

# **GEP-NET:**

## **CNS Manifestations of Primary Hyperparathyroidism**

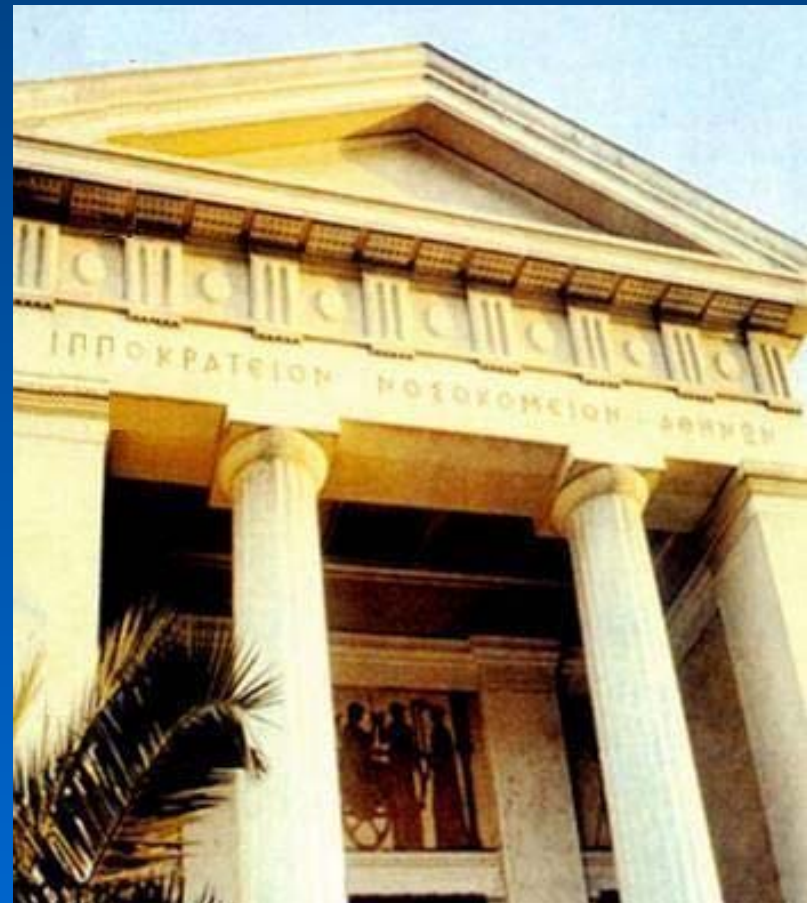
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## **Delirium as the predominant manifestation of hyperparathyroidism: reversal after parathyroidectomy.**

KLEINFELD M, PETER S, GILBERT GM.

**J Am Geriatr Soc 32:689-90, 1984**

A 67-year-old woman who had primary hyperparathyroidism presented with delirium rather than dementia as the predominant psychologic manifestation.

After surgical removal of a parathyroid adenoma, there was a dramatic improvement in mental status.

Psychologic retesting at six weeks after discharge showed her to be well oriented to time, place, and person, with no impairment of cognitive capacity.

## **New onset of neuropsychiatric symptoms in the elderly: possible primary hyperparathyroidism.**

WATSON LC, MARX CE. *Department of Psychiatry, University of North Carolina at Chapel Hill, NC 27599-7105, USA.*

**Psychosomatics 43:413-7, 2002**

Hypercalcemia due to primary hyperparathyroidism may be accompanied by neuropsychiatric symptoms, ranging from mild depression and cognitive changes to extreme agitation and psychosis.

Surgical intervention almost invariably reverses these symptoms.

