Gallium-67 Breast Uptake in a Patient with Hypothalamic Granuloma (Sarcoid)

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An unusual case is presented of bilateral breast uptake of [^{67}Ga]citrate in a patient with a hypothalamic granuloma in the absence of galactorrhea is presented. A possible mechanism for this incidental finding is elevated prolactin levels, as other causes of gallium breast uptake such as drug therapy, and intrinsic breast disease, were not present.

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Uptake of gallium-67 (^{67}Ga) citrate in the breast is well documented [*1–12*). Its accumulation in the mammary tissue with subsequent excretion into human milk has been demonstrated by physical and chemical studies (*3,7,10*). Several physiologic, pathologic, and drug-induced states have been linked to this phenomenon (*1–9,11,12*).

We present a case of bilateral gallium breast uptake in a patient with a hypothalamic granuloma (sarcoid) and discuss the possible anatomic and physiologic basis for this scintigraphic finding.

CASE REPORT

A 36-yr-old white female with a previously documented suprasellar mass was admitted with a 1-mo history of increasing headaches and vomiting. The patient was well until 1½ yr prior to admission when 4 mo after the birth of her first child, menses did not resume. (The patient did not subsequently breastfeed). Prolactin levels drawn at an outside hospital were elevated and a head computed tomographic (CT) scan showed a suprasellar mass. Replacement hormone therapy was initiated at the outside hospital for presumed panhypopituitarism although thyroid function studies were normal. The patient subsequently developed symptoms of diabetes insipidus for which she received antidiuretic hormone therapy.

On physical examination, there was no evidence of galactorrhea. Visual fields were full and visual acuity was 20/20. Motor, sensory, and cerebellar testing were all normal. The remainder of the examination was unremarkable. As part of the diagnostic evaluation, an elevated prolactin level of 35.1 ng/ml (nl 15–20 ng/ml) was found. CT scan of the sella again revealed a suprasellar mass. In order to evaluate this mass further, an MRI (Figs. 1*A* and *B*) was obtained that clearly demonstrated a hypothalamic mass. A PPD skin test, as well as controls, were negative but the patient was receiving cortisone therapy. Previous PPDs prior to steroid therapy, however, were negative. Histoplasmosis antibody test was within normal limits.

Following this initial workup the patient underwent a right frontal craniotomy with biopsy. At surgery, a swollen and fixed optic chiasm surrounded by a gray-yellow nonresectable hypothalamic mass was found. Biopsy revealed a granulomatous tumor that in view of the pathology and tumor location was felt to be most consistent with sarcoid. Acid-fast stains and stains for fungi were negative. Because of the specimen size, special histologic stains could not be performed. In order to investigate granulomatous involvement in other sites, a gallium scan was obtained revealing a normal distribution of the radiotracer except for intense bilateral breast uptake (Figs. 2*A* and *B*).

The patient had an unremarkable postoperative course and was discharged on antidiuretic hormone, progesterone and estrogen replacement. Hydrocortisone replacement was to begin following discharge. Postoperatively, the patient's menses returned and she experienced only one episode of headache and vomiting. Blood work after discharge showed a normal Total T4, binding ratio, free T4, T3, and TSH. Despite negative ACE (angiotensin converting enzyme) the patient was still felt to have sarcoid.

DISCUSSION

The breast is the primary site of action of prolactin (*13*). Together with other hormones such as estrogen and progesterone, it is responsible for the development of mammary tissue and the stimulation of lactation (*13,14*). Prolactin is crucial in the synthesis of milk proteins (*13,14*), and, in fact, is necessary to maintain

