Thyroid carcinoma with rhabdoid phenotype: Case report with review of the literature

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ABSTRACT

Objective: This paper aims to comprehensively document a rare case of thyroid carcinoma with rhabdoid phenotype and literature review of this disease.

Methods: A 59-year-old man presented with a rapidly enlarging, painful left lateral cervical mass. CT scan revealed a tumor over the left thyroid gland with multiple left cervical lymphadenopathy over left level II–IV and level VI. Fine-needle aspiration cytology reported carcinoma, type undetermined. Total thyroidectomy with central compartment and left neck dissection was performed.

Results: Pathology report showed rhabdoid phenotype of thyroid carcinoma. Final staging was pT4N1M1.

Conclusions: Although WHO classification of thyroid tumor histology does not define this disease entity, few cases were reported. In the last 20 years, English literature review revealed only 12 cases about thyroid carcinoma with rhabdoid phenotype. Major treatment of thyroid carcinoma with rhabdoid phenotype is surgery, and the benefit of adjuvant therapies as radiotherapy or systemic chemotherapy is not clear. The prognosis of thyroid carcinoma with rhabdoid phenotype is extremely poor, with mean survival of only 6 months.

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1. Introduction

The rhabdoid cell has been first described in kidney in 1978 [1] and then extrarenal origin as epithelial, endocrine, mesenchymal, and melanocytic tumor with rhabdoid phenotype were also noted later [2]. The rhabdoid phenotype is a pathological presentation associated with aggressive nature not only in thyroid gland but also in other organs [3]. In literature review, the median survival is only 6 months in thyroid tumor [4]. Here, we reported a case of poorly differentiated papillary thyroid carcinoma with rhabdoid phenotype. A discussion of rhabdoid phenotype of thyroid carcinoma was also described.

2. Case presentation

A 59-year-old male presented at our clinic with an enlarging painful left neck mass for 2 months. He also
experienced symptoms as hoarseness, dysphagia, and ody-nophagia but there was no dyspnea. There was no family history of thyroid disease, and he also denied history of radiation exposure to head and neck region. Physical examination revealed an ill-defined mass over level II–IV of left side neck. Nasopharyngoscopy revealed freely movable bilateral vocal cords without visible lesion over the larynx or pharynx. Neck ultrasonography showed a 3.7 cm × 2.2 cm hypoechoic left thyroid tumor with ipsilateral multiple enlarged lymph nodes, the largest being around 2.6 cm. Serum thyroid hormones and thyroid-stimulating hormone were within normal range. Fine-needle aspiration cytology reported carcinoma type undetermined, while computed tomography (CT) revealed left thyroid hypo-dense tumor with coarse calcification, sternocleidomastoid muscle invasion and left level II–V and VI lymphadenopathies (Fig. 1A). Total thyroidectomy, central compartment and left level II–V neck dissection were performed.

On pathological examination, the tumor measured 8.5 cm × 7 cm × 4 cm with calcification, cystic degeneration, and extra-thyroidal extension. Histologically, the tumor exhibits extensive poorly differentiated cells characterized by large cell size, abundant cytoplasm, eosinophilic inclusion, and eccentric nuclei containing distinct nucleoli compatible as rhabdoid cell (Fig. 2), mixed with focal area of conventional papillary thyroid carcinoma (PTC). Rhabdoid cell component in this case was positive for TTF-1 (Fig. 3A) and vimentin (Fig. 3C), but negative for thyroglobulin (Fig. 3B), chromogranin, HBME-1 (Fig. 3D), or chromogranin A. The DNA sequence analysis showed V600E missense mutation (T1799A) in the BRAF gene.

Post-operative PET-CT was arranged, showing multiple uptake foci over paratracheal area, left pulmonary hilum, body of T-4, right 6th rib and right iliac bone. Final staging of this case turned out to be pT4N1M1. By a multi-disciplinary conference, I-131 ablation with 200 cCi was arranged 6 weeks post-operatively. The post-therapeutic whole body scan, however, revealed no I-131 uptake at the metastatic foci. Then this patient underwent post-operative radiotherapy, and 1 year later, he lost follow-up.