# CNS Manifestations of Hyperparathyroidism

Hyperparathyroidism is accompanied by under-recognized psychiatric, cognitive and neurologic manifestations

These manifestations affect quality of life and, albeit rarely may even prove life-threatening for the patients or their environment

# CNS Manifestations of Hyperparathyroidism

- Irritability
- Fatigue
- Lack of concentration
- Lassitude
- Sleep disturbance
- Lack of sexual and emotional interests
- Depression (~ 1 out of 4 patients)
- Intelligence, memory and levels of anxiety are rather not significantly affected

# Major depression due to primary hyperparathyroidism: a frequent and correctable disorder.

Wilhelm SM, Lee J, Prinz RA. Am Surg. 70:175-9, 2004

*University Hospitals of Cleveland, Department of Surgery, Case Western Reserve University, Cleveland, Ohio 44106, USA*

- 35 of 360 patients (10%) that underwent parathyroidectomy for primary HPT between 08/1994 and 09/2002 met DSM IV-TR criteria for major depression.
- Postoperatively:
  - **90 %** stated depression no longer impacted their ability to work or activities of daily living
  - **52 %** reported an improved quality of life
  - **27 %** discontinued preoperative antidepressant medication
  - **27 %** reduced their antidepressant medication dose
- *The reduced need for antidepressant medication (in up to 54 % of patients), **resulted in savings of \$ 700 to 3000 per patient/year***

**Primary hyperparathyroidism: neuropsychiatric manifestations and case report.** ROSENTHAL M, GIL I, HABOT B. *Shmuel Harofe Geriatric Center, Beer-Yaakov, Israel.* *Isr J Psychiatry Relat Sci.* 34:122-5, 1997

An elderly patient with primary hyperparathyroidism and dementia was admitted to a psychogeriatric department because of delusions of new onset.

While hospitalized he had three episodes of delusions that coincided with mild hypercalcemia.

Treatment for the hypercalcemia resulted in rapid remission of the delusional state, but no change in his cognitive abilities or in the severity of dementia.

# Psychosis resulting in suicide in a patient with primary hyperparathyroidism.

OZTUNC S, GUSCOTT RG, SONI J, STEINER M.

Can J Psychiatry 31:342-3, 1986

A patient presenting to the psychiatric unit with symptoms of depression and found to have an organic psychosis.

Elevated serum calcium was detected on admission leading to the diagnosis of primary hyperparathyroidism.

The surgical removal of a parathyroid adenoma was followed by a rapid return of biochemical abnormalities to normal ranges.

In spite of appropriate psychiatric management and fluctuations in the patient's clinical condition, the organic psychosis was unaltered and culminated in suicide 4 months after admission.



# Hypercalcemia in the etiology of puerperal psychosis.

RILEY DM, WATT DC.

*Biol Psychiatry* 20:479-88, 1985

Serum calcium of 53 recently delivered mothers hospitalized for severe puerperal psychiatric illness compared with that of 35 female psychiatric patients and that of 49 normal postnatal women.

Mean corrected and ionized serum calcium values in puerperal psychiatric patients with no personal or family history of psychiatric disorder markedly above the normal range. They were also significantly higher than those of the puerperal psychiatric patients with a personal or family history of psychiatric illness and those of the two control groups.

Modest positive correlation between the degree of hypercalcemia and the severity of the psychiatric illness.

The follow-up of 16 puerperal psychiatric patients indicated that the fall in ionized serum calcium levels correlated positively and significantly with the improvement in rated symptomatology.

Patients with severe puerperal psychiatric disorder can be divided etiologically into two groups:

- The larger proportion is psychiatrically vulnerable,
- In the remainder (about 1/3 of the total), the psychiatric illness appears to be related to a disorder of calcium homeostasis in the puerperium.

# Psychiatric symptoms and cerebrospinal fluid monoamine metabolites in primary hyperparathyroidism.

JOBORN C, HETTA J, RASTAD J, AGREN H, AKERSTROM G, LJUNGHALL S.

*Department of Internal Medicine, University Hospital, Uppsala, Sweden.*

**Biol Psychiatry 23:149-58, 1988**

Prospective study, 32 patients with primary hyperparathyroidism

Compared with a healthy reference group, the patients had pronounced psychiatric symptomatology [CPRS score 17.2 +/- 9.0 (SD) versus 4.4 +/- 2.0], mainly affective in character

The severity of symptoms was not related to the serum calcium or PTH. The majority of the patients had low CSF concentrations of monoamine metabolites (5-HIAA, HVA, and MHPG) and, in particular, those with the most severe psychiatric symptoms had low values for 5-HIAA

**Neuropsychiatric disorders in primary hyperparathyroidism.** HAYABARA T, HASHIMOTO K, IZUMI H, MORIOKA E, HOSOKAWA K. *Jpn J Psychiatry Neurol* 41:33-40, 1987

Two middle-aged women with hypercalcemia (noted during treatment of depression and paranoid state) and with normal metabolism of magnesium, were diagnosed with PHPT.

