very useful for predicting prognosis for patients with meningiomas.

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Technetium-99m-HMPAO Brain SPECT in Anorexia Nervosa

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Eating disorders have been redefined in recent years. Brain imaging techniques are useful in demonstrating the association between the morphologic and the functional cerebral changes in these cases. We report ^{99m}Tc-HMPAO brain SPECT findings in two patients with anorexia nervosa, before and after the treatment. While the detailed neurologic and laboratory examinations, including EEG and cranial CT, were within normal limits before therapy, SPECT study revealed diffuse bilateral hypoperfusion in frontal, parietal and frontotemporal areas which was more prominent in the left hemisphere. Post-treatment SPECT studies obtained after a clinical remission period of 3 mo showed normal brain perfusion in both patients. The pre- and post-treatment SPECT studies accurately reflect the functional state of the patients, and this technique may be used to follow-up the effect of treatment and predict the clinical response to therapy in patients with eating disorders.

Key Words: technetium-99m; HMPAO brain SPECT; computerized tomography; anorexia nervosa

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Anorexia nervosa is a behavioral disorder characterized by refusal to maintain body weight at or above a minimally normal weight for age and height. There is a significant disturbance in the individual's perception of the shape or size of the body and denial of the seriousness of the current low body weight (*1*).

There is an increased interest in the functional and structural cerebral changes in psychiatric disorders in the last decade. Recent studies with brain imaging techniques not only investigate the basic pathological condition in a specified disease, but also help to identify the activation phases and to discriminate the different clinical states, such as remission and exacerbation of the same disease process (*2*).

The limited number of brain imaging studies in anorexia nervosa failed to give uniform results, the main pathological finding being the cerebral cortical atrophy detected in some patients using CT (*3*). MRI studies revealed a smaller cross-sectional area of the pituitary gland and thalamus (*4,5*). An early PET study in anorectic patients revealed normal cortical glucose metabolism (*6*), while another study showed increased metabolism of the caudate nucleus in anorexic state returning to normal levels after realimentation (*7*). In a recent PET study, the underweight anorectic group showed a global hypometabolism and an absolute, as well as relative, hypometabolism of glucose in cortical regions most marked in the frontal and parietal cortices as compared to controls (*8*).

These confusing results obtained by the neuroimaging studies are mainly due to methodological discrepancies and patient selection criteria. Moreover, evaluating the patients in remission will probably lead to a better understanding of eating disorders. In this study, we investigated cerebral blood flow using ^{99m}Tc-HMPAO brain SPECT of two patients with anorexia nervosa, both at the time of diagnosis and after remission of symptoms.

CASE REPORTS

Patient 1

A 16-yr-old woman presented with a 14-mo history of intentional loss of weight (17% of the initial weight), refusal of eating because of morbid fear of weight gain, and amenorrhea for the previous 8 mo. She also had provocative vomiting.

During the last year of her college education as a successful student, although not overweight, she began dieting with the intention of losing weight. Initially, the weight loss was not recognized by the family. Gradually, she started to drop out of classes, while spending most of her time at home. Ten months after the onset of symptoms, obvious weight loss as well as the emergence of binge and purge cycles alarmed the family and she was brought for treatment.

During the initial visits, the psychiatric evaluation of the patient revealed defective self-regulatory functions, regressive pseudo-

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oedipal conflicts and an immature ego. Psychometric examinations ruled out additional psychiatric disturbances and depression. The Eating Attitudes Test (EAT) score was 68 (*9*), while the Hamilton Depression Rating Scale (*10*) score was 14. The Minnesota Multiphasic Personality Inventory (MMPI) (*11*) profile of the patient was inconsistent with any comorbid Axis I and II disorders. Laboratory tests including the serum glucose or electrolytes, urinalysis and endocrine profile were within normal limits, and no organic pathology consistent with the weight loss or secondary amenorrhea was found. Cranial CT as well as EEG were within normal limits.

After the diagnosis of binge eating and purging type anorexia nervosa was established by two independent interviewers according to Diagnostic Statistical Manual of Mental Disorders-IV (DSM-IV) diagnostic criteria (*1*), the patient was introduced to a therapeutic program, with dietary counseling and individual psychotherapeutic measures. The therapy was initially supportive, followed by both supportive and cognitive-behavioral measures. Pharmacotherapy was given as fluovoxamine 100 mg daily during the first 8 mo of the treatment. Furthermore, the patient participated in outpatient group therapy.

During the second year of the treatment, there was an apparent improvement in her behavioral pattern and interpersonal relationships. The symbiotic pattern was not evident, and the individualization process was more conspicuous. She had remissions in binge/purge cycles lasting for long periods, and her weight was normalized. The EAT score decreased to 20.

