Letter to the Editor

FAP associated cribiform morular variant of PTC: striking female prevalence and indolent course

Dear Sir;

Ito et al. reported on a large series of 32 patients with cribiform-morular variant (CMV) of the papillary thyroid carcinoma (PTC) detected and treated in a single surgical center between 1991 and 2010. In particular, 19 were sporadic CMV, whereas 12 were with Familial Adenomatous Polyposis (FAP) [1].

We would like to comment on the latter group, i.e. FAP associated CMV-PTC, and to compare data from Ito’s series with those from our large series of 18 subjects with FAP associated PTC, in order to detect similarities and differences. In 16 of 18 of our patients we detected the germ-line APC mutation, which was 5’ to codon 1220 in 14 of 16 (the 2 remaining having mutations at codon 1309) [2-4].

Ito et al. report that in 7 of their cases the APC gene mutation was detected, but we were able to find only 2 mutations (512, exon 9) [5], which were in accordance with our report, suggesting a statistically significant genotype-phenotype correlation. Age of patients was 28.6 year, that was similar to that in our series, as well as the relative detection of FAP and CMV (FAP diagnosis precedent in 7 and subsequent in 5). In our series, diagnosis was concomitant in 1/3, whereas in 1/3 FAP preceded and 1/3 PTC preceded.

The most interesting feature, also similar in both series, was the striking prevalence of FAP associated PTC in females (Patients were all females both in our series and in the Ito’s series). But in a review of the literature after year 2000, the F:M ratio was 80:1, far exceeding the F:M ratio of 2,5 in sporadic PTCs.

Another interesting feature was the indolent course of PTC in FAP patients. In our series, we always performed total thyroidectomy, except in 3 siblings who decided to have hemithyroidectomy. Two had CMV, the last, a 36 yer-old aunt of two systers, had conventional PTC. Despite the presence of lymphonodal metastases, in our cases, none of the 3 had recurrence, either lymphonodal or in the thyroid remnant, with a follow-up longer than 15 years (>180 months) for all 3 siblings.

The last comment concerns FAP associated and sporadic CMV. 1) Even if CMV is an histologic variant which is associated with FAP in more than 50% of cases, not all FAP associated are CMV, even in the same kindred with the same documented APC germ-line mutation. 2) FAP associated PTC occurs quite exclusively in females and, despite multicentricity and lymphonodal involvement has an indolent behaviour (only 1 death because of thyroid related complications out of 200 FAP associated PTCs). On the contrary, sporadic CMV-PTC often occurs in males and there have been various reports of aggressive behaviour.

Therefore, we suggest caution before stating that, despite similar features, these tumors should be considered as a single entity. On the contrary, they should be considered distinct diseases for both demographic features and biological behaviour or prognosis. In particular, we do not support a more conservative approach in sporadic CMV than in FAP associated PTC.

References