3. Discussion and review of the literature

The rhabdoid cell is a special type of cell characterized by abundant cytoplasm with eosinophilic globular inclusions and eccentric with vesicular nuclei [5]. The initial concept of the rhabdoid cell has been used for a subtype of Wilms’ tumor with a rhabdomyosarcomatous pattern first described by Beckwith and Palmer in 1978 [1]. In 1991, Chetty and Govender identified it in a poorly differentiated follicular thyroid carcinoma [5].

Thyroid tumors with rhabdoid phenotype are rare; only 12 cases (include this case) have been reported in recent literature (Table 1). Eight of the 12 cases were female. The patients’ age ranged from 29 to 77 years with a mean of 56.4 years. All cases have extra-thyroidal extension at the time of diagnosis and cervical or distant metastases are common clinical presentations. Thyroid tumor with rhabdoid phenotype shares many features of anaplastic carcinomas, including microscopic undifferentiated cells with immunohistochemical
or ultra-structural epithelial differentiation [4]. Thus, prognosis is extremely poor, with mean survival of only 6 months [4].

The theory of rhabdoid tumor formation may be de novo or through secondary progression from other types of tumors [3]. In previous reports, the background lesion of rhabdoid tumor of the thyroid included follicular carcinoma in five cases, PTC in three, anaplastic carcinoma in three, and pure rhabdoid thyroid carcinoma without any background thyroid lesion in one. Because PTC was detected over the thyroid lesion in this case, the rhabdoid tumor was considered secondary progression from PTC.

Grossly, thyroid tumor with rhabdoid phenotype is a solid white or gray mass with irregular margins. Morphologic features include large pleomorphic cells with abundant cytoplasm, typical eosinophilic inclusions, and eccentric nuclei with distinct nucleoli [4]. Immunohistochemically, rhabdoid tumor of the thyroid gland always shows positive vimentin expression. Expressions of TTF-1, cytokeratin, epithelial membrane antigen (i.e., AE1/AE3, Cam5.2, CK8, CK18), smooth-muscle actin, myoglobin, and desmin can also be observed at lower frequency [7]. The rhabdoid tumor cells of the present case are immune-reactive to vimentin and TTF-1, but negative for HBME-1 and thyroglobulin.

Genetic analysis in the present case shows V600E BRAF mutation. BRAF, located over chromosome 7, is the most common genetic alteration in PTC and is useful for differentiating difficult thyroid tumors [8]. T1799A, located on exon 15, is a missense point mutation in the kinase domain,

