CLINICAL STUDY OF A PATIENT SUFFERING FROM
INTENSE THIRST AND POLYURIA (DIABETES IN-
SIPIDUS) AND PRESENTING X-RAY EVIDENCE
OF MALIGNANT PROCESSES IN THE CRA-
NIAL BONES, POSSIBLY LATE METAS-
TASES OF MAMMARY CARCINOMA

ERNEST S. CROSS, M.D.

BALTIMORE, Md.

Recently there came under our observation a patient who had developed intense thirst and polyuria, which seemed to be associated with the appearance of malignant metastases in the bones of the skull. The case would seem to be of sufficient importance to put on record.

ANAMNESIS

The patient, who was brought to us for consultation by her family physician, was a woman of 58 years, the wife of a well-to-do business man.

She complained chiefly of excessive thirst, of very frequent urination, of weakness, of peculiar morning vomiting and of marked disability in the lower part of the back.

The family history was negative except that one sister had died of metastases of a cancer of the breast.

The patient herself had ordinarily been well except for chronic constipation. She had had four children and three miscarriages, and had passed the menopause at 43 with no remarkable symptoms. At 48 the left breast was removed by a competent surgeon because of a tumor, supposed to be a carcinoma.

The present illness had its beginning seven months before consultation. The patient noticed pain in the back and in various joints, especially the shoulders, knees and hips; but there was neither redness nor swelling and the pain in the various joints was inconstant and variable. The development of bilateral sciatic pain forced the patient to remain in bed for a short time.

Simultaneously with the development of these symptoms referable to the locomotor system, there appeared intense thirst and frequent urination. There was also marked anorexia, slight nausea and some morning vomiting of mucoid froth.

Gradually the sciatica and joint pains grew less and the patient was able to get about, though she still suffered from marked disability of the back. The gastric symptoms, however, continued as did

the polydipsia and the polyuria. At times a little clotted blood appeared in the throat, apparently coming from the posterior nares. There were two attacks of diffuse erythema of the legs, each attack lasting a day or two, to be followed by scaling. Twice there was transient diplopia while motoring. There was weakness and much loss of weight. The patient stated that, at times, she voided more than a gallon of urine in twenty-four hours. There was some itching of the skin. There was no headache. All the teeth had been removed four months before consultation.

STATUS PRAESENS

Examination at the time of our consultation showed a pale, feeble woman, still well nourished despite much recent loss of weight. Pupils and eye muscles showed no abnormalities. Ears and hearing were normal. The tonsils were small, slightly irregular, and showed a few occluded crypts. There was no thyroid struma. A few small retrocervical glands could be felt, but otherwise there was no glandular enlargement. The scar of the left breast operation was in excellent condition. The lungs were negative. The heart was normal. The pulse rate was 96. The blood pressure measured 120 to 130 systolic and 80 diastolic. There was no appreciable thickening of the peripheral blood vessels. There was a little tendency to round back, and the movements of the whole spine were very stiffly carried out. The most discomfort appeared to be localized in the lumbar region. The abdomen showed nothing remarkable. The deep reflexes and abdominal reflexes were normal. The sign of Babinski was negative. Neither sciatic region was tender and Kernig's maneuver caused no unusual discomfort.

LABORATORY REPORTS

During the weeks just preceding consultation, numerous careful, special examinations had been made in the hope of throwing more light upon the condition. The main results of these tests follow.

Blood Examination: Red blood cells, 3,752,000; hemoglobin, 75 per cent; white blood cells, 5,800; blood Wassermann, negative; blood sugar, 121 mg. per cent; blood nitrogen, 30.5 mg. per cent; blood creatinin, 1.5 mg. per cent.

Urine Examination: Sp. gr., 1,002; acid; no albumin; no sugar; in the sediment no casts, but occasional pus cells were found. Tests of the urine were made repeatedly with negative results, except for persistently low specific gravity (usually about 1,002). The amounts of urine were always large for each twenty-four hours.

Examination of Stomach Contents: Free HCl, 12 acidity per cent; total acid, 40 acidity per cent; lactic acid, absent. The stomach contents were examined on several different occasions; once small blood clots were present in the stomach washings.

