DESTRUCTION OF THE HYPOPHYSIS WITH RADIO-ACTIVE COLLOIDAL CHROMIC PHOSPHATE IN CANCER OF THE PROSTATE

PHILIP C. JOHNSON, M.D., KELLY M. WEST, M.D., AND BOB J. RUTLEDGE, M.D.

Radioisotope Service, V. A. Hospital, and Departments of Medicine and Neurosurgery, University of Oklahoma School of Medicine, Oklahoma City, Oklahoma

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TREATMENT of metastatic cancer of the prostate by hypophysectomy has been reported by several investigators.8,10,14 This therapy has been tried in the hope that the tumor cells might be dependent to some degree upon the secretion of adrenal androgens, or upon growth hormone or some other secretion of the hypophysis. The number of cases of cancer of the prostate treated by destruction of the pituitary body is not yet great enough to evaluate adequately the effectiveness of this treatment. Luft and Olivecrona8 were able to find in the literature 3 cases of cancer of the prostate in which remission occurred after hypophysectomy. They added 5 of their own, making a total of 8 remissions in 16 patients treated by surgical hypophysectomy. Precise interpretation of these data is difficult since orchiectomy had not been performed in all instances. For instance, the patient of Luft and Olivecrona,8 who had the longest remission (over 24 months), had not had orchiectomy prior to hypophysectomy. It is entirely possible that the prolonged remission in this case may have been caused entirely by the cessation of testicular function. The patient reported by Scott14 who had a good remission after hypophysectomy also had not had orchiectomy. On the other hand, the reported data are not complete enough to exclude the possibility that at least some of the patients who received no benefit from hypophysectomy might not have been completely hypophysectomized.

The technical difficulties of performing a complete hypophysectomy have limited the use of this operation.1 In order to avoid surgical hypophysectomy, external irradiation of the pituitary body has been tried. Because of the location of the pituitary body and its resistance to irradiation, it had not been possible to achieve complete permanent interruption of pituitary function with this method.7 However, the recent use of high-energy proton irradiation of the pituitary body may have solved this difficulty.9 Internal irradiation of the gland has been tried with several radioisotopic techniques including the implantation of yttrium pellets,16 radon seeds,5 and gold.1,6

Recently, Rothenberg et al.11 attempted the direct injection of radioactive colloidal chromic phosphate containing P-32 into the substance of the gland in 6 patients with neoplasms. Phosphorus-32 would seem to offer some advantages over the other radioisotopes used for this purpose, because of its
relatively long half-life, its energetic beta particle, and because it does not produce gamma radiation. To our knowledge, this preliminary report of Rothenberg et al. and one other preliminary report by the same group12 are the only articles published describing the use of radioactive colloidal chromic phosphorus for destroying the pituitary gland. They performed this procedure in 3 cases of carcinoma of the breast, 2 cases of thyroid carcinoma and 1 case of prostatic carcinoma. For this purpose, they injected 2 ml. of colloidal chromic phosphate containing 10 mc. of P-32 directly into the pituitary substance. We have performed this procedure in 6 patients with far-advanced carcinoma of the prostate in order (1) to evaluate the effect of destruction of the pituitary body on cancer of the prostate, and (2) to investigate the clinical usefulness of this particular method of destroying the pituitary body. The results obtained are presented.

TECHNIC

After a frontotemporal flap is turned, the frontal lobe is retracted gently until the diaphragm sellae is identified. With the exception of the first patient, 0.5 to 1.5 ml. of a solution containing 9-10 mc. of P-32 (Table 2) as colloidal chromic phosphate was injected into the substance of the gland, using a 25-gauge needle. Three ml. of this solution were injected into the pituitary body of the first patient. The subsequent patients received less than 1.5 ml. of the chromic phosphate solution because injections of aqueous methylene blue into the normal pituitary body at autopsy showed that volumes greater than this resulted in marked overflow of the dye. At least four sites of injection were used in an attempt to distribute the radioactivity throughout the gland. Methylene blue was added to the colloidal material so that leakage of the radioactive solution superiorly could be detected and removed by washing with copious amounts of saline. The pituitary stalks in Cases 4, 5 and 6 were clipped and severed prior to the injection of P-32.

Preliminary studies performed on normal pituitary glands at autopsy had shown us that the injected material diffuses fairly evenly throughout the substance of the gland. Usually, any excess of injected material escapes from the sella by migrating laterally and inferiorly under and between layers of the dura mater. Dye can be identified beneath the dura mater behind the posterior clinoids when more than 1 ml. is injected. There is also leakage superiority out through the top of the sella when large volumes are injected, but when the injected volume is less than 1 ml. this does not usually occur. Since the sella has a capacity of less than 1 ml. it would seem reasonable to limit the volume injected to less than this amount in order to minimize leakage and in this way avoid excessive irradiation of nearby neurologic structures.

CASE MATERIAL

The patients chosen for this procedure had far-advanced metastatic carcinoma of the prostate gland. Each had had symptomatic improvement following orchiectomy except Patient 2 who had not improved after this procedure and Patient 4 who had refused orchiectomy. All patients required narcotics for relief of pain. Each of these patients had become refractory to estrogen therapy before pituitary destruction was attempted. All patients had biopsy proof of prostatic carcinoma. Table 1 summarizes the clinical and