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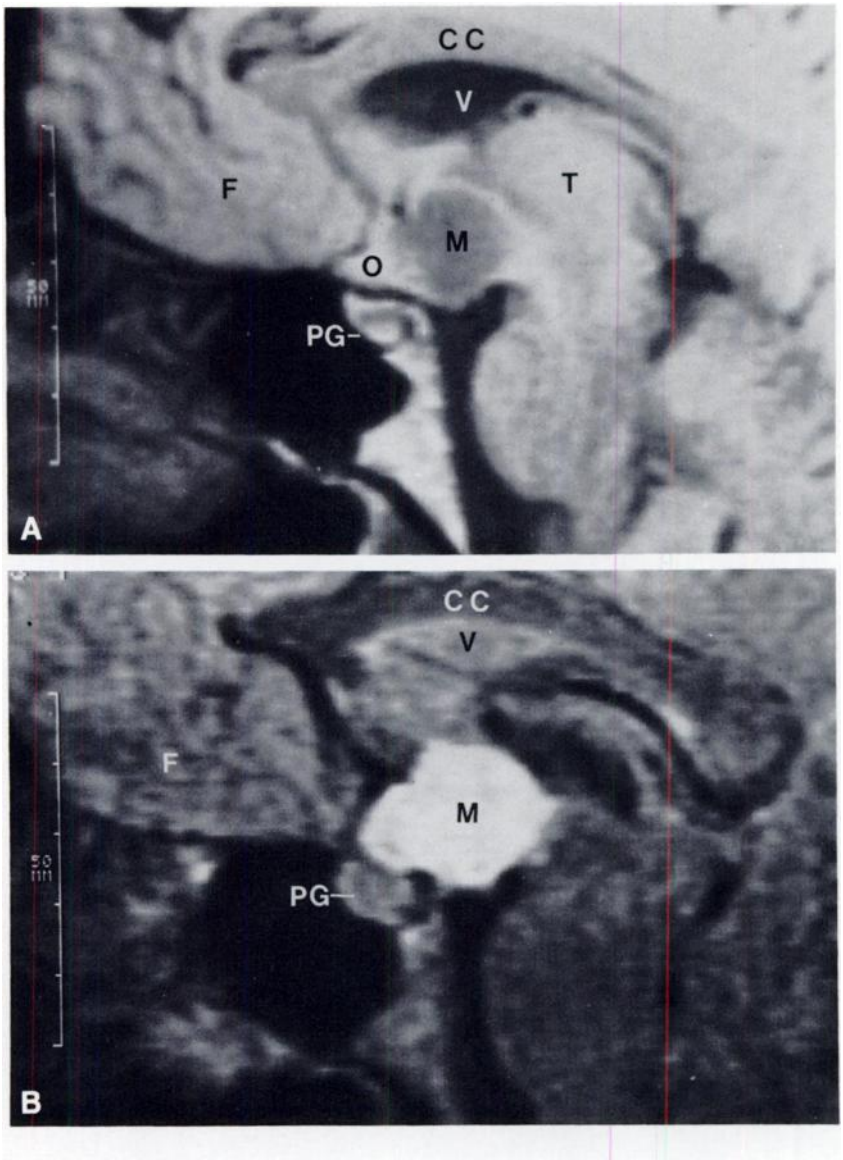

FIGURE 1
A: Sagittal (T_1-weighted) MR image of the sella and suprasellar region clearly demonstrating a hypothalamic mass (M) of intermediate signal intensity. B: Sagittal (T_2-weighted) MR image at a similar location showing the mass (M) with a higher signal. PG = Pituitary gland, T = Thalamus, CC = Corpus callosum, V = Lateral ventricles, F = Frontal lobe, O = Optic chiasm.

lactation once it has been initiated (*13*). It is this milk production (high in lactoferrin) which is likely one element responsible for ^{67}Ga uptake in the prolactin stimulated breast. It is known that ^{67}Ga when injected intravenously binds to transferrin. It has been shown experimentally, however, that ^{67}Ga binds preferentially to lactoferrin rather than to transferrin when challenged with both agents (*10*). In studies of human milk, it has also been shown that when ^{67}Ga is incubated with lactoferrin from human milk, it is noted to bind preferentially to the lactoferrin and not to other milk proteins. Since lactoferrin constitutes ~15% of the total protein content of milk (*15*), the presence of lactoferrin in human milk and the affinity of ^{67}Ga for lactoferrin may well be a mechanism of ^{67}Ga uptake in the prolactin stimulated breast.

Several other etiologies for ^{67}Ga uptake in the breast have been described (*1–9,11,12*). Some of these cases are related also to elevated prolactin levels (*2–4,6,9*) and these include normal physiologic responses (e.g., puberty, pregnancy, and the postpartum period). Drug therapy can also produce breast uptake of ^{67}Ga and these include drugs such as reserpine, imipramine, metochlopromide, meprobramate, and phenothiazines (*7–9*). Some of the drug-induced breast uptake of ^{67}Ga may be a result of drug-induced hyperprolactinemia. It is of note, however, that previous reports of drug-induced ^{67}Ga uptake in the breast make the point that the uptake in this scenario is not as intense as that seen in the postpartum state (*9*).

There are other causes of ^{67}Ga uptake in the breast unrelated to high prolactin levels and these include diseases intrinsic to the breast such as primary adenocarcinoma, lymphoma, fibrocystic disease, sclerosing adenosis, cystosarcoma phylloides, abscess, and metastasis (*3,5,9,11,12*).