Patient 2

An 18-yr-old woman presented with a 16-mo history of weight loss (19% of her initial weight). Although she was underweight, she had provocative vomiting in order to prevent weight gain. She had amenorrhea for the previous 7 mo.

Being the last child of a conservative family, she was described as a quiet and conscientious student. The refusal of eating started during the adolescence period when she became an attractive girl and began to think about marriage. Progressive weight loss promoted anxiety and concern within the family, and several physicians were consulted without reaching a definitive diagnosis. During that time, binge-purge cycles emerged so that she decided to come to the psychiatry outpatient department without informing her family.

Psychiatric evaluation revealed impulsiveness, disturbance of interpersonal relationships and preoccupation with body image. She reported a decline in academic performance. The MMPI profile revealed no comorbid Axis I or II disorder (*11*). The Hamilton Depression Rating Scale (*10*) score was 12, while the EAT (*9*) score was 55. The results of detailed laboratory tests, including CT and EEG, were within normal limits.

A diagnosis of binge eating and purging type anorexia nervosa was made by two independent psychiatrists and outpatient treatment with dietary counseling, as well as psychotherapeutic measures was instituted. For the initial 6 mo of treatment, 20 mg fluoxetine was given daily. One year after the patient's admission, her eating pattern improved and her weight increased by 10 kg. She restarted her education and formulated long-term plans to cope with family conflicts.

MATERIALS AND METHODS

The SPECT study consisted of two steps. Pretreatment SPECT was performed after intravenous injection of 592–666 MBq ^{99m}Tc-HMPAO 4–6 wk after the diagnosis of anorexia nervosa was established and the laboratory tests were completed. Patients were neither dehydrated nor on drug treatment. The patients did not have any binge-purge cycles and unprescribed drug intake before the study. Images of the head were acquired over 60 angles through 360°, with each angle being collected for 30 sec on a dual-headed rotating gamma camera equipped with a high-resolution collimator. Images were obtained in a quiet and semidark room with the patient's eyes open. Total acquisition time was approximately 30 min. Data were stored on a computer in a 64 × 64 matrix. After the patient remained free of symptoms for at least 3 mo and off medication for at least 6 mo, the SPECT study was repeated with the same dose of ^{99m}Tc-HMPAO and the same acquisition parameters as the pretreatment study.

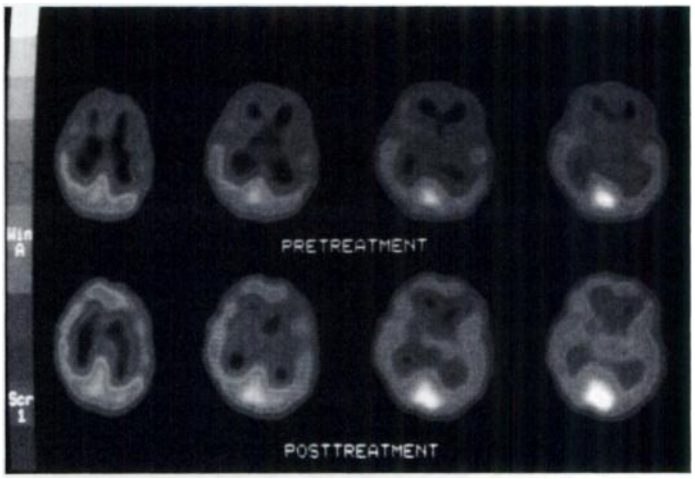

FIGURE 1. Upper row: pretreatment SPECT study; four sequential transaxial consecutive slices of Patient 1 show diffuse hypoperfusion in frontal, frontoparietal, parietal and frontotemporal cortices which is more prominent in the left hemisphere. Lower row: post-treatment SPECT study; four sequential transaxial slices of the same patient show that cortical hypoperfusion is no longer apparent.

After doing backprojection, image reconstruction was performed using Butterworth and Ramp filters with an attenuation coefficient of 0.12, cutoff frequency of 0.39 and power factor of 10. Transaxial slices were obtained parallel to the orbito-meatal line. Transaxial, coronal and sagittal slices were generated in the pixel size of 6 mm. Slices were analyzed visually and quantitatively. For quantitative analysis, the mean counts/pixel was calculated for 11 regions of interest (ROIs) on four sequential transaxial slices and for one ROI outlining the cerebellum. Pairs of ROIs were mirrored from the right hemisphere to the left using a semiautomated technique. Count density was calculated for each ROI and region-to-cerebellar ratios were obtained for pretreatment and post-treatment studies. From these normalized values, the asymmetry between pretreatment and post-treatment studies of the same region was expressed as follows:

$$\% \text{ Asymmetry index} = 100 \times 0.5 \frac{(\text{Region post-treatment} - \text{Region pretreatment})}{(\text{Region post-treatment} + \text{Region pretreatment})}.$$

RESULTS

At the initial evaluation, the results of the EEG and CT studies were within normal limits, while SPECT revealed bilateral frontal, parietal and frontotemporal hypoperfusion. The left hemispheric hypoperfusion was more prominent. At the end of 1.5 yr of treatment, with the patients having been in remission for 3 mo, a control SPECT was obtained (Fig. 1, 2). Interestingly, the previously demonstrated hypoperfusion was no longer seen. Asymmetry indexes between post-treatment and pretreatment studies ranged from 3%–8%, compatible with the visual analysis of both of the patients.