Case 1: antipsychotics were effective, though transiently, for the mental symptoms other than physical ones. A preoperative EEG showed the presence of sporadic slow waves

Case 2: levodopa and hypercalcemia might have acted synergistically. A preoperative EEG showed the presence of low voltage activity.

After the operation, their mental symptoms disappeared  
as the blood level of calcium was depressed in both  
cases

There was no recurrence for a follow up period of 12  
and 18 months, respectively.

After the operation, the EEG showed an improvement to  
regular hypersynchronous alpha activity in both cases

**Preliminary report: functional MRI of the brain may be the ideal tool for evaluating neuropsychologic and sleep complaints of patients with primary hyperparathyroidism.**

*PERRIER ND, COKER LH, RORIE KD, BURBANK NS, KIRKLAND KA, PASSMORE LV, TEMBREULL T, STUMP DA, LAURIENTI PJ. Department of Surgical Oncology, University of Texas M. D. Anderson Cancer Center  
World J Surg 30:686-696, 2006*

## **METHODS:**

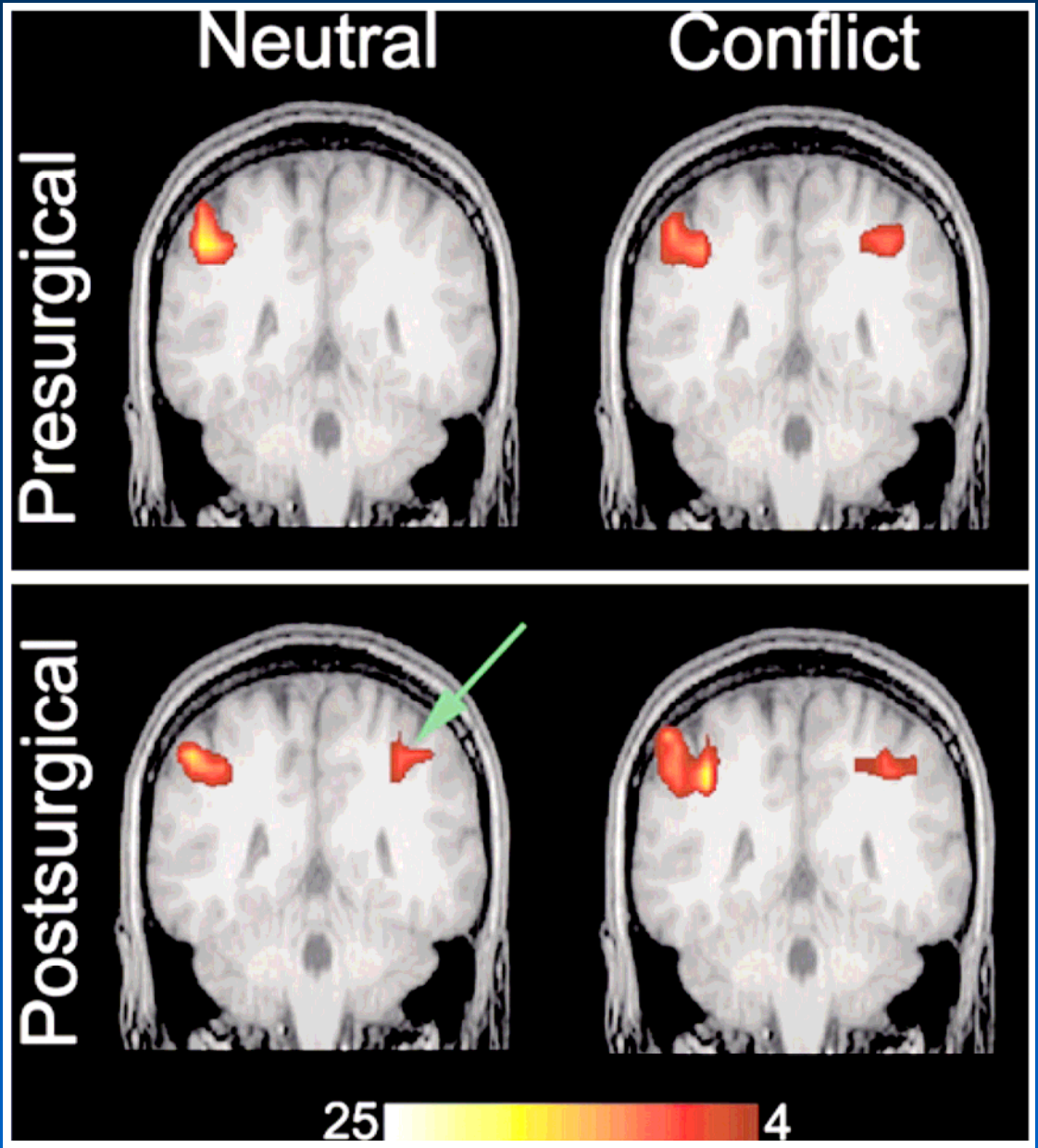
*Prospective analysis before and after parathyroid-ectomy to obtain pilot data on 6 patients with PHPT:*

