Case Report

Papillary thyroid carcinoma associated with glioblastoma in a neurofibromatosis 1 patient: An unusual and rare combination of multiple primary malignancies

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ABSTRACT

Introduction: Papillary Thyroid carcinoma (PTC) is the most common endocrine malignancy and accounts for 1–2% of all cancer cases. Second malignancies in women diagnosed with thyroid cancer are of concern given the young average age at diagnosis. The concurrent occurrence of thyroid cancer and malignant brain tumor such as glioblastoma (GBM) was rarely seen and reported. However, the simultaneous association of these 2 conditions, namely PTC and GBM, in a neurofibromatosis type 1 (NF1) patient, has never been reported before in the literature.

Case presentation: The authors report the first case of an extremely rare association combining papillary thyroid carcinoma, glioblastoma, and a neurofibromatosis 1 in a 34-year-old female patient with primary generalized tonic-clonic seizures.

Clinical discussion: NF1 can be associated with PTC and GBM independently. In this current case, NF1 was accompanied by both PTC and GBM. With the exception of the present case, to our knowledge, there has been no previous case report in the literature in which these 3 entities were associated. The reason for the rarity of this combination of these neoplasms in patients with NF1 remains not clear, but it may be explained by the low incidence of combined occurrence of PTC and GBM.

Conclusion: This is the first reported extremely rare coexistence of GBM and PTC in a female NF1 patient. Further genetic investigations could improve our understanding of this combination and change our therapeutic approaches.

1. Introduction

Papillary Thyroid carcinoma (PTC) is the most common endocrine malignancy and accounts for 1–2% of all cancer cases. It disproportionately affects young women less than 45 years age, three to four times greater than men [1]. Its prognosis remains very good with a 10-year survival rate of over 99% for women diagnosed before the age of 45 years [2]. Second malignancies in women diagnosed with thyroid cancer are of concern given the young average age at diagnosis and excellent survival. Thereby, many studies highlighted a positive association between thyroid cancer and breast, prostate, kidney, salivary glands, brain, scrotum cancer, and even leukemia. The concurrent occurrence of thyroid cancer and malignant brain tumor such as glioblastoma (GBM) was rarely seen and reported [3]. However, the simultaneous association of these 2 conditions, namely PTC and GBM, in a neurofibromatosis type 1 (NF1) patient, has never been reported before in the literature.

In the present case, the authors report the first case of an extremely rare association combining papillary thyroid carcinoma, glioblastoma, and a neurofibromatosis 1 in a female patient. The authors will proceed with a review of the current literature regarding this rare entity.

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This case report has been reported in line with the SCARE Criteria [4].

2. Case presentation

A 34-year-old female patient with neurofibromatosis type 1 (NF1) was admitted in our department of neurosurgery complaining of primary generalized tonic-clonic seizures non followed by neither coma nor motor or sensory palsy associated with progressive raised intracranial pressure made of frontal headache, vomiting and bilateral blurred vision. Painkillers could alleviate the patient’s headache but it still reoccurred repeatedly. As surgical history, she was diagnosed with papillary thyroid carcinoma (PTC) and she underwent a gross total thyroidectomy followed by Radioactive iodine ablation therapy (RAI) at a dose of 30 mCi 2 years ago. No local recurrence or distal metastases were found during follow-up examinations. On admission, neurological examination was unremarkable. She was in consciousness and cooperative in answering questions. Her bilateral pupils were sensitive to light reflection. Physical examination showed stable vital signs with a body temperature of 36.8 °C, a heart rate of 86 beats per minute and blood pressure around 90/50 mm Hg. No obvious abnormality was found in cardiac, lung, and abdominal examination. The rest of physical examination revealed one large café-au-lait spot of the antero-internal aspect of the right arm, multiple freckles of the posterior part of the left shoulder, two neurofibromas of the posterior aspect of the right arm, and axillary freckling (Fig. 1). There were no Lisch nodules on his iris at the slit-lamp examination. We carried out a complete biological assessment. The results of the complete blood count, and urine analysis serum biochemistry were normal. The electrocardiogram and chest X-ray also revealed normal results. Our patient was clinically euthyroid. Tumor marker tests showed an increase of thyroglobulin level reaching 44.23 ng/mL (normal range: 1.4–78.0 ng/mL). Autoimmune antibodies such as anti-thyroglobulin and anti-microsomal antibodies were not performed.

Cerebral CT scan has showed a median parieto-occipital lesion isodense in its center and hyperdense in the periphery, measuring 50 × 60 mm in diameter with extension into the splenium of corpus callosum and with heterogeneous and annular enhancement after contrast injection (Fig. 2). Investigation was completed by a Brain MRI showing the periventricular parietal-occipital lesion in isosignal on the T1-weighted sequence. The patient was subjected to surgery and tumor resection was performed with a subtotal excision (Fig. 3).}

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Fig. 1. Patient’s body photograph showing different skin manifestations of NF1. A: café-au-lait macules of the antero-internal aspect of the right arm (black arrow); B: multiple freckles of the posterior part of the left shoulder; C: Two neurofibromas of the posterior aspect of the right arm (black arrows); D: axillary freckling.
sequences enhancing intensely and heterogeneously in annular fashion after chelate gadolinium injection. This mass was surrounded by a significant perilesional oedema on Flair (Fluid attenuated inversion recovery) sequence (Fig. 3). There were a few foci of intratumoral bleeding in on the Gradient echo T2*-weighted image.