Feces: Occult blood was found in the stool on one occasion.

Cerebrospinal Fluid: Clear; 5 cells; Wassermann reaction negative; tests for globulin, negative.

X-RAY STUDIES

Five months before our examination evidence of infectious arthritis of the thoracic and lumbar spine was visible in roentgenograms, but nothing further could be made out. Three weeks before consultation various long bones had been studied by means of the x-ray, on suspicion of a possible malignant condition, but nothing was found, and the arthritic changes in the spine were regarded as sufficient explanation of the symptoms in the back. The gastrointestinal tract had also been carefully studied roentgenologically, but no evidence of any lesion in the stomach or intestines beyond adhesions in the right upper quadrant of the abdomen was obtained.

NOSE AND THROAT EXAMINATION

An ulcer had been found on the left aspect of the nasal septum. It was believed that this might explain the occasional appearance of blood in the nasopharynx, the blood clots once found in the stomach content, and, perhaps, also the occult blood in the feces.

SUMMARY

On summing up the situation, the principal features were as follows:

1. Loss of weight and strength.
2. Gastric symptoms, including nausea, morning vomiting and anorexia.
3. Polyuria and polydipsia.
4. Disability of the spine.

Of these, the fourth was easily explicable, apparently, on the basis of x-ray findings of infectious arthritis of the spine. No local cause had been found for the gastric symptoms. The loss of weight and strength and the general appearance of the patient made one fearful of a malignant process somewhere in the body, but none had been revealed. The urinary studies, blood findings and blood pressure were all rather against the polyuria being a manifestation of chronic nephritis, and there was nothing to suggest that it was of hysterical origin.

EFFECT OF INJECTIONS OF PITUITRIN

It seemed best to investigate next the effects of pituitrin upon the polyuria. The amount of urine excreted during the twenty-four hours preceding was found to be 3,000 cc. One milligram of pitui-

trin was injected, hypodermically, twice a day for two days. During the first twenty-four hours after injection the urinary output was 2,500 cc., the amount of water ingested 2,000 cc. During the second twenty-four hours the urinary output was 2,000 cc., and the amount of water ingested was the same. The nausea was definitely less and the nocturia was reduced to two urinations the first night of the test and to one the second night.

EYES AND EYE GROUNDS

The eye grounds were carefully examined and found to be perfectly healthy. Central vision was good. The fields of vision, however, showed marked contraction for form and for colors. The ophthalmologist's report reads: "Without knowing anything of the general complaint of the patient, the markedly contracted fields point strongly toward hysteria."

X-RAY FINDINGS IN THE SKULL

X-ray studies of the skull showed normal paranasal sinuses, including the sphenoidal sinus. The sella turcica was of the flat, open type with no sign of any destruction of the base, or of the clinoid processes. Scattered through the cranial bones, particularly in the parietal and frontal regions, there were numerous rarefied areas of bone destruction, showing no evidence of new bone formation; the process in the bones was apparently invasive in character, in every way resembling the changes in malignancy.

COURSE AND TERMINATION

The patient's condition changed but little while under our observation. The cutaneous itching was controlled by a mild carbolic ointment. The polyuria became less marked and required no further use of pituitrin. The gastric symptoms persisted. About two weeks after our examination the patient gradually became dull, then comatose, and died on the third day of the coma, according to the report of the family physician, with evidence of increased intracranial pressure.

DISCUSSION OF SPECIAL FEATURES

The case presents a number of interesting possibilities and problems.

(1) In the first place, what was the origin of the apparently malignant processes in the bones of the skull? The lesions were multiple and certainly metastatic in origin. Repeated careful search was made for a primary, malignant process in the body; none was found, though this does not, of course, exclude the existence of such a lesion. Can we connect the sup-

posed left breast cancer, removed ten years earlier, with these metastases? The possibility must, of course, be kept in mind. Ordinarily, we feel pretty safe, in a cancer case, if the patient is entirely well three years after operation; and after five years, one is accustomed to look upon the cancer as cured. Crouzon and others, however, have reported late multiple metastases in the brain in two cases after removal of the breast for cancer. In one of these, the metastases occurred eighteen years after, and, in the other, twenty years after operation. The interval in our case was ten years.

