headaches had disappeared. Examination disclosed an acuity of 20/50, right, and a right temporal field defect with splitting of the macula (Figure 1, C). Optic discs were pale bilaterally, particularly on the left. Lumbar puncture yielded clear, xanthochromic fluid under a pressure of 125 cm of water containing 31 RBC/mm^3 and a protein of 111 mg/100 ml. Electroencephalography disclosed a right frontal-right central theta focus. Pneumoencephalogram showed no definite abnormality, but carotid arteriograms disclosed a pedunculated aneurysm arising from the right anterior cerebral artery with filling of both anterior cerebral arteries from the right side (Figure 2, A, B).

He entered the hospital again in July of 1957 following a left-sided focal seizure. At the time of admission he was alert and had, in addition to his previous signs, left lower facial paresis, deviation of tongue to the left, moderate weakness of left arm and leg, and a left extensor plantar response; left corneal reflex was absent. Over a 30-hour period these signs gradually disappeared.

When re-evaluated in May of 1959 the patient stated that for the previous one and one-half years he had noted gradually diminishing libido and sexual potency and fatigue on minor exertion. He complained of increasing constipation during the past 2 months. On examination he moved sluggishly and had slow, thick speech. He had thin skin, diminished facial hair, and a female escutcheon; chest and axillary hair was absent. Testes were small and soft, and the prostate gland was small. He had normal olfactory perception, slight left exotropia, and prolonged relaxation of the deep tendon reflexes. X rays of the skull disclosed a rounded linear calcification, 4½ cm, in the suprasellar region with destruction of posterior clinoids. Laminograms showed no calcification within the aneurysm. Laboratory evidence of panhypopituitarism was present (Table 1). The patient

had a macrocytic anemia with normal bone marrow. On the twenty-second hospital day he suddenly became unresponsive, rolled to the right in bed with eyes tonically deviated to the right, raised his right arm, and developed stertorous breathing with coughing. After 2 minutes he became increasingly responsive and made smacking movements with lips and tongue. Blood pressure was 130/80 mm Hg; pulse rate was 88/min. He remained lethargic and disoriented to place and time for the subsequent 17 hours. Blood pressure fell to 100/60 mm Hg, and pulse rate increased to 90/min. Serum electrolytes drawn at that time were: sodium 116, chloride 85, and potassium 4.4 mEq/liter; non-protein nitrogen was 23 mg/100 ml; and carbon dioxide combining power was 19.6 mEq HCO$_3$⁻/liter. Following therapy with intravenous hydrocortisone and saline, the patient's mentation improved, and electrolytes returned to normal levels. Phenolsulfonphthalein excretion was 70% in 60 minutes. Maintenance therapy of cortisone acetate, 25 mg, and sodium chloride, 2 g daily, was begun. Desiccated thyroid, 90 mg daily,

TABLE 1. Endocrine Studies

Test	Date	Therapy	Result
Urinary gonadotrophin*	6/ 2/59	None	Negative at 5 units
Urinary 17-ketosteroids†	6/ 3/59	None	6.2 mg/24 hours
Water load test‡	6/11/59	None	450 ml urine in 5 hours
	6/15/59	Corticotropin, 60 units I.M., daily for 3 days	1,000 ml urine in 5 hours
24-Hour I^{131} uptake§	6/ 2/59	None	19%
	6/ 8/59	Thyrotropin, 10 units I.M., daily for 3 days	51%
Serum protein-bound iodine‖	6/ 2/59	None	3.5 µg/100 ml
	4/ 4/60	None	1.6 µg/100 ml
	8/28/61	Desiccated thyroid, 90 mg/day orally Cortisone, 25 mg/day orally	4.4 µg/100 ml
Basal metabolic rate	8/30/61	Desiccated thyroid, 90 mg/day orally Cortisone, 25 mg/day orally	−20

* Performed at the Gynecological-Endocrinology Laboratory, Peter Bent Brigham Hospital, Boston, Massachusetts.   Normal value for elderly males, positive at 5 to 50 units.

† Performed at the Boston Medical Laboratory, Boston, Massachusetts.   Normal value for males, 10 to 22 mg/24 hours.