After combining clinical manifestations with radiological examination, several diagnoses were thus evoked including glioma, brain metastasis and primary cerebral lymphoma with NF1. As part of further assessment, a thoraco-abdominopelvic CT scan was performed which revealed no abnormalities. Our patient underwent, thus, an open brain biopsy under general anesthesia through a right parietal craniotomy in supine position with her head placed in a 3-pin skull fixation device. On macroscopic appearance, the mass had a poorly demarcated gelatinous necrotic and hemorrhagic aspect, formed by alternating areas of firm whitish and yellowish areas. Infiltration beyond the visible tumor margin was obviously present.

Immediate postoperative course was uneventful and patient reported partial improvement of headaches. The final histopathological and immunohistochemical finding showed a large focus of ischemic necrosis formed by proliferation in high density layers of glial cells, round and were hyperchromatic voluminous bilobed, sometimes reniform with marked cytonuclear pleomorphism. The nuclei sometimes fusiform with significant perilesional oedema on Flair (Fluid attenuated inversion recovery) sequence (Fig. 3). There were a few foci of intratumoral bleeding in on the Gradient echo T2*-weighted image.

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Fig. 3. Axial cerebral MRI showing a periventricular parietal-occipital mass in isosignal on T1-weighted sequences (A) enhancing intensely and heterogeneously in an annular fashion after Gadolinium injection (B). Note the significant surrounded perilesional oedema on Flair sequence (C). Few foci of intratumoral bleeding (red arrows) on the Gradient echo T2*-weighted image (D). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Fig. 4. Representative histology of the tumor (GBM) on hematoxylin and eosin-stained sections showing highly cellular proliferation composed of poorly differentiated and atypical tumour cells with prominent microvascular proliferation (blue arrow) (A: H&EEx100). A focus of ischaemic necrosis (blue star) is surrounded by palissading tumour cells and microvascular proliferation with glomeruloid appearance (blue arrow) (B: H&EEx200). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)
triodothyronine (T3) indirectly affects glioma growth via the modulation of microglia [19]. We suggest that the combination of GBM and PTC is not a hazardous coincidence. Likewise many scientific article mention the risk of second primary malignancy in women particularly with PTC [11,20]. Certainly, it is rarely seen but we should be aware of this concurrent occurrence. This type of tumor is the most common anatomopathological form of thyroid cancer. It affects mainly young women. Usually, PTC gives cerebral metastasis in 1–10% of cases. Moreover, patients younger than 40 years of age at the time of diagnosis of thyroid cancer had a 39% increased risk of a second cancer, whereas the risk was 6% in older patients [21]. It is obvious to attribute this increase of risk to younger age and the good prognosis of the thyroid cancer, but radiiodine ablation therapy and the role of thyroid hormone are suggested to be an involved element. A retrospective analysis indicated that RAI treatment increased the probability of occurrence of a second primary cancer, as it was seen in our patient, compared with non-radioactive iodine treatment [21].

Our present case was therefore an extremely rare combination of certain neoplasms occurring at different times in a patient with NF1. To our knowledge, NF1 can be associated with PTC and GBM independently. In this current case, NF1 was accompanied by both PTC and GBM. With the exception of the present case, to our knowledge, there has been no previous case report in the literature in which these 3 entities were associated. The reason for the rarity of this combination of these neoplasms in patients with NF1 remains not clear, but it may be explained by the low incidence of combined occurrence of PTC and GBM.

4. Conclusion

This is the first reported extremely rare coexistence of GBM and PTC in a female NF1 patient. Further evaluation of genetic factors between these neoplasms could improve our understanding of the etiology of this combination and change our therapeutic approaches.

Ethics approval and consent to participate

Not applicable.

Consent for publication

A verbal consent was obtained.
Written informed consent for participation in the study was obtained from the patient.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

None.

Authors’ contributions

MB, FK, MM: Conceptualization, Methodology, Software.
MB, MZ, HM, SS, CM: Data curation, Writing- Original draft preparation.
MB, NM, LA, SM: Visualization, supervision, Writing- Reviewing and Editing.
MZB: Validation.

All authors have read and approved the manuscript, and ensure that this is the case.

Registration of research studies

1. Name of the registry:
2. Unique identifying number or registration ID:
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Guarantor

Mehdi Borni was responsible for the work and the conduct of the study, had access to the data, and controlled the decision to publish.

Provenance and peer review

Not commissioned, externally peer reviewed.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Patient perspective

During hospitalization and at the discharge, the patient was given the opportunity to share her perspective on the intervention she received and she was satisfied with the care.

Declaration of competing interest

The authors declared no potential conflicts of interests with respect to research, authorship and/or publication of the article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103556.

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