

Cerebral Blood Flow Abnormality Observed With Tc-99M Hmpao Spect in Reversible Dementia Caused by Hypothyroidism

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ABSTRACT

The clinical presentation of hypothyroidism varies considerably and may be dominated by cognitive deficits and psychological symptoms. A 49 year-old male patient came to our clinic with symptoms of forgetfulness, decrease in communication, difficulty in remembering and learning, and difficulty in building sentences. Due to these complaints he was diagnosed as suffering from depressive pseudodementia and possible Alzheimer's disease by other physicians. His routine blood investigation revealed a decrease in T3 and T4 levels, an increase in TSH level, and high levels of antithyroid antibodies. In addition, thyroid ultrasound showed diffuse hypoechogenity of the thyroid gland. The patient was diagnosed as suffering from Hashimoto's Thyroiditis. In addition, his depressive and dementia symptoms were thought to be caused by hypothyroidism. Neuropsychological testing supported the diagnosis of depression and dementia. No pathological findings were found in the patient's cranial magnetic resonance imaging (MRI), but single-photon emission computed tomography (SPECT) analysis labelled with 99m Technetium hexamethylpropyleneamineoxime (Tc-99m-HMPAO) demonstrated regional cerebral hypoperfusion, as is mostly seen in degenerative dementias. After treatment with L-thyroxine, his depressive symptoms and impairment in the neuropsychological testing mostly disappeared. However, cerebral hypoperfusion in his following brain SPECT continued over an observation period of one year. In this article, we aim to review neuropsychiatric disorders related to hypothyroidism and the importance of SPECT analysis in their diagnostic investigations.

Keywords: hypothyroidism, dementia, SPECT

ÖZET

Hipotroidiyle Ortaya Çıkan Reversibl Demansta Tc-99M HMPAO Spect Tetkikinde Gözlenen Serebral Kan Akımı Anormalliği

Hipotiroidin klinik tablosu oldukça değişken olup bazen bilişsel etkilenim ve psikiyatrik belirtiler ile kendini gösterebilmektedir. Kırk dokuz yaşında erkek hasta, nöroloji polikliniğine unutkanlık, içe kapanma, öğrenmede ve kelime bulmada güçlük yakınması ile başvurmuştur. Daha önceden bir yıl süreyle benzer şikâyetlerle gittiği hekimler tarafından depresif psödodemans ve muhtemel Alzheimer Hastalığı ön tanılarıyla izlenen hastanın rutin biyokimyasal incelemelerinde T3 ve T4 düzeylerinde düşüklük ve TSH düzeylerinde yükseklik saptanmıştır. Tiroid antikorları yüksek olarak saptanan hastanın tiroid ultrasonografisinde diffüz hipoekojenite saptanmış ve bu bulgular ile hastaya Hashimoto Tiroiditi tanısı konmuştur. Klinik depresyonu ve demansı nörokognitif testlerle doğrulanan hastanın şikâyetlerinin hipotiroidiye bağlı olabileceği düşünülmüştür. Kranial manyetik rezonans görüntüleme (MRG)'sinde patoloji saptanmayan hastanın, Technetium-99m-hegzametilpropilaminoksime (Tc-99m-HMPAO) ile işaretli beyin tek foton emisyon bilgisayarlı tomografisinde (single photon emission computed tomography: SPECT) daha çok dejeneratif demans tablolarında görülmesi beklenen bölgesel serebral hipoperfüzyon izlenmiştir. Hastanın L-tiroksine tedavisi sonrası, depresif belirtileri gerilemiş, nörokognitif testlerindeki bozulma tama yakın düzelmiştir. Ancak, bir yıllık takip süresince tekrarlanan SPECT incelemelerinde daha önceden saptanan patolojinin devam ettiği izlenmiştir. Bu makalede olgumuz temelinde hipotiroidi ile ilişkili nöropsikiyatrik bozukluklar ve bu tablolardaki tanısız yaklaşımlarda SPECT incelemesinin yeri tartışılmıştır.