We know, also, that carcinoma of the breast is the commonest cause of bone metastases in women, just as carcinoma of the prostate is the commonest cause in men. The order of frequency of the bones showing such metastases in women is as follows: Ribs, thoracic spine, lumbar spine, ilia, femur, skull and humerus. In this connection, it may be said that we were a little suspicious of a malignant process in the lumbar spine, though at the time of the x-ray examination there was no visible evidence of it.

(2) It would seem highly probable that the intense thirst and the polyuria exhibited by the patient should be viewed as evidence of the existence of a mild diabetes insipidus. The patient said that she had frequently voided more than a gallon of urine in twenty-four hours, though even this is, of course, a small amount in comparison with the quantities passed in many of the reported cases of diabetes insipidus. Many such cases have certainly suffered from diseases of the pituitary gland or of the floor of the third ventricle in its neighborhood. In our case, it seems reasonable to infer the presence of a metastatic growth in the region of the pituitary or of the floor of the third ventricle. Negative x-ray findings in the region of the sella would be expected, unless the growth had been of sufficiently long standing to bring about bone destruction. Many of the reported cases of diabetes insipidus have shown tumors in the region of the pituitary when examined post mortem.

(3) Can our case be related to the remarkable condition recently reported by Christian? His case was an exceedingly interesting one, that of a child of five years presenting the symptom complex of: (1) Extensive defects in the bones of

the skull; (2) exophthalmos, and (3) diabetes insipidus. There were also less marked defects in the pelvic bones. Christian cites two other cases showing similar bony defects in the skull; one was that of a young boy with dystrophia adiposogenitalis and exophthalmos; the other that of a girl of four years with exophthalmos and diabetes insipidus. In the latter case, the x-ray revealed a defect in the right ilium and a spindle-like thickening in the upper part of the right femur. These two cases cited by Christian had been reported by Schüller, and in both instances, basilar intracranial tumors presumably existed; basilar tumors would not account, however, for the areas of bone destruction seen in the cranium in both cases nor for the additional defects in the pelvis and femur seen in one of the cases, particularly since the physical condition of both children was too good to allow one to accept the theory of the existence of metastases. Christian believes that the bony defects in all three cases are to be explained by changes in the function of the pituitary gland.

It does not seem probable that our case falls in the group just cited, since the x-rays in our patient revealed irregular-shaped, scattered areas, suggestive of an invasive, destructive process, whereas in the three cases reviewed by Christian, the bony margins of the defects were very sharply and clearly defined.

CONCLUSIONS

In retrospect, we should be inclined to regard the case reported here as one of multiple, malignant metastases in the bones of the skull, at the base of the brain, and, possibly, also in the lumbar spine. It is probable that the involvement of the base of the brain affected the mechanism regulating water metabolism, so that symptoms of mild diabetes insipidus developed. The origin of the metastases is uncertain, but it is quite possible that they were secondary to the breast cancer removed ten years before.

BIBLIOGRAPHY

- Baetjer, Frederick H. & Waters, Charles A.: *Injuries and diseases of the bones and joints*. N. Y., 1921. Paul B. Hoeber. 349 p.
- Christian, H. A.: Defects in membranous bones, exophthalmos and diabetes insipidus: an unusual syndrome of dyspituitarism. *M. Clinics N. Am.* (Phila. & Lond.), 1920, iii, No. 4, 849-872.
- Crouzon, O., Behague, P., & Bertrand, I.: Concréreuses multiples du cerveau Bull. et mém. Soc. méd. d hôp. de Par., 1920, 44, 500.
- Futcher, T. B.: Diabetes insipidus, with a report of five cases. *Johns Hopkins Hosp. Rep.* (Balt.), 1902, 10, 197-247.
- Schüller, A.: Ueber eigenartige Schädeldefekte im Jugendalter. *Fortsch a. d. Geb. d. Röntgenstrahlen* (Hamb.), 1915, 23, 12-18, 1 pl.