Radiation Necrosis of the Brain in Acromegaly*

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Radiation necrosis of the brain is a rare but serious complication of the treatment of acromegaly. This report describes 3 cases, each from a different institution, in which large doses of external irradiation produced significant delayed destructive lesions of cerebral tissue. In each case, craniotomy was necessary, in one bilaterally, for the removal of necrotic gliomatous masses. To our knowledge, no similar cases have been published, although reports of radiation damage and malignant changes in brain and spinal cord in other conditions have occasionally been recorded.

The large amounts of irradiation used probably do not reflect upon the institutions involved, but attest to the difficulty of control of acromegaly by non-surgical means in certain instances. Until recently, 2 factors have prejudiced such control. 1. Satisfactory measurement of human growth hormone activity has been unavailable, and except for the serum phosphorus level, other laboratory data are unreliable. Furthermore, clinical evaluation of the patient, or estimation of acral volume, are inexact criteria of activity. 2. Beneficial effects of irradiation are difficult to assess since they are gradual, often transitory and incomplete, sometimes leading to repeated courses of treatment. At the present time, with modern radio-immuno-assay measurements of human growth hormone and the remarkable safety and rapid effectiveness of total surgical hypophysectomy, the control of acromegaly can be more accurate. The serious complications of radiation therapy described in these 3 cases can be avoided.

Case Report

Case 1. A.B. A 58-year-old Italian-American man was admitted to the Long Island College Hospital in June, 1953, in a drowsy, non-cooperative state. In the previous 10 years he had shown an insidious change in behavior from a hard-driv-

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Pathological Findings. The specimen showed edematous gyri with a 2×5×4 cm. congested yellowish-brown area which on microscopic examination revealed large areas of necrosis and hemorrhage alternating with other areas where extensive neutrophilic infiltration intermingled with lymphocytes, macrophages and gitter cells. The small blood vessels were congested, their walls hyalinized and the site of fibrinoid degeneration. The Virchow-Robin spaces were filled with lymphocytes and neutrophiles. The pathological diagnosis was "localized necrosis of the cerebrum, cause undetermined."

Case 2. E.Z. This man developed symptoms of acromegaly in 1948 at the age of 35 and the diagnosis was reliably established on clinical grounds in late 1950. The sella turcica was not enlarged and the visual fields were normal. In December, 1950, he received 2000 r low voltage therapy to the pituitary from 3 ports, right and left temporal and vertex. There was little symptomatic response and a 2nd course of 2100 r was administered through similar ports in March and April, 1952. There was some improvement in headache and acral enlargement following this treatment but the polyphagia, polydypsia and profuse malodorous perspiration and paresthesias continued.

The patient was first seen at the Memorial Hospital in New York in February, 1954. The active nature of the acromegalic process was indicated by the finding of a serum phosphorus of 5.0 mg.%. There was slight enlargement of the sella turcica by x-ray. Visual fields were normal and there was a normal glucose tolerance test. In March, 1954, a 3rd course of radiation was given over a period of 2 weeks through two 5 cm. temporal ports for a total of 3000 r. The x-ray beam of the 22.5 million electron volt betatron was used which gives a calculated dose to the brain, in line with the beam, approximately the same as delivered to the hypophysis. There was measurable clinical improvement but the headaches were worse and it was decided to give further therapy to tolerance. Accordingly the 4th course of pituitary irradiation was given in May, 1954, consisting of 3026 r with the betatron. After several months, jaw pain and headaches diminished considerably and the serum phosphorus fell to 3.4. There was measurable decrease in the size of his hands and feet.

The patient had now received a total of 10,126 r to the pituitary and it was delighted with his good clinical response. However, in November, 1954, his headache recurred along with a measurable increase in the size of his hands and feet, loss of libido, increased weakness and a rise in serum phosphorus to 4.5 mg.%. Surgical hypophysectomy was advised and refused. In January, 1955, 8 months after the last course of x-ray, his head-ache greatly increased and papilledema was discovered. Several seizures occurred.

In May, 1955, he was re-admitted to the Memorial Hospital with marked impairment of recent memory, deterioration of abstract thinking, emotional lability and depression. There was a striking loss of ability to use his most recently learned language, English, although facility with Italian, German, Yugoslavian, and Jewish was preserved. Visual fields were normal. Papilledema was present. Radiation necrosis of the brain was suspected and the patient was transferred to the New York Hospital under the care of Dr. Bronson Ray.

Operation. A ventriculogram showed inadequate filling of the right frontal horn with a moderate shift to the left. A right frontotemporal craniotomy was carried out. The brain was found to be tense and the arachnoid gray and thickened. The temporal lobe convolutions were flattened and there was a yellowish-brown discoloration of the lobe. There was a general vasocular suffusion over the brain and the small vessels were more prominent than usual. The middle and frontal portion of the temporal lobe was soft to palpation. The temporal lobe was resected from the middle cerebral artery to behind the vein of Labbé. The brain had a soft necrotic appearance and, in the sub-cortical area, could easily have passed for infiltrating glioma. The optic nerves were normal but the arachnoid about the chiasm was unusually thick. There was no evidence of a bulging of the diaphragma sellae.

Pathological Findings. The external surface of the temporal lobe appeared smooth and brown-tinted. The internal surface was soft and spongy, and 2 firm, apparently fibrotic nodules, were present. Microscopically, these nodules showed marked gliosis with small areas of necrosis and deposits of calcium. In other regions there were many diffusely scattered polymorphonuclear leucocytes and a marked increase in microglia. There was considerable thickening of the walls of the smaller blood vessels and a collection of lymphocytes surrounded them. The capillaries were so numerous that a few areas resembled granulation tissue. In these regions there were many macrophages filled with hemosiderin and numerous lymphocytes.

The postoperative course was satisfactory. There was an incomplete left upper homonymous quadrantic defect in the visual field. The patient was rather placid and childlike and showed a marked defect in memory. The papilledema disappeared in 4 months and about this same time a considerable improvement in mentality occurred. He became moderately well-oriented and was able to obey simple commands, and go about New York City alone. He was last heard from in 1964 when he sought help from the Welfare Department.