Anahtar Kelimeler: hipotiroidi, demans, SPECT

INTRODUCTION

Thyroid dysfunction may induce various neuropsychiatric disorders, and hypothyroidism is one of the common causes of treatable dementia (Yilmaz et al. 2005). In the general population, the prevalence rate of autoimmune thyroiditis (Hashimoto's disease) is about 5% to 12% (depending on the criteria used for definition), and it manifests with characteristic high titers of autoantibodies (Flynn et al. 1998, Placidi et al. 1998). Research in the area of regional cerebral blood flow (rCBF) in hypothyroidism has been continuing since 1998. One of the most helpful assessment tools in this area is brain SPECT. The changes in rCBF in SPECT studies have been reported to be reversible or irreversible. In addition, the pattern of this rCBF abnormality has not yet been fully understood (Dugbarney 1998, Zettinigg et al. 2003). We have described a patient with hypothyroidism dementia and clinicoradiological response to treatment.

CASE

A 49 year-old male patient, an attorney at law, came to our clinic with symptoms of fatigue, forgetfulness, difficulty in remembering and learning, and difficulty in building sentences. He was diagnosed as suffering from depressive pseudodementia and possible Alzheimer's disease and at that point was treated with a combination of serotonin reuptake inhibitor and acetylcholinesterase inhibitor (20 mg/day paroxetine, 5mg/day donepezil) over the following 12 months. No pathological findings were found in the patient's cranial magnetic resonance imaging (MRI), MRI angiography and carotid-vertebral Doppler ultrasonography assessments. The patient's routine blood work revealed a TSH: 15.65 mIU/ml (normal range: 0.34-5.60 mIU/ml), freeT4: 0.61 ng/dl (normal range: 0.58-1.64 ng/dl), freeT3: 2.6 pg/ml (normal range: 2.99-6.11 pg/ml), anti-thyroid auto-antibody: 212 IU/ml (normal range: 35 IU/ml) and a diffuse hypoechogenicity of the thyroid gland in ultrasound was detected. In light of these findings, the patient was diagnosed with Hashimoto's Thyroiditis by the endocrinologist. His Mini-Mental State Examination (MMSE) score was 30/30 and Hamilton Depression Scale (HAM-D) score was 14/52. The patient was started on a course of escitalopram 10 mg/day after stopping paroxetine treatment and L-thyroxine 0.1 mg/day by a psychiatrist and an endocrinologist, respectively. Acetylcholine esterase inhibitor treatment was also stopped. Neuropsychological tests were administered by a psychologist. These tests included Wechsler Adult Intelligence Scale Revised (WAIS-R) and Wechsler Memory Scale Revised (WMS-R). Technetium-99m-HMPAO brain single-photon emission computed tomography (SPECT) was used to evaluate cerebral perfusion. Neuropsychological testing and brain SPECT were repeated in the third and sixth months of, and after one year of L-thyroxine supplementation.

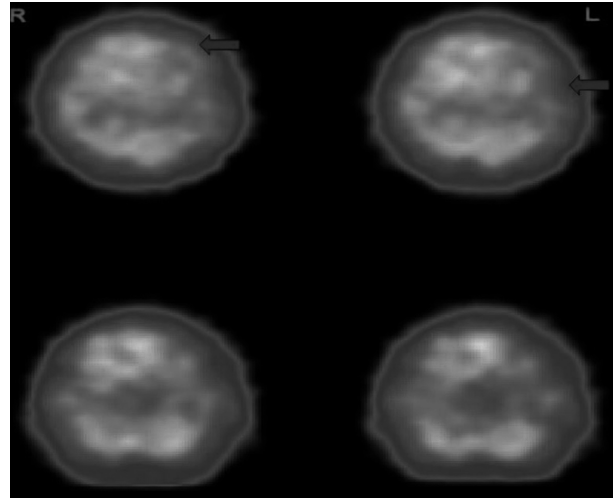


Figure-1: Hypoperfusion in the left parietotemporal lobe and the left frontal lobe at the transversal plane of Tc-99m-HMPAO brain SPECT.

tium-99m-HMPAO brain single-photon emission computed tomography (SPECT) was used to evaluate cerebral perfusion. Neuropsychological testing and brain SPECT were repeated in the third and sixth months of, and after one year of L-thyroxine supplementation.

