Appearance of Hyperostosis Frontalis Interna on Indium-111 Leukocyte Scans: Potential Diagnostic Pitfall

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The appearance of hyperostosis frontalis interna on an [^{111}In]leukocyte scan is reported. Recognition of the potential for normal accumulation of ^{111}In-labeled white blood cells within this common process involving the skull is necessary to avoid misdiagnosis.

J Nucl Med 27:495–497, 1986

Whole-body scintigraphy of indium-111- (^{111}In) labeled leukocytes is a well-established clinical tool for the detection of occult inflammatory processes (*1–5*). Several hours after injection, the normal distribution of the radiolabeled leukocytes includes the liver, spleen, and bone marrow. Activity accumulated in any other site is considered abnormal. The occasional accumulation of leukocytes in areas not associated with abscesses, however, has created potential pitfalls in the accurate diagnosis of inflammatory processes (*6,7*). We report a case in which focally increased activity in the frontal regions of the calvarium was correlated with a diploic thickening of the frontal bones (hyperostosis frontalis interna) shown by transmission computed tomography (TCT).

CASE REPORT

A 79-yr-old female was admitted for myocardial infarction. Two days later, she acutely developed symptoms of left hemispheric cerebral infarction which was confirmed by TCT. Simultaneously, she developed a fever without obvious cause and became progressively obtunded. Amikacin sulfate was begun. Two weeks later, persistence of the fever and the new development of abdominal pain prompted an [^{111}In]white blood cell (WBC) scan. Twenty-four hours after autologous leukocytes labeled with 500 μCi of ^{111}In had been injected, images revealed an abnormal focus of inflammatory cells accumulating in the region of the rectosigmoid (Fig. 1A) and increased activity in the frontal regions of calvarium (Fig. 1B). A repeat TCT (Fig. 2A) again revealed the mass effect and contrast enhancement pattern of a left MCA infarction. The contralateral side was normal, however, and there was no evidence for cerebritis, meningitis, or any other bilateral inflammatory process. Bone windows and lateral scout view revealed the characteristic findings of hyperostosis frontalis interna, with thickening of the internal tables of the frontal bone and widening of the diploic space (Fig. 2B).

On sigmoidoscopy there were the typical changes of pseudomembranous enterocolitis and cultures grew *Clostridium difficile*. After vancomycin therapy was instituted, fever and abdominal symptoms subsided.

DISCUSSION

The demonstration of inflammatory bowel disease, including pseudomembranous colitis, with [^{111}In]WBC scintigraphy has been previously reported (*13,14*). Cytopathic effects of the *Clostridium difficile* toxin are responsible for the clinical and pathologic manifestations of pseudomembranous colitis. This diagnosis should be entertained in any patient on aggressive antibiotic therapy who manifests symptoms of colitis and exhibits colonic accumulation of [^{111}In]WBCs. Appropriate alteration of antibiotic therapy usually leads to resolution.

We are unaware of any other report of increased cranial [^{111}In]WBC activity associated with hyperostosis frontalis interna. In a review of 53 prior [^{111}In]WBC whole-body scans in our clinical experience, this is the only patient to have demonstrated a focal increase in the activity of the frontal bones in a bilateral and

Received Mar. 12, 1985; revision accepted Nov. 26, 1985.