‡ 1,500 ml water are administered orally over a 15 to 45-minute period, and urine is collected over the following 5 hours.   Normal excretion is considerably in excess of 800 ml urine.

§ Twenty-four hour radioactive iodine uptake.

‖ Performed at the Boston Medical Laboratory, Boston, Massachusetts.   Normal value, 4 to 8 µg/100 ml.

TABLE 2. Urinary 17-Hydroxycorticoids

Date	Day	Therapy	17-Hydroxy-corticosteroid/24 hr*	
			mg	mg/g urine creatinine†
10/23/61	1	Dexamethasone, 2 mg orally		
10/24/61	2	Dexamethasone, 2 mg orally	5.2‡	
10/25/61	3	Dexamethasone, 2 mg orally		
10/26, 27/61	4, 5	Dexamethasone, 2 mg/day, orally Corticotropin, 40 units I.V., daily		
10/28/61	6	Dexamethasone, 2 mg orally Corticotropin, 40 units I.V.	24.1	
10/29/61	7	Dexamethasone, 2 mg orally Corticotropin, 40 units I.V.		
10/30/61–11/1/61	8–10	None		
11/2/61	11	None	3.7	9.2
11/3/61	12	Methopyrapone, 500 mg orally every 4 hr	6.4	10.7
11/4/61	13	None	0.6	4.6

* Determined by Dr. I. N. Rosenberg, Boston City Hospital.   Normal value, 3 to 12 mg/24 hr (Porter-Silber).

† 17-Hydroxycorticosteroid expressed/g urine creatinine during the test with methopyrapone. Patient became extremely drowsy and uncooperative on day 13, and a complete 24-hour urine was not obtained.

‡ Previous maintenance therapy of 37.5 mg cortisone/day orally was discontinued 2 days prior to this determination.

was added in April of 1960 when protein-bound iodine was 1.6 μg/100 ml.

In July 1961 he inadvertently discontinued cortisone, developed increasing lethargy, and 10 days later became unresponsive following a generalized seizure. On admission he was stuporous. Blood pressure was 90/60 mm Hg, pulse rate, 96/min, and respiratory rate, 20/min. Serum electrolytes were: sodium 110, chloride 75, and potassium 3 mEq/liter. Carbon dioxide combining power was 21.5 mEq HCO_3^- liter; blood sugar was 108 mg/100 ml. The patient remained lethargic for 12 hours but gradually responded to intravenous administration of cortisone and salt. Examination several days after admission revealed an alert, euphoric man with a blood pressure of 120/70 mm Hg and pulse rate of 84/min. Urine specific gravity was 1.020 after 24 hours of fluid deprivation. Truncal obesity with diffuse muscular wasting of extremities was apparent (Figure 3). The skin was thin, dry, pale, and showed diminished turgor. Scalp hair was fine. Lateral eyebrow alopecia and

