Author's response to reviews

Title: Simultaneous medullary and papillary thyroid cancer: description of two cases

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Author's response to reviews: see over
Response to Reviewer Comments #1

Dear Reviewer,

Thank You for Your general comments on this manuscript “SIMULTANEOUS MEDULLARY AND PAPILLARY THYROID CANCER: DESCRIPTION OF TWO CASES”. Thank you very much for Your collaboration and interest for reviewing our paper.

Following the reviewers suggestions, a major revision of the English language was made, key point and additional information were added, showing the key aspects of the manuscript and the salient issues regarding this paper. We agree with Your suggestion. We elaborated and clarified several points.

Point#1 (introduction)
We agree with Your suggestion. We changed with the term “endoderm”.

Point#2 (case 1)
We cancelled the mention of our surgical department.

Point#3 (case 2)
Corrected. We elaborated the sentence.

Point#4
Corrected

Point#5
Corrected

Point#6
Corrected

Point#7
Corrected. We elaborated the sentence.
Point#8
We agree with Your suggestion. We elaborated and clarified several points. Case 2 section was shortened.

Point#9 (discussion)
Corrected

Point#10 (discussion)
We agree with Your suggestion. We elaborated and clarified several points in the Discussion Section.

Thank You very much for Your collaboration

Kindest Regards,

Gianlorenzo Dionigi
Response to Reviewer Comments #2

Dear Reviewer,

Thank You for Your general comments on this manuscript “SIMULTANEOUS MEDULLARY AND PAPILLARY THYROID CANCER: DESCRIPTION OF TWO CASES”.

Thank you very much for Your collaboration and interest for reviewing our paper. Following the reviewers suggestions, a major revision of the English language and typos was made, key point and additional information were added, showing the key aspects of the manuscript and the salient issues. We agree with Your suggestion. We elaborated and clarified several points.

POINT #1 (abstract)
The information provided in the abstract was elaborated and clarified; additional information was added. In particular, the sentence “same thyroid gland” was changed with “thyroid gland”. Moreover, we think that Case 2 is peculiar for the long follow up (about 16 years disease free).

POINT#2 (Introduction)
We elaborated and clarified several points of the Introduction Section.

For the tumorigenesis we reported that point mutations of RET proto-oncogene have been demonstrated to be causative of the familial form of medullary thyroid cancer, both isolated FMTC and associated to MEN 2A and 2B. Thyroid carcinomas are frequently associated with genetic alterations. Moreover, somatic rearrangements of RET designated as RET/PTC (from papillary thyroid carcinoma) were identified in papillary thyroid carcinoma before RET was recognized as the susceptibility gene for MEN2.

POINT#3

Case 1
1. No pentagastrin testing pre-and postoperatively was perform
2. No immunhistochemical examination was performed in the small nodule of the isthmus (0.4cm) (Figure 1)
3. Tumor categories (TNM) and stage are given
5. Analysis of tumor tissue for the RET oncogene mutations was negative (exons)
6. Six months postoperative serum calcitonin and TG level was within normal range.
7. At present, the specimen has not yet been examinated for ret/PTC translocation
8. The patient did not undergo any external radiation therapy previously.

Case2
Thank You for Your question.
Case 2 is “retrospective” (i.e. May 1990), therefore some dates were missing. The case was taken from the our Pathologist records. The completeness of these data was optimized by collecting from different sources. Patient notes, referral routes (clinical endocrinologists, internists), surgeons and hospital records. We elaborated and clarified several points of the Case 2 Section.

1. We mean that US showed ipo-echogenity area/signal of the nodule.
2. We do not have data of TG; during follow up calcitonin levels were between 300 and 200 pg/ml
3. Case 2 is of May 1990. During that period the diagnostics for MTC involve blood, urine and biochemical examination as well as imaging modalities. Imaging was achieved by a variety of techniques such as radiological morphological imaging methods, for example, sonography, computerized tomography (CT) and finally, nuclear functional imaging methods. Many molecular imaging and therapy modalities for MTC (such as metaiodobenzylguanidine) were under investigation or being developed during that period.
4. RET analysis was not performed in this patient in that period
5. The tumor categories given by pathologist were pT2, N+

POINT#4 (DISCUSSION)

We agree with Your suggestion. We elaborated and clarified several points.
1. Ret/PTC translocation is elaborated in the Introduction Section.
2. Our patients did not present characteristics of MEN 2A syndrome. However, the association of MEN 2A and PTC is intriguing and has been discussed recently.
3. We think that the clinical consequences of this cases are the fact that the treatment of thyroid cancer should be based on individual findings instead of general recommendations.

Thank You very much for Your collaboration

Kindest Regards,
Gianlorenzo Dionigi