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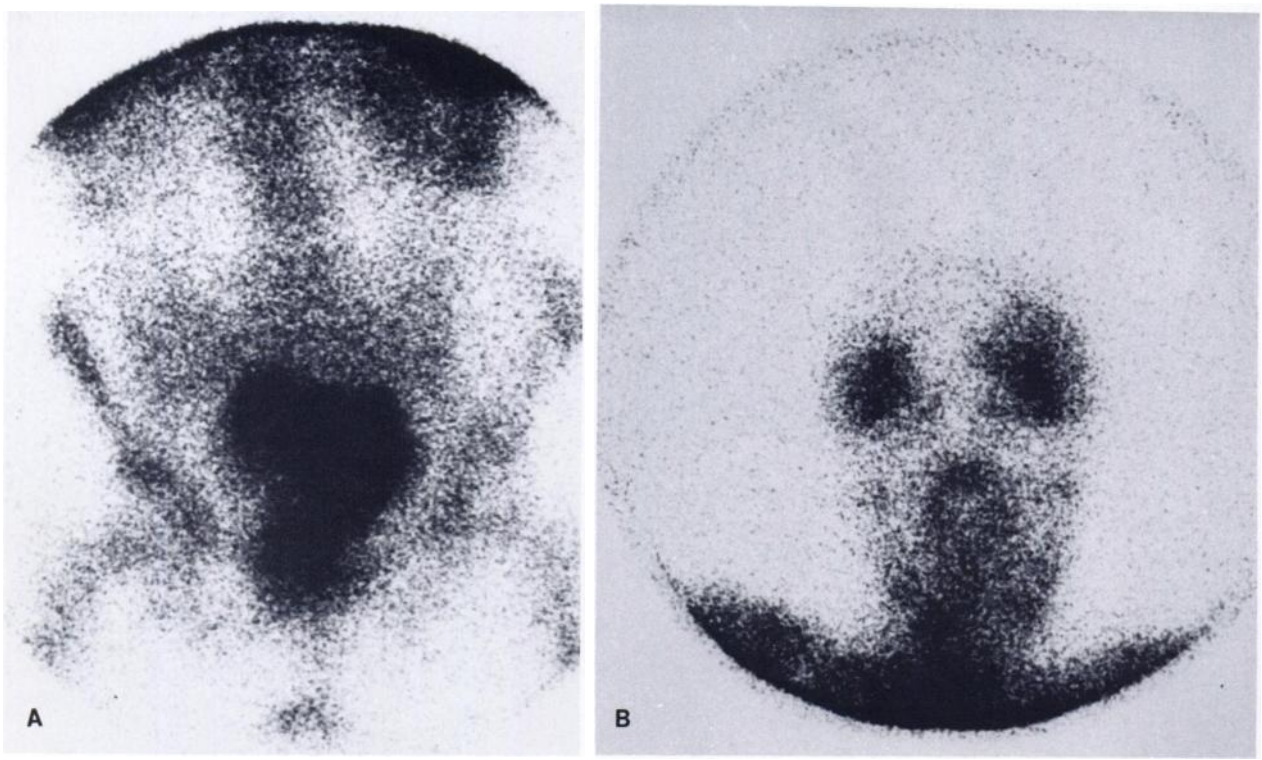

FIGURE 1
A: Anterior pelvis view at 24-hr demonstrates rectosigmoid accumulation of labeled white cells. B: Anterior view of head with ^{111}In activity in frontal regions of calvarium