- **Functional magnetic resonance imaging (fMRI)**
- **Formal neuropsychologic tests**
- **Health-related quality of life (HRQL) measures that included sleep assessment**
- **Changes in cortical activation under both conflict and neutral conditions (distracting tasks)**

Functional MR image showing activity in the posterior parietal cortices during neutral and conflict conditions.

The arrow points to the portion of the parietal cortex in the right hemisphere that was active during the neutral condition, following surgical intervention.

The functional images are overlaid on a template brain image.



## RESULTS:

Postoperatively the patients demonstrated improvements in sleep and social behavior

They tended to experience less fatigue and their processing speed on cognitive tests improved

Functional MRI demonstrated postoperative changes in medial prefrontal cortex activity during cognitive processing of conflict and non-conflict tasks

Postoperative changes were also noted in the dorsolateral prefrontal cortex and parietal cortex with shifts in activations



## CONCLUSIONS:

Preliminary findings reflected a generalized improvement in processing efficiency postoperatively compared with a patient's preoperative state, and the HRQL measures showed improved sleep

These findings mirror those expected with sleep dysfunction. Longitudinal assessment with advanced brain imaging technology, neuropsychological, and sleep evaluations is warranted to further explore cognitive, sleep, and HRQL improvement after parathyroidectomy

These data support the feasibility and willingness of patients with PHPT to undergo fMRI assessment

## Should primary hyperparathyroidism be treated surgically in elderly patients older than 75 years?

CHIGOT JP, MENEGAUX F, ACHRAFI H. *Department of General and Gastrointestinal Surgery, Hopital de la Pitie, Paris, France.*

**Surgery 117:397-401, 1995**

A retrospective study of the charts of 78 patients older than 75 years (mean age, 79.1 years) with PHPT who underwent neck exploration during a 15-year period.

**RESULTS:** The most common presenting symptoms were neurologic and psychiatric disorders (47 patients).

Preoperative localization investigations, performed in 72 patients, were successful in 42 of them (sensitivity, 58%). Single adenoma, double adenomas, and hyperplasia were found in 74 patients (95%), three patients, and one patient, respectively.

Overall postoperative mortality was 3.8% (3 patients) with no death since 1984

Significant complications occurred in three patients (4%): one myocardial infarction, one pulmonary embolism, and one cerebral hemorrhage

Average length of postoperative hospital stay was **4 days**

Among patients who could be followed up (65 cases with a mean follow-up of 3 years), 94% reported an improvement in their symptoms. This was especially marked for fatigue and intellectual function

## **Focused, minimally invasive radio-guided parathyroidectomy: a feasible and safe option for elderly patients with primary hyperparathyroidism.**

BEN HAIM M, ZWAS ST, MUNZ Y, ROSIN D, SHABTAI EL, KURIANSKY J, OLCHOVSKY D, ZMORA O, SCARLAT A, AYALON A, SHABTAI M. *Department of Surgery, Endocrine Surgery Service, Sheba Medical Center, Tel Hashomer, Israel.*