the previously noted decrease in facial and body hair were apparent. He was inappropriately cheerful. Remote memory was defective. He could not identify the odors of peppermint, vanilla, cloves, or garlic but perceived correctly the tastes of sugar and salt. Visual acuity in the right eye was 20/200, and the right visual field snowed further constriction in the inferior nasal quadrant (Figure 1, D). Plantar responses were flexor. Vibration sense in the toes was slightly impaired, but no other sensory abnormality was found. Lumbar puncture showed clear, faintly xanthochromic fluid under 150 cm of pressure containing 2 RBC and 4 lymphocytes/mm³. Protein was 124 mg/100 ml, and the Wassermann reaction was negative. Roentgenograms of skull again revealed a curvilinear area of calcification in the suprasellar region with erosion of posterior clinoids and thinning of sella turcia (Figure 2, C, D). A right internal carotid arteriogram showed marked bowing of the right anterior cerebral artery with a small projection arising from its medial aspect (Figure 4, A, B).
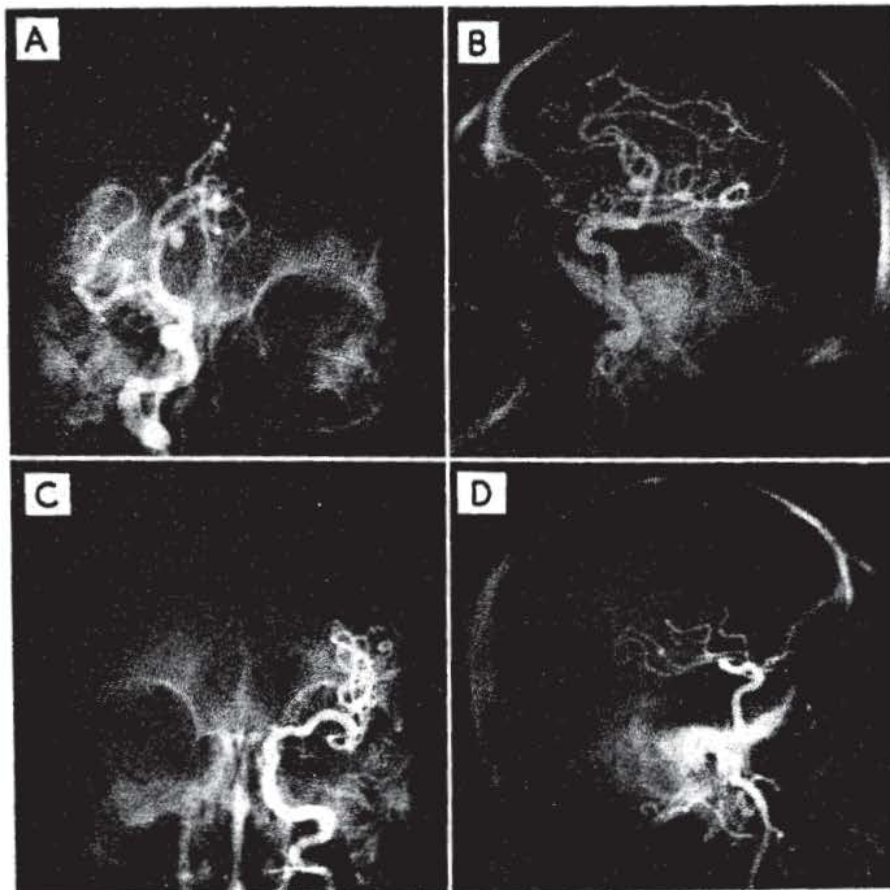

FIGURE 4. Right carotid arteriogram performed in 1961 showing the stalk of the aneurysm arising from the anterior cerebral artery without filling of the aneurysm lumen (A, B). The left anterior cerebral artery arises from the right internal carotid. Left carotid arteriogram in 1961 outlines left middle cerebral artery without filling of anterior cerebral artery (C, D).

One of the 2 vessels arising distal to this projection crossed the midline and appeared to supply regions of the left hemisphere in the distribution of the left anterior cerebral artery. The left internal carotid arteriogram showed no left anterior cerebral artery arising from the carotid (Figure 4, C, D). The electroencephalogram was abnormal, with a basic pattern of 4 to 6 cycles/sec theta waves and 3 cycles/sec delta waves over the frontal regions. Studies to confirm the diagnosis of impaired production of adrenocorticotropic hormone were carried out (Table 2).

DISCUSSION

Intracranial aneurysms alter neurological function by sudden bleeding, compression of local nervous structures, or disturbances of cerebral blood flow, and at times these events occur concurrently. Aneurysms of the internal carotid artery or proximal portions of anterior or middle cerebral arteries cause 2 relatively distinct compressive syndromes, depending upon their location. Infraclinoid aneurysms impair oculomotor and trigeminal function but only rarely disrupt visual pathways, whereas supraclinoid aneurysms usually cause visual field defects without disturbing the function of other cranial nerves (1). Although aneurysms simulating tumors of the sellar region most frequently arise from supraclinoid vessels, infraclinoid aneurysms may, by expansion upward, cause similar symptoms (3, 5). Clinical differentiation of aneurysm from tumor of the sellar region is usually difficult, but a history of supra-orbital pain, sudden disturbance in visual fields, monocular amblyopia, or signs of impairment of oculomotor and trigeminal nerve function suggests aneurysm. Calcification in the walls of the aneurysm can be seen in skull films, but may be mistaken for calcified tumor unless the calcification forms a fine, dense line (18). Arteriography is the most useful single diagnostic test, but it can be misleading if the aneurysm has thrombosed. Direct visualization at operation may be deceptive, since a clotted aneurysm may not pulsate and therefore may appear to be a tumor mass. Aneurysms causing amblyopia with field defects previously were considered uncommon, since Jefferson (1) found only 66 cases in the literature prior to 1937. However, he reported 15 additional cases, and subsequent reports of this association are numerous (2).

