TERT Promotor Mutation as a Prognostic Indicator in Papillary Thyroid Carcinoma

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Background

Papillary thyroid carcinoma (PTC) is generally considered a curable disease. However, not all PTC behaves the same. Knowledge of tumor genetics offers an important tool for guiding clinical decision making and risk stratification in PTC. We present an interesting case of a patient initially thought to have intermediate risk PTC, who later presented with distant metastatic disease, associated with a high-risk tumor mutation.

Case Description

A 69-year-old female with a history of PTC presented for endocrine medical management. Thirteen years prior, she had a left hemithyroidectomy after fine needle aspiration (FNA) of a nodule showed atypia of undetermined significance (AUS). Surgical pathology revealed PTC and a completion thyroidectomy was performed, demonstrating multifocal microcarcinoma. She received 105 mCi I-131 and a post-therapy scan showed a large focus of uptake (1.6%) in the lower neck without distant metastasis. Whole body scan (WBS) one year later showed uptake of 0.2%. Stimulated thyroglobulin (Tg) level was 5.5 mg/dL, which was similar to Tg levels with TSH suppression. She was lost to follow-up for several years until she presented for evaluation of a new mandibular mass. A positron emission tomography (PET) scan showed evidence of bone metastasis in the left mandible (Fig 1) as well as pulmonary metastases (Fig 2). Excisional biopsy confirmed metastatic PTC and genetic testing showed the presence of a telomerase reverse transcriptase (TERT) gene promotor mutation. Mutations for BRAF, RET and NTRK fusion were not detected. The patient had repeat I-131 therapy, which showed uptake only in the mandibular mass. Her stimulated Tg level was over 200 ng/mL. Her mandibular mass increased further in size and she was referred to medical oncology. Tyrosine kinase inhibitor (TKI) chemotherapy was initiated. After two months of therapy, the mass regressed and Tg levels improved to 39 ng/mL.

Imaging

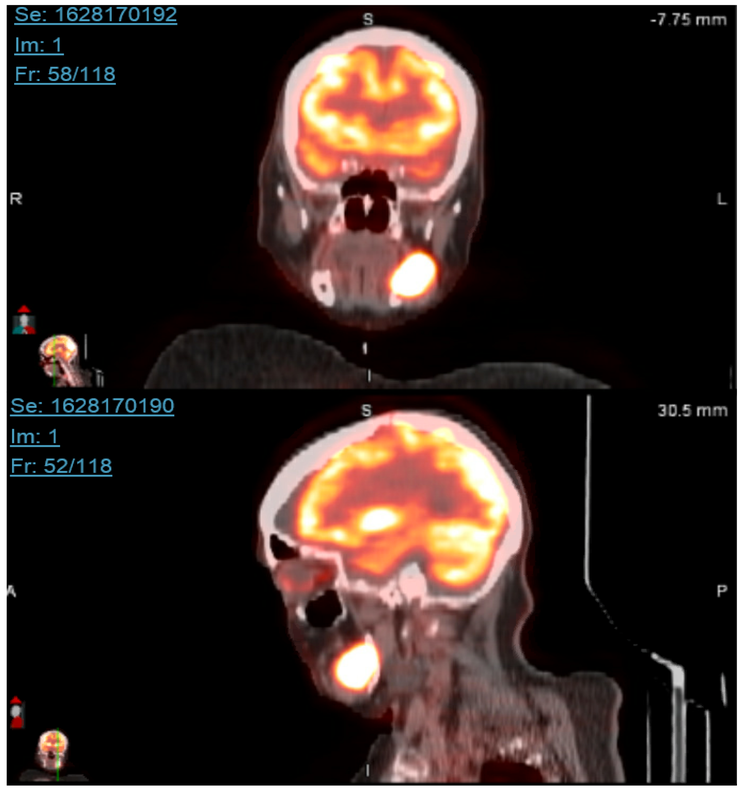

Figure 1. Coronal and sagittal PET scan images revealing increased fluorodeoxyglucose (FDG) uptake in the patient's left mandible, consistent with bone metastases.

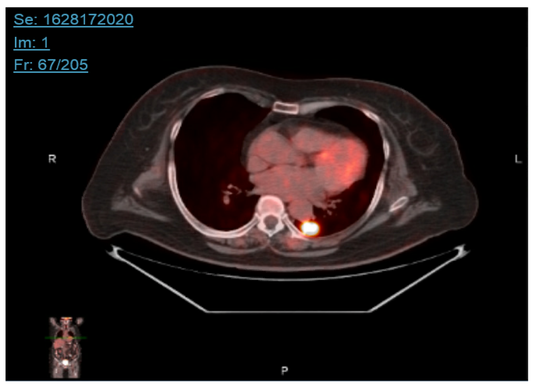

Figure 2. Axial PET scan image showing increased FDG uptake in a left lower lobe lung mass, consistent with pulmonary metastases.

Discussion

TERT promotor mutations in PTC were first identified in 2013 [1]. The mutations cause de novo formation of E-twenty-six (ETS) transcriptional factor binding sites, resulting in increased telomerase activity and creating a pathway for malignant transformation at the cellular level [2]. TERT mutation is associated with high-risk and aggressive tumor behavior [1]. Identification of these mutations can guide risk stratification and medical decision-making at the time of diagnosis. In our case, the complicated clinical course might have been anticipated if the presence of a TERT mutation was known after the initial surgery. This case underscores the value of genetic testing in PTC tumors for accurately prognosticating the clinical trajectory and providing individualized care to patients.

References

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