**Isr Med Assoc J 5:326-8, 2003**

22 pts  $\approx$  70 years (70-88 years, mean 76.3 +/- 5.9),  $\text{♁}:\text{♀} = 13:9$  with:

- biochemically proven PHPT
- a single parathyroid adenoma identified by localization studies (sestamibi SPECT scan and ultrasonography)

underwent 23 operations over 29 months

Immediate preoperative sestamibi scintigraphy and marking of focal adenoma uptake followed by intraoperative hand-held gamma probe were used for the removal of the parathyroid adenoma by unilateral minimal access surgery

In 20 of the 22 patients (91%), surgery cured PHPT (1 patient with persistent hypercalcemia -missed adenoma- was treated with a successful repeat operation). There were no complications and no morbidity postoperatively

Mean postoperative serum calcium, phosphorous and PTH were  $9.6 \times 1.2$  mg/dl,  $3.0 \times 0.5$  mg/dl and  $35.2 \times 24$  pg/ml respectively vs mean preoperative  $11.7 \times 1.3$  mg/dl,  $2.5 \times 0.5$  mg/dl and  $160.9 \times 75.4$  pg/ml, respectively. In all 20 patients, serum Ca levels remained normal after long-term follow-up (mean  $17.7 \times 9.6$  months)

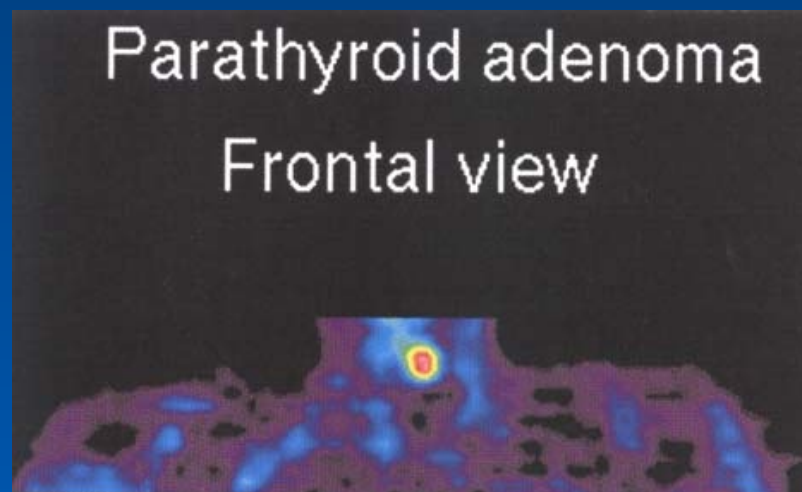
## **CONCLUSIONS:**

Minimally invasive, **radio-guided focused parathyroidectomy** for a **single adenoma** is a safe and effective method to cure hyperparathyroidism in the elderly

Success of surgery is directly related to the surgeon's experience and to the **precise localization marking** provided by **sestamibi scintigraphic SPECT localization** and **concurrent sonographic findings**

# Evaluation of preoperative localization utilizing PET with L-[methyl-C]methionine (MET) in comparison to computed tomography (CT) and ultrasound (US) and to characterize MET accumulation in the different histopathological parathyroid tissue subgroups in correlation with biochemical parameters

Following surgery of the neck for thyroid or parathyroid disease the normal anatomy and fasciae planes are obscured. In the reoperative patient with hyperparathyroidism (HPT) preoperative localization of the enlarged hyperparathyroid tissue is therefore important for the success of repeated surgery.



**MET- PET offers promising potential in the preoperative localization and metabolic characterization of abnormal parathyroid tissue in patients with hyperparathyroidism**

# Conclusions

Parathyroidectomy improves symptoms in many patients, however, alternatives that would provide symptom relief, without surgical intervention would be preferable, especially in the elderly patients, who are more susceptible to psychiatric and cognitive manifestations.

Calcimimetics and non-surgical interventions such as alcohol infusion or ultrasound-guided laser thermal ablation of parathyroid adenomas may represent future alternative therapies.