From the proximity of carotid and anterior cerebral arteries to the hypophysis, pituitary failure might be expected to result from large aneurysms of these vessels. Yet the presumed rarity of hypopituitarism in association with such aneurysms led to the acceptance of pituitary failure as a sign of tumor rather than aneurysm. Although only 7 well-documented cases of panhypopituitarism have resulted from cerebral aneurysm (3, 5–8, 17), other reported cases have had some clinical or laboratory features consistent with partial pituitary failure (1, 3, 9–16). This emerging association of cerebral aneurysm with pituitary failure diminishes the value of hypopituitarism as a consideration in the differential diagnosis between cerebral aneurysm and tumor.

The patient's clinical course was consistent with the gradual progression of signs and symptoms of anterior pituitary hypofunction beginning with secondary gonadal failure confirmed by an absence of urinary gonadotrophin, and finally resulting in thyroid and adrenal deficiency. Thyroid responsiveness to administered thyrotropin indicated secondary rather than primary hypothyroidism (Table 1). Similarly, a good response to parenterally administered adrenal cortical stimulating hormone was demonstrated by the correction of the patient's inability to excrete normally an orally administered water load (19) and the marked rise in urinary excretion of 17-hydroxysteroids (Tables 1 and 2). Further evidence of secondary adrenal hypofunction was obtained by employing a recently described test to evaluate the ability of the pituitary to secrete corticotropin (20). If pituitary corticotropin production is not impaired, the administration of methopyrapone (SU-4885) [1,2-bis-(3-pyridyl)-2-methyl-1-propanone] results in a marked increase in urinary 17-hydroxysteroids. In our patient this normal increase did not occur, strengthening the suspicion of decreased ability to secrete corticotropin (Table 2). Indeed, he became markedly obtunded during the test when all replacement therapy with adrenal steroids was discontinued. Whether the severe endocrine disturbance in this patient resulted from impaired vascular supply, direct destruction of the pituitary gland, or interference with the presumed hypothalamic control of adenohypophysis cannot be resolved with certainty. Intracranial extrasellar lesions with or without radiologic evidence of changes in the sella may be associated

with clinical or laboratory evidence of diminished pituitary function (21, 22).

Localized cranial pain was the initial complaint in the present case, as it was in the patients described by Gallagher, Dorsey, Stefanini, and Looney (6) and van Staveren and Smits (5). Following gradual loss of vision, monocular blindness appeared suddenly without acute headache or nuchal rigidity, thereby implicating compressive effects rather than bleeding. Although later contrast studies demonstrated that the aneurysm arose from the right side, it presented as a mass compressing the left optic nerve anterior to chiasm since the right monocular field was initially unrestricted (Figure 1, A). Similar monocular amblyopia occurred in 6 of the 7 cases with associated panhypopituitarism previously reported, although White and Ballantine's case (3) had antecedent bitemporal hemianopsia.

This patient had several types of seizures, including psychomotor spells, grand mal attacks, and at least one left-sided focal seizure with postictal paralysis of the left extremities. The multiple seizure patterns suggested diffuse involvement, greater in the right hemisphere. The large size of the aneurysm makes it likely that medial temporal lobes, olfactory trigones, and orbital gyri were directly compressed and consequently might be expected to initiate abnormal discharge. Uncinate attacks and generalized seizures are not uncommon in patients with aneurysms of the sellar region (1). Hyposmia occurred late in the clinical course and was probably secondary to direct compression of the olfactory tracts. This development is considered to be unusual with aneurysms of the sellar region (1).