Table 1
Clinicopathological and treatment of thyroid carcinoma with rhabdoid phenotype.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (year)/sex</th>
<th>pTNM (stage)</th>
<th>Background</th>
<th>Treatment</th>
<th>Prognosis</th>
<th>Author [reference]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43/F</td>
<td>pT4N0M1</td>
<td>Follicular</td>
<td>HT</td>
<td>Lost to follow-up</td>
<td>Chetty and Govender (1999) [5]</td>
</tr>
<tr>
<td>2</td>
<td>56/F</td>
<td>pT4N0M0</td>
<td>Follicular</td>
<td>HT</td>
<td>Alive, 1 month later</td>
<td>Chetty and Govender (1999) [5]</td>
</tr>
<tr>
<td>3</td>
<td>65/F</td>
<td>pT4N0M1</td>
<td>Follicular</td>
<td>HT</td>
<td>DOD, 3 months later</td>
<td>Chetty and Govender (1999) [5]</td>
</tr>
<tr>
<td>4</td>
<td>60/F</td>
<td>pT4N1M1</td>
<td>Papillary</td>
<td>TR</td>
<td>DOD, 5 months later</td>
<td>Sumida et al. (2001) [10]</td>
</tr>
<tr>
<td>5</td>
<td>42/F</td>
<td>pT4N1M1</td>
<td>Follicular</td>
<td>HT</td>
<td>DOD, 3 years later</td>
<td>Albores-Saavedra and Sharma (2001) [6]</td>
</tr>
<tr>
<td>6</td>
<td>56/F</td>
<td>pT4N0M1</td>
<td>Papillary</td>
<td>TT</td>
<td>DOD, 4 years later</td>
<td>Albores-Saavedra and Sharma (2001) [6]</td>
</tr>
<tr>
<td>7</td>
<td>67/F</td>
<td>pT4N1M1</td>
<td>Papillary</td>
<td>TT</td>
<td>DOD, 5 months</td>
<td>Lai et al. (2005) [4]</td>
</tr>
<tr>
<td>8</td>
<td>59/M</td>
<td>pT4N+M1</td>
<td>Anaplastic</td>
<td>HT+ERT+CT</td>
<td>DOD, 15 months later</td>
<td>Carda et al. (2005) [9]</td>
</tr>
<tr>
<td>9</td>
<td>62/M</td>
<td>*</td>
<td>Anaplastic</td>
<td>TT</td>
<td>Lost to follow-up</td>
<td>Carda et al. (2005) [9]</td>
</tr>
<tr>
<td>10</td>
<td>77/M</td>
<td>pT4N1M0</td>
<td>Anaplastic</td>
<td>HT + ND</td>
<td>DOD, 6 months later</td>
<td>Sato et al. (2006) [3]</td>
</tr>
<tr>
<td>11</td>
<td>61/F</td>
<td>pT4N0M0</td>
<td>Anaplastic</td>
<td>TT + ERT + CT</td>
<td>DOD, 5 months later</td>
<td>D’Antonio et al. (2010) [7]</td>
</tr>
<tr>
<td>12</td>
<td>59/M</td>
<td>pT4N1M1</td>
<td>Papillary</td>
<td>TT + ND + RAI + CT</td>
<td>Alive, 1 year later</td>
<td>Current case</td>
</tr>
</tbody>
</table>

F, female; M, male; HT, hemithyroidectomy; TT, total thyroidectomy; TR, tumor resection; ERT, external beam radiotherapy; ND, neck dissection; RAI, radio-iodine ablation therapy; CT, chemotherapy; DOD, die of disease; * incomplete stage of thyroid tumor or not mention of stage in the original article.
which activates the BRAF kinase and MAP kinase pathways by V600E amino acid substitution in the protein product [8]. Because 35–70% of PTC exhibit BRAF mutation [8], this also supports the possibility that rhabdoid tumor in our case may arise from PTC through tumor progression.

Surgery and I-131 ablation therapy were performed in the present case. Poor radio-iodine uptake was confirmed by the 200 mCi I-131 post-therapeutic whole body scan. Rapid disease progression at the neck and lung developed within 1 month by positron emission tomography–computed tomography and he later only received symptomatic palliative care. Treatment for thyroid carcinoma with rhabdoid phenotype is not standardized because of the extremely low incidence. Feasible options include surgery, radiotherapy, radio-iodine therapy and chemotherapy [3,5,7–10]. These treatment modalities can be combined to maximize local and systemic control. Surgery was arranged in most reported cases, aiming at complete macroscopic resection with clear microscopic margin over the thyroid and the metastatic neck lymphadenopathies. Adjuvant therapies including post-operative external-beam radiotherapy, systemic chemotherapy (with regimen of ifosfamide, liposomal doxorubixin, taxol and cisplatin), and radio-iodine ablation were also reported [3,5,7–10]. However, no clear benefit can be demonstrated due to the few case number.

4. Conclusion

Thyroid tumor with rhabdoid phenotype is a highly aggressive thyroid malignancy with poor prognosis. It could be a secondary progression from differentiated thyroid carcinoma such as PTC or follicular thyroid carcinoma. Surgery was performed in most cases and the benefit of adjuvant therapy was not clear.

Consent

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

Conflicts of interest

None.

Acknowledgement

Many thanks to this patient who kindly consented to have his case published.

References