THE EFFECT OF PITUITARY-STALK SECTION ON THYROID FUNCTION AND GONADOTROPIC-HORMONE EXCRETION IN WOMEN WITH MAMMARY CARCINOMA*

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(Received for publication February 23, 1969)

The rationale of attempting to modify the course of advanced mammary carcinoma by transecting the pituitary stalk has been discussed in a previous publication. Preliminary observations on the small group of patients reported previously were sufficiently encouraging to warrant an extension of these studies in a larger group of women. Studies have been carried out to compare the known effects of hypophysectomy with the physiological alterations that occur in humans when the pituitary gland is isolated surgically from its normal anatomical connections with the hypothalamus. A detailed study of adrenal function in these patients has revealed that the ACTH feedback mechanism virtually is abolished following section of the stalk, although the ability of the adrenal glands to secrete cortical hormones in response to "stress" is diminished only in proportion to the adrenal atrophy that occurs. Additional studies of adrenal function and the course of mammary carcinoma following section of the stalk will be reported subsequently. The present paper will report the effect of pituitary-stalk section on thyroid function and gonadotropic-hormone excretion.

MATERIALS AND METHODS

Thirty-four women between the ages of 32 and 69 years were selected for operation. All of them had advanced mammary carcinoma. Many had been treated previously by mastectomy and oophorectomy or with exogenous hormones such as androgens and estrogens. The pituitary stalk was visualized through a right frontal craniotomy and divided. In the early cases a plate of tantalum was placed between the divided ends of the stalk. Autopsy material in some instances showed that revascularization of the pituitary body by the hypophyseal-portal vessel system had occurred in some patients around the margins of the plate. For this reason in later cases the entire pituitary fossa was covered by a sheet of polyethylene in addition to the metal plate.

The 24-hour uptake of I\(^{131}\) was measured after the oral administration of carrier-free N\(^{131}\)\(_{2}\) using formula No. 2 as described by the Oak Ridge Institute for Nuclear Studies. When serial counts were obtained correction was made for radioactivity remaining in the gland from previous studies.

The protein-bound iodine was measured by a modification of the method described by Barker. The gonadotropin assay was carried out on 24-hour collections of urine which were stored in a refrigerated container without preservatives. Aliquots were shipped promptly by air to another laboratory for assay. The gonadotropin content was

* These investigations were supported by research grants from the National Institutes of Health, Grants CY 3348(C4S1) and A 1022, The Elsa U. Pardee Foundation, The United Fund, and by an Institutional Grant from the American Cancer Society.

† The PBI values and gonadotropin assays were performed by Bio-Science Laboratories, Los Angeles, California.
assayed by the immature-mouse uterine-weight method after preliminary concentration of the urine on kaolin.

RESULTS

The effect of section of the stalk on the $^{131}$I uptake is charted in Fig. 1. In this hospital a 24-hour uptake of 15 per cent is considered to be the lower limit of the normal range. Twelve patients had a normal uptake of $^{131}$I before operation and in all of these individuals the postoperative uptakes were reduced sharply. In 11 of them the postoperative values fell within the hypothyroid range and in 1 the postoperative values were within the low euthyroid range. The fall in $^{131}$I uptake occurred as early as the second postoperative day (the earliest that it was measured).

The $^{131}$I uptake values of 7 patients were abnormally low before operation. Many of the patients previously had been subjected to multiple diagnostic and surgical procedures and it is possible that some of the low uptake values resulted from exposure to iodine in either inorganic or organic form. In 2 of these individuals the uptake tended to rise in subsequent determinations and in 1 instance it reached the euthyroid range. Because of technical difficulties the pituitary stalk of this patient could not be severed and other parameters of her endocrine function remained normal. None of the other patients regained uptake levels above 15 per cent during the period of observation although upward trends were noted in some patients.

Effect on PBI. Data are available on 17 patients before and after operation. These data are plotted in Fig. 2. The two elevated values were obtained in individuals who were clinically euthyroid. One of them was known to have had bronchography many months previously. All but 1 patient exhibited a postoperative fall in her protein-bound iodine level. An additional patient had a postoperative rise in PBI level but later became hypothyroid with a PBI of 3.2 µg per 100 ml. of plasma. In 9 patients one or more values fell below 4µg. per cent. Symptoms of hypothyroidism which were judged to be sufficiently severe to require substitution therapy were encountered in only 4 patients. Late postoperative rises in PBI levels occurred in 4 patients after an initial fall. One of the 3 patients whose postoperative values fell to the hypothyroid range regained a normal level after many months.

Effect on Gonadotropic-Hormone Excretion.