Dementia, in the case reported by Gallagher and associates (6), accompanied the severe endocrinopathy, but these authors did not describe the patient's intellectual functioning after treatment with replacement hormones. Deterioration of intellect apart from the effect of lethargy was not mentioned in the other cases of panhypopituitarism resulting from aneurysm. The mild dementia in our patient was characterized by slowness of thought, impaired recent and remote memory, and carelessness of personal appearance. Since these symptoms preceded any endocrinopathy and were not corrected by replacement therapy, they are probably attributable to cerebral compression, but

hypoxia from diversion of a substantial proportion of cerebral circulation may have contributed to the dementia.

The consistent elevation of spinal fluid protein and xanthochromia with mild pleocytosis persisted without significant change for over 20 years, even after the aneurysm clotted spontaneously. Chronic basal arachnoiditis is the most likely explanation for this finding in the absence of known chronic venous obstruction. Similar basal arachnoiditis was discovered at operation in the patient described by Rhonheimer (16). This reactive tissue response and the subsequent clotting of the vessel may have served to prevent rupture of the aneurysm.

Arteriography is of critical importance in the diagnostic evaluation of a parasellar mass. The arterial contrast studies of 1953 outlined an apparently small aneurysm, but these films also showed bowing of the anterior cerebral artery which is considerably greater in diameter than the aneurysm. This latter observation, combined with the patient's long-standing amblyopia and the early erosion of the sella turcica, indicates that the aneurysm had attained its large size early in the clinical course but had clotted peripherally. Surgical excision of the aneurysm was contemplated but considered excessively hazardous in view of its large size. The repeat arteriogram in 1961 revealed complete thrombosis of the aneurysm which produced a radiographic picture suggestive of a sellar tumor. However, even without the previous arteriographic demonstration, aneurysm rather than tumor was suggested by headaches, monocular amblyopia, and the fine linear calcification in skull films.

SUMMARY

A patient with an aneurysm of the anterior cerebral artery was observed for over 20 years. He developed, sequentially, a visual field defect, seizures, mild progressive dementia, and, finally, severe panhypopituitarism. The importance of considering cerebral aneurysm in the differential diagnosis of pituitary failure is discussed.

SUMMARIO IN INTERLINGUA

Un patiente con aneurysma del arteria antero-cerebral—tenite sub observation durante plus que 20 annos—disveloppava successivemente perdita del vision, un disordine convulsive, leve dementia, hyposmia, e panhypopi-

tuitarismo. Ben que le aneurysma habeva su origine al latere dextere, illo causava initialmente cecitate del oculo sinistre in consequentia de compression del nervo optic. Postea le patiente disveloppava convulsiones psychomotori e de grand mal, sequite de leve grados de dysfunction intellectual. Finalmente, panhypopituitarismo se manifestava, comenciante con dysfunction gonadal. Quando le aneurysma esseva primo demonstrate per arteriographia in 1953, illo esseva partialmente thrombotificate. In 1961 le thrombose esseva complete.

Le supponite raritate de hypopituitarismo in association con aneurysma resultava in le interpretation del dysfunction pituitari como un signo supportante le these de tumor plus tosto que de aneurysma in le diagnose differential de massas suprasellar. Tamen, ben documentate casos de panhypopituitarismo in association con aneurysma esseva reportate septe vices in recente tempores, e multe exemplos additional de partial disfallimento pituitari como effecto de aneurysmas cerebral es describite in publicationes plus ancian. Le assi documentate association de aneurysma cerebral con hypopituitarismo reduce le valor del constatation de dysfunction pituitari como factor discriminatori in le diagnose differential de aneurysma e tumor sellar.

