A PROSPECTIVE STUDY ON JUVENILE PRIMARY HYPERPARATHYROIDISM POPULATION

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INTRODUCTION
Primary hyperparathyroidism (PHPT) is the third most common endocrine disorder in adults and its typical presentation is an incidentally discovered asymptomatic hypercalcemia. It occurs in patients between the age of 50 and 60 years, with an annual incidence of 30 cases per 100,000 individuals and males/females ratio of approximately 2:1. PHPT is uncommon in young people and children. Since the first case described in 1930 by Pemberton and Geddie, studies on Juvenile PHPT (J-PHPT) are few, mostly retrospective and on limited numbers.

The estimated incidence of J-PHPT is 2.5 in 100,000 and without information on sex, J-PHPT seems to be clinically symptomless more frequently than the adult form and typically presents with signs or symptoms of hypercalcemia, skeletal complications, and/or nephrolithiasis. It’s still controversial if this finding is due to a real biologic difference that accounts for the distinct features between PHPT in young and older patients or it’s a bias due to infrequent biochemical testing of children and adolescents.

AIM OF WORK
The aim of the study was to evaluate the clinical, biochemical, densitometric, histological characteristics and outcome in patients with J-PHPT, comparing sporadic (S) and familial (F) J-PHPT.

MATERIALS AND METHODS
PATIENTS
It’s a monocentric prospective study at a referral center. Two hundred patients/year were evaluated in our center in a period of 9 years (2006-2014) and 154 patients with J-PHPT, namely age of <40 years (range 12-40 years), were enrolled in the present study. Patients were fully evaluated at diagnosis and at the last follow-up visit (median follow-up 2 years) by: clinical evaluation, biochemical data collection, densitometric analysis, histology after parathyroidectomy (PTx). Patients were classified in F and S-J-PHPT on the basis of i) familial clinical history, ii) absence of familial PHPT features at physical examination; ii) neuroendocrine markers, calcitonin, pituitary hormones in the normal range at diagnosis and last follow-up visit; iv) serum calcium in first-degree relatives in the normal range. One hundred and twelve patients had S-J-PHPT and 42 patients F-J-PHPT. The latter group included 31 patients with Multiple Endocrine Neoplasia Type 1 Syndrome (MEN1) and 11 with Familial Isolated Hyperparathyroidism (FIHP).

GENETIC ANALYSIS
DNA of index cases of MEN1 and FIHP families was purified from peripheral blood with a commercial kit (Qiagen Blood Minitkit) and the entire coding regions and splice sites junctions of MEN1 gene, were PCR-amplified and a sequencing reaction was performed. In FIHP patients, negative to MEN1 testing, CASR, CDC73, CDKN1B and AIP genes were also analyzed as above described.

RESULTS
Clinical data from all patients are reported in Figure 1. For MEN1 patients we also reported the distribution of pituitary, neuroendocrine and cutaneous lesions (Fig. 1).

In both groups a more severe disease in term of serum Ca++ (S-J-PHPT p=0.039, F-J-PHPT p=0.027), PTH (S-J-PHPT p=0.045, F-J-PHPT p=0.7) and 3rd distal radius Z score (Sporadic p=0.001, Familial p=0.0002) was observed in males compared with females. In contrast, age was not significantly correlated with the severity of disease in term of Ca++ (p=0.4), PTH (p=0.2) and Z score in both groups (p=0.7). In both groups baseline serum Ca++ was significantly associated with PTH levels and severity of bone disease (lumbar, hip and 3rd distal radius Z score) (p<0.001).

When the patients, in the overall group, were stratified for age, ≤25 (n=31) and > 25 years (n=123), serum calcium levels was statistically higher (p <0.024) and 3rd distal radius Z score significantly lower (p=0.009) in younger patients.

In Figure 3 we reported the results of genetic analysis of MEN1 and FIHP patients.

CONCLUSIONS
In conclusion, J-PHPT seems to be a symptomatic disease confirming literature’s data. J-PHPT is more severe in males than in females and has a higher rate of persistence/recurrence disease, even in S-J-PHPT patients. The severity of disease is independ from age and the clinical characteristics are similar between Sporadic and Familial patients.