In our case, the prominent bilateral breast uptake occurred in the presence of an elevated prolactin level but in the absence of galactorrhea, breastfeeding, or any other known breast pathology. In addition, such levels

of prolactin elevation and degree of ^{67}Ga uptake would not be a normal physiological response in a 4-mo postpartum state (*9–14*). Drug-induced uptake of ^{67}Ga in the breast can occur, although the amount of uptake which has been reported does not equal that of the postpartum state (*9*). The very intense breast uptake of ^{67}Ga in our case, therefore, was felt to be most likely secondary to the known elevated prolactin levels. In view of the fact that it is known that infiltrating hypothalamic tumors, specifically sarcoid, can produce hy-

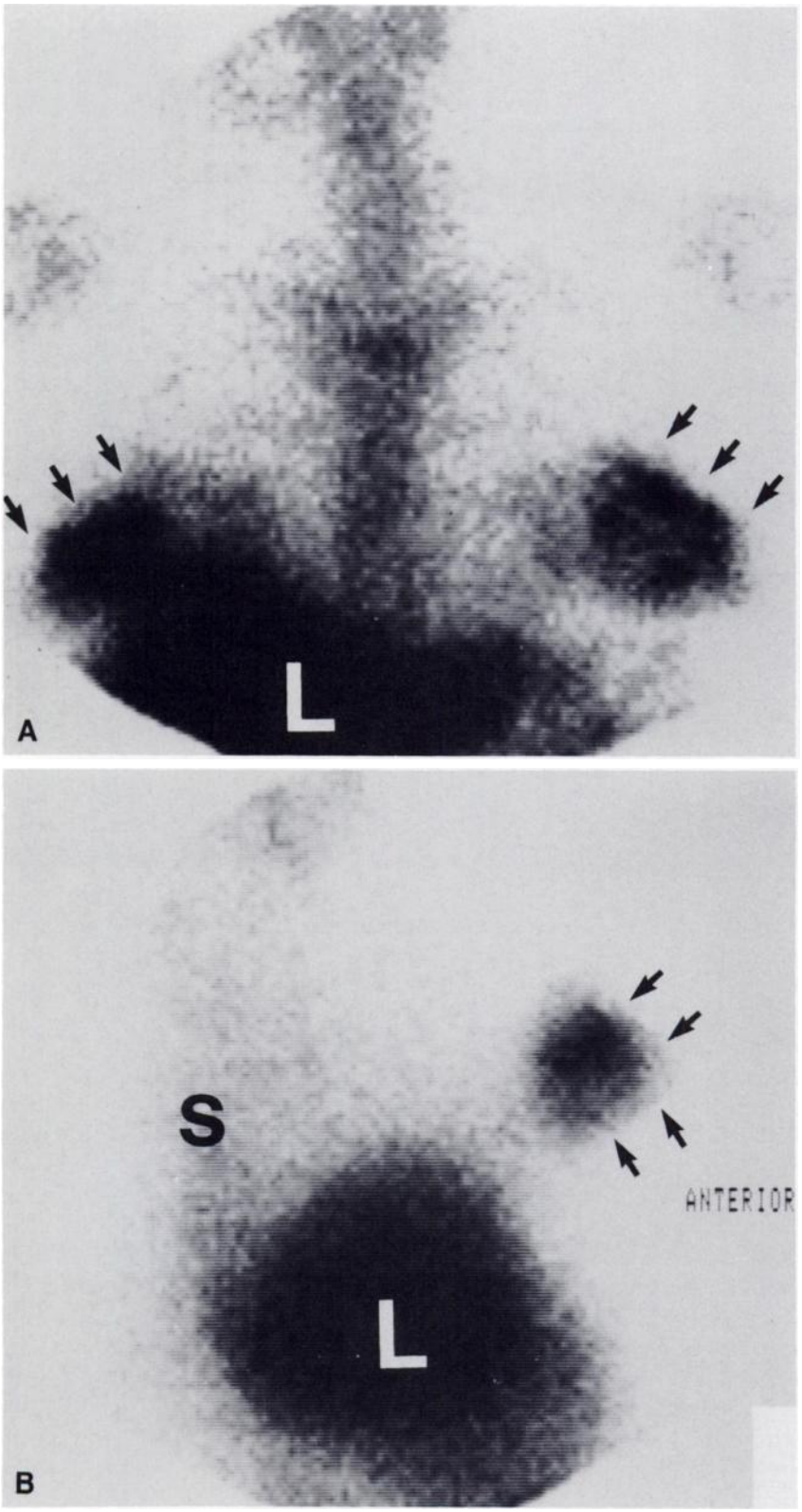

FIGURE 2
A: Anterior and B: Right lateral views of the chest at 96 hr post-i.v. administration of 5.3 mCi of [^{67}Ga]citrate clearly demonstrating prominent bilateral breast uptake (arrows) (L = liver, S = spine).

perprolactinemia (*16*), the intense uptake in our patient can best be explained by an unusual anatomic and physiologic interruption of the hypothalamic-pituitary axis by the hypothalamic granuloma (sarcoid). We postulate that this lesion produced uninhibited secretion of prolactin and resulted in the marked uptake of ^{67}Ga within the breasts.

The nuclear medicine physician should be aware of all possible mechanisms for this incidental scintigraphic finding since the physician may be the first one to lead the clinician to the discovery of unsuspected pathologic conditions.

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