In the first analysis, minimal impairment in performance was found in attention and in immediate memory index of visual memory tests. On the other hand, significant impairment was found in measures of immediate and delayed memory index of verbal memory tests and delayed memory index of visual memory tests. SPECT analysis demonstrated a significant rCBF decrease in the left parietotemporal lobe and the left frontal lobe (Figure-1). At the end of the third month of the pharmacological treatment, the thyroid hormone levels and the TSH were at normal levels, but the decline in verbal memory and in delayed memory index continued in neuropsychological tests. The HAM-D score was 10/52. At the end of the sixth month, the delayed memory index was found to be normal in neuropsychological tests, with a HAM-D score 3/52. After psychiatric evaluation, escitalopram medication was gradually stopped. The hypoperfusion continued in the same region on the SPECT assessment. After one year of follow-up, his antithyroid antibodies and thyroid hormone levels had been normalized by the L-thyroxine treatment. Despite his clinical improvement and a good performance in neuropsychological testing, there was no change in the patient's brain SPECT

DISCUSSION

Thyroid disease should be considered primarily in patients presenting with depression and cognitive decline

(Hall et al. 1992). The patient was diagnosed primarily as suffering from pseudodementia and possible Alzheimer's disease by other physicians previously. But later on, after endocrinological evaluation, he was diagnosed as having Hashimoto's Thyroiditis due to the decrease in thyroid hormone levels. Then, we thought his symptoms were related to hypothyroidism. Although the clinical presentation of hypothyroidism is heterogeneous, patients with a progressive dementia or depression should be evaluated for evidence of chronic autoimmune thyroiditis with T3, T4, TSH, and antithyroid antibodies (Dayan and Daniels 1996).

Forchetti et al. (1997) reported reversible cerebral hypoperfusion in a case of subclinical hypothyroidism caused by Hashimoto's Thyroiditis during the hypothyroid state. Autoimmune cerebral vasculitis or disruption of the cerebral microvasculature by autoantibody or immune complex deposition was suspected as a cause of the encephalopathy in their case. In the current case, anti-thyroid auto-antibody was positive, as in their patient, and the same mechanism may have been involved. In comparison to the above mentioned example in our case hypoperfusion in SPECT was not diffuse and it persisted despite thyroid hormone levels being normalized.

Brain SPECT showed hypoperfusion in left parietotemporal and left frontal lobes in our case. In the literature, although the hypoperfusion in SPECT studies is usually observed as being diffuse, it is found in bilateral temporoparietal and frontal regions in patients with autoimmune thyroiditis (Zettinig et al. 2003).

The area of the brain involved in this case was the left hemisphere. These findings demonstrate some similarities with Alzheimer's disease (Jagust et al. 2001). Decreased rCBF has been previously reported in some cases of

hypothyroidism (Krauzs et al. 2004). The mechanism of this abnormality in these cases, as in ours, has not yet been fully understood.

Follow-up studies are needed to determine the longer-term persistence of perfusion abnormalities in this disorder.

REFERENCES

- Dayan CM, Daniels GH (1996) Chronic autoimmune thyroiditis. *N Engl J Med*; 335: 99-107.
- Dugbartey AT (1998) Neurocognitive aspects of hypothyroidism. *Arch Intern Med*; 158: 1413-1418.
- Flynn SD, Nishiyama RH, Bogos ST (1998) Autoimmune thyroid disease: immunological, pathological, and clinical aspects. *Crit Rev Clin Lab Sci*; 26: 43-93.
- Forchetti CM, Katsamakis G, Garron DC (1997) Autoimmune thyroiditis and a rapidly progressive dementia: Global hypoperfusion on SPECT scanning suggests a possible mechanism. *Neurology*; 49: 623-629.
- Hall RCW, Popkin MK, Vaul RD, et al (1992) Psychiatric manifestations of Hashimoto's thyroiditis. *Psychosomatics*; 23: 337-342.
- Jagust W, Thisted R, Devous S (2001) SPECT perfusion imaging in the diagnosis of Alzheimer's disease. A clinical-pathologic study. *Neurology*; 56: 950-956.
- Krauzs Y, Freedman N, Lester H, et al (2004) Regional cerebral blood flow in patients with mild hypothyroidism. *J Nucl Med*; 45: 1712-1715.
- Placidi GP, Boldrini M, Patronelli A (1998) Prevalence of psychiatric disorders in thyroid-diseased patients. *Neuropsychobiology*; 38: 222-225.
- Yılmaz M, Çıtak S, Karamustafaloğlu O (2005) Hipotiroidizme bağlı psikotik bozukluk: bir olgu sunumu. *Klinik Psikofarmakoloji Bülteni*; 15: 22-26.
- Zettinig G, Asenbaum S, Fueger BJ, et al (2003) Increased prevalence of subclinical brain perfusion abnormalities in patients with autoimmune thyroiditis: Evidence of Hashimoto's encephalitis? *Clin Endocrinol*; 59: 637-643.