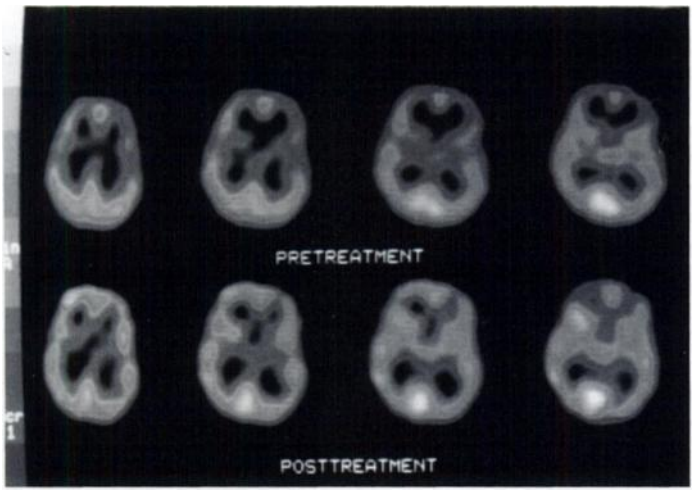

FIGURE 2. Upper row: pretreatment SPECT study; four sequential transaxial consecutive slices of Patient 2 show hypoperfusion in the same regions as in Patient 1. Lower row: post-treatment SPECT study of the same patient shows that cortical perfusion is normal.

DISCUSSION

Metabolic factors such as protein loss and fluid retention due to malnutrition were proposed to be causally related with the early CT and EEG findings in anorectic patients (*17,18*). Validating this hypothesis, our patients with normal CT and EEG findings neither had fluid-electrolyte disturbances nor protein malnutrition. Moreover, the absence of cortical atrophy in our cases can be interpreted as a positive prognostic factor because of lack of structural changes (*8*).

Previous studies demonstrated a close correlation between cerebral blood flow and the neural activity (*2*). Our study shows bilateral frontal and parietal hypoperfusion in two untreated and underweight anorectic patients. Similarly, cerebral hypometabolism more prominent in the frontal and parietal cortices was observed in a recent PET study (*8*). The reversibility of perfusion abnormalities after treatment in our cases is striking.

Although identical cerebral blood flow changes were reported in patients with depression (*12–14*) and other psychiatric disorders (*15,16*), none of our patients was depressed or had comorbid Axis I and II disorders. Moreover, no medication was administered during the SPECT studies. This suggests that observed changes in cerebral blood flow in our patients may be directly related in some way to the disease process.

Apart from the metabolic factors in these patients, one must take into account other disturbances such as sensitivity to cognitive cues. As a matter of fact, Nozoe et al. (*2*) proposed that the cognitive functions related to feeding may considerably influence the cerebral blood flow of the frontal cortex. Similarly, Delvenne et al. (*8*) hypothesized a primary corticocerebral dysfunction in these patients supported by cognitive studies. Although, the mechanism of the cerebral hypoperfusion observed during the active disease period, and re-establishment of normal cerebral perfusion in remission in our cases, is unknown our patients showed improvement not only in the pathological eating habits but also in the cognitive-behavioral domain during remission. It is difficult to establish a cause-effect relationship between the cerebral hypometabolism and eating behavior in anorexia nervosa. Whether severe dieting in these patients causes a metabolic imbalance ending up in cerebral hypometabolism as well as cognitive-behavioral symptoms or a primary corticocerebral dysfunction leads to a disorder with pathological eating habits can only be answered by future studies. Although this study does not exclude some unknown direct effects of different eating habits on cerebral metabolism, the cognitive factors also can be accounted for by the changes in cerebral perfusion and cerebral neural activity.

CONCLUSION

The reversible cerebral hypoperfusion demonstrated in the pre- and post-treatment SPECT images without a CT abnormality suggests that perfusion differences in this study reflect the functional state of these patients. The cognitive factors appear to play an important role. Although the limited number of cases in this study precludes definite conclusions and makes additional studies mandatory, SPECT can be used to monitor treatment and the images can add much to the clinical descriptions of the psychiatric disturbances.

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