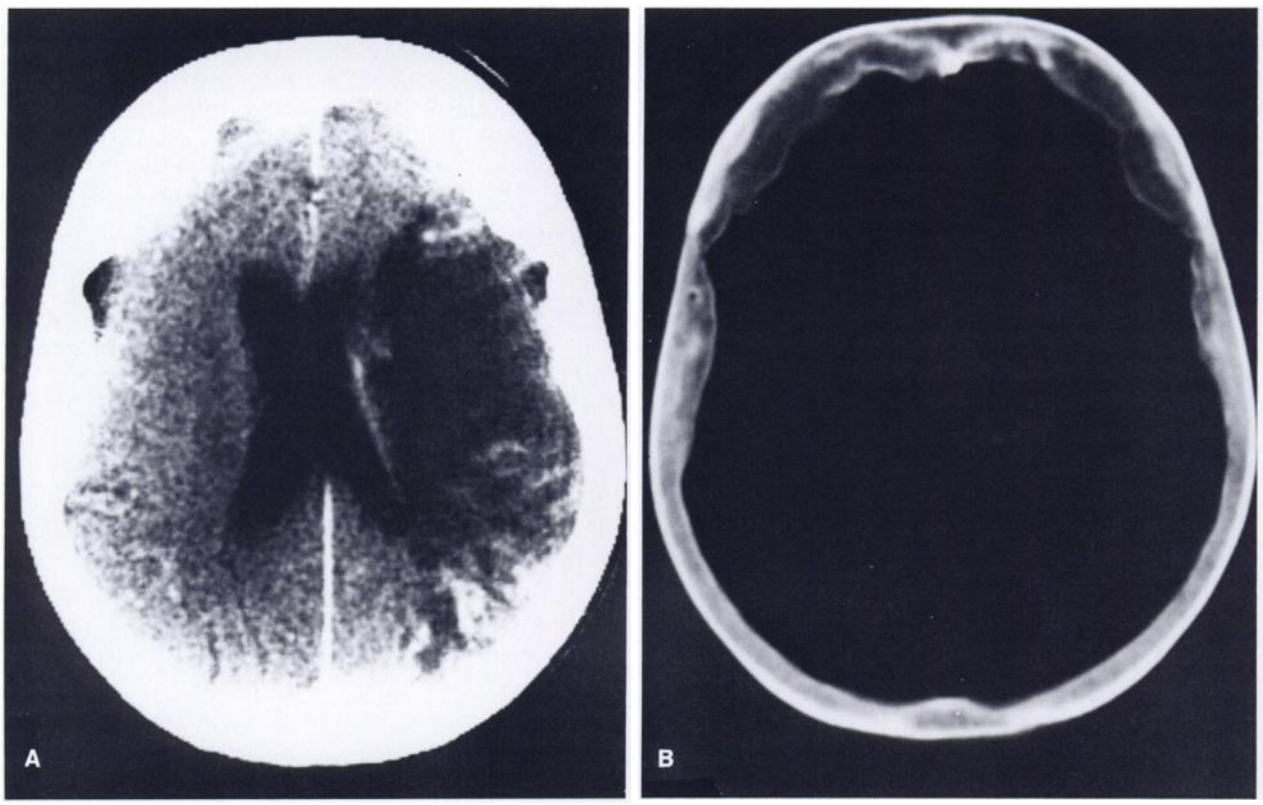

FIGURE 2
A: Transmission CT of left middle cerebral infarct. There are no associated abnormalities on right. B: CT scan at bone window settings demonstrating characteristic changes of hyperostosis frontalis interna

symmetrical fashion. The tracer activity seen in the calvaria of the other 53 patients was much less intense and never focal.

In this case, we considered the possible accumulation of [^{111}In]WBCs within a cerebral infarction, as has been previously reported (*6*). Perivascular accumulation of polymorphonuclear leukocytes within the area of a cerebral infarction occurs to a minor degree within the first 24 hr, but this is never a major component in the brain's pathologic response to the ischemic insult (*8*). In this case, the ^{111}In activity was symmetric and accumulated in an area anatomically separate from the area of infarction as demonstrated by the CT scan. For these reasons, we believe that it is very unlikely that the infarction was the cause of the ^{111}In activity.

A recent case report of the bilateral accumulation of [^{111}In]WBCs in a patient with meningitis has also been reported (*9*). However, the CT scan in our patient was not consistent with meningitis or other intracranial inflammatory cause for the reported activity, and the patient's subsequent clinical course was not in keeping with this diagnosis.

Hyperostosis frontalis interna, a benign disorder of the skull, predominately affects the inner table of the frontal bone. It is usually seen in women over the age of 40 yr, although men may also be affected (*10,11*). Pathologic examination reveals excessive diploic bone with thinning of the inner and/or outer tables of the skull (*12*).

Investigations into the use of ^{111}In-labeled leukocytes have demonstrated that activity will appear in the bone marrow normally (*1,6*). Whether this activity is the result of accumulation of leukocytes or some other ^{111}In compound within the bone marrow is not known.

The increased diploic space with associated bone marrow in hyperostosis frontalis interna could result in the increase in ^{111}In activity observed in this patient. It is not known what percentage of patients with hyperostosis frontalis interna will demonstrate increased uptake of activity on [^{111}In]leukocyte scan. Knowledge of the potential appearance of symmetrical activity in the frontal bones in this condition should prompt follow-up skull radiographs in the future to help clarify this association.

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