REFERENCES

1. JEFFERSON, G.: Compression of the chiasma, optic nerves, and optic tracts by intracranial aneurysms. *Brain* 60: 444, 1937.
2. JEFFERSON, G.: Further concerning compression of the optic pathways by intracranial aneurysms, in *Clinical Neurosurgery: Proceedings of the Congress of Neurological Surgeons, New Orleans, Louisiana,* The Williams & Wilkins Company, Baltimore, 1955, p. 55.
3. WHITE, J. C., BALLANTINE, H. T.: Intrasellar aneurysms simulating hypophyseal tumors. *J. Neurosurg.* 18: 34, 1961.
4. WEINBERGER, L. M., ADLER, F. H., GRANT, F. C.: Primary pituitary adenoma and the syndrome of the cavernous sinus, a clinical and anatomic study. *Arch. Ophthal.* 24: 1197, 1940.
5. VAN STAVEREN, P. J., SMITS, M. W.: Infraclinöideaal aneurysma met hypofysaire uitvalverschijnselen. *Ned. T. Geneesk.* 103: 1525, 1959.
6. GALLAGHER, P. G., DORSEY, J. F., STEFANINI, M., LOONEY, J. M.: Large intracranial aneurysm producing panhypopituitarism and frontal lobe syndrome. *Neurology (Minneap.)* 6: 829, 1956.
7. DRIESEN, W.: Über zwei ungewöhuliche Operationsbefunde bei raumforderden intrasellären Prozessen. *Zbl. Neurochir.* 19: 28, 1959.
8. VAN'T HOFF, W., HORNABROOK, R. W., MARKS, V.: Hypopituitarism associated with intracranial aneurysms. *Brit. Med. J.* 2: 1190, 1961.
9. BRAMWELL, B.: Two enormous intracranial aneurysms. *Edinburgh Med. J.* 32: 911, 1887.
10. KÜMMELL, R.: Zur Kenntnis der Geschwülste der Hypophysengegend. *Muench. Med. Wschr.* 58: 1293, 1911.
11. SJÖQVIST, O.: Über intrakranielle Aneurysmen der Arteria Carotis und deren Beziehung zur ophthalmoplegischen Migräne. *Nervenarzt* 9: 233, 1936.
12. MCKENDREE, C. A., DOSHAY, L. J.: Visual disturbances, of obscure etiology, produced by focal intracranial lesions implicating optic nerve; study of six cases of optic nerve compression with proven lesions. *Bull. Neurol. Inst. N. Y.* 5: 223, 1936.
13. WERNER, S. C., BLAKEMORE, A. H., KING, B. G.: Aneurysm of internal carotid artery within skull; wiring and electrothermic coagulation. *JAMA* 116: 578, 1941.
14. ESCAMILLA, R. F., LISSER, H.: Simmonds' disease; clinical study with review of literature; differentiation from anorexia nervosa by statistical analysis of 595 cases, 101 of which were proved pathologically. *J. Clin. Endocr.* 2: 65, 1942.
15. SCHIEFFER, W., MARGUTH, F.: Intrasellare Aneurysmen (Klinik, Differentialdiagnose und Behandlung). *Acta Neurochir. (Wien)* 4: 344, 1956.
16. RHONHEIMER, C.: Zur Symptomatologie der sellaren Aneurysmen. Ein Beitrag zur Differentialdiagnose der Chiasmasyndrome. *Klin. Mbl. Augenheilk.* 134: 1, 1959.
17. KAHANA, L., LEBOVITZ, H., LUSK, W., MCPHERSON, H. T., DAVIDSON, E. T., OPPENHEIMER, J. H., ENGEL, F. L., WOODHALL, B., ODOM, G.: Endocrine manifestations of intracranial extrasellar lesions. *J. Clin. Endocr.* 22: 304, 1962.
18. ALBL, H.: Aneurysma der Carotis interna, einen Hypophysentumor vortäuschend, ein Beitrag zur Diagnose intrakranieller Aneurysmen. *Fortschr. Röntgenstr.* 39: 890, 1929.
19. SOFFER, L. J., DORFMAN, R., GABRILOVE, L.: *The Human Adrenal Gland,* Lea & Febiger, Philadelphia, 1961, p. 276.
20. LIDDLE, G. W., ESTEP, H. L., KENDALL, J. W., JR., WILLIAMS, W. C., JR., TOWNES, A. W.: Clinical application of a new test of pituitary reserve. *J. Clin. Endocr.* 19: 875, 1959.
21. OPPENHEIMER, J. H., FISHER, L. V., JAILER, J. W.: Disturbance of the pituitary-adrenal interrelationships in diseases of the central nervous system. *J. Clin. Endocr.* 21: 1023, 1961.
22. HOKFELT, R. L., LUFT, R.: The effect of suprasellar tumours on the regulation of adrenal cortical function. *Acta Endocr. (Kbh.)* 32: 177, 1959.