Ultrasonographic Features of Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma

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Received March 21, 2011; accepted May 19, 2011
Available online June 30, 2011

Diffuse sclerosing variant of papillary thyroid carcinoma (DSVPTC) is a rare entity. The purpose of this article is to analyze the sonographic findings of DSVPTC. The sonograms of 17 patients (12 females and 5 males) ranging in age from 8 years to 49 years (mean 24.1 years) with histopathologically proven DSVPTC were retrospectively analyzed. Of the 17 patients, 70% (12 of 17) had thyroid masses ranging from 0.4 cm to 4.5 cm in diameter. Diffused and scattered microcalcifications with heterogeneous hypoechoegenicity were noted in all cases. Involvement of supra/infraclavicular lymph nodes and cervical lymph nodes were found in nine cases (53%), whereas involvement of only cervical lymph nodes was seen in six cases (35%). Regional lymphadenopathy was not observed in two cases (12%). Among the thyroid lesions with or without underlying mass, the blood flow pattern were Adler Score III in eight cases (47%), Score II in two cases (12%), Score I in five cases (29%) and Score 0 in two cases (12%). Sonography is an important diagnostic tool that may help diagnosis of DSVPTC.

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correctly diagnosed by ultrasonography (US) and cytological examination preoperatively. On the other hand, DSVPTC is a rare entity. Few case reports and case series have been reported in the literature [3–6]. Because of its rarity, the sonographic features have not been well described. In this study, we report the sonographic findings of 17 patients with histopathologically proven DSVPTC. To our knowledge this is the largest series in the literature dealing with ultrasonographic features of DSVPTC.

Material and Methods

The retrospective study was approved by the institutional review board. A search for “DSVPTC” was conducted in the clinical database and in sonograms that were stored in picture archiving and communication system at our institution. The sonograms of 17 patients with surgicopathologically proved DSVPTC were available in our picture archiving and communication system, which was installed in 2002. The demographic data, sonograms, histopathological data, and surgical records were reviewed. The sonographic features in terms of size, margin, contour, echogenicity, calcification, color Doppler blood flow, and lymph node involvement were retrospectively reviewed by two sonologists in consensus.

Blood flow in the diseased area was categorized according to Adler score grading [7]. Score 0: no blood flow inside the diseased area; Score I: very small amount of blood flow or stellate blood flow; Score II: moderate blood flow, 2–3 blood vessels; Score III: profuse blood flow, more than 4 blood vessels present in the diseased area. US was performed by high frequency transducers ranging from 7.5 MHz to 12 MHz. The entire thyroid gland including regional lymph nodes sites (both sides of neck, supra/infracriclavelar regions) were examined for possible lymphadenopathy. Preoperatively, five patients underwent US-guided fine needle aspiration biopsy (FNAB). The areas with abundant diffuse microcalcifications having no underlying masses were especially targeted during FNAB. Among them, two patients were found to have metastasis in the regional cervical nodes. The sonograms of the other 12 cases featured ill-defined hypoechoic masses with malignant features, including marked hypoechoegenicity, irregular margins, presence of calcification, absence of a hypoechoic halo around the nodule, lymphadenopathy, and local invasion of adjacent structures.

Results

Of the 17 patients, 12 were female and 5 were male. The ages ranged from 8 to 49 years (mean 24.1 years). The surgical management and imaging findings of these cases with DSVPTC are shown Table 1. Among 17 cases, ultrasound revealed 12 cases of DSVPTC with associated mass. They showed diffused, scattered microcalcifications and heterogeneous hypoechoegenicity with ill-defined masses ranging from 0.4 cm to 4.5 cm (Fig. 1). The other five cases had similar sonographic features but without mass (Fig. 2). Heterogeneous hypoechoegenicity and diffusely scattered microcalcification on sonograms corresponded to lymphocytic infiltration and psammoma bodies on pathological examination (Figs. 1B and 2B). Regional lymphadenopathy or nodal metastasis was found in 15 of 17 cases (Figs. 1D and 1E). All cases except two had regional lymphadenopathy. Six cases had only cervical lymph node involvement. All nodes revealed poorly differentiated corticomedullary junction on sonogram. Calcified lymph nodes seen on sonogram corresponded to psammoma bodies on histopathological examination. Of the 17 cases, five cases without underlying associated masses on the diseased thyroid gland had US-guided FNAB (Fig. 3).

No distant metastasis was reported in this study. Near or total thyroidectomy was carried out in all cases. Postoperative radioiodine I-131 was used to ablate the residual cancer in thyroid tissue and metastatic lymphadenopathies for possible risk of recurrence. The follow-up US after surgery revealed recurrent regional lymphadenopathies in four cases, including one case that featured punctuate microcalcifications in an enlarged node greater than 1 cm in diameter (Fig. 4). The nodal calcifications seen on sonogram were proven to be psammoma bodies on histopathological investigation. Second stage surgery was done to remove residual lymphadenopathies in this case. The other three patients did not undergo second stage surgery and followed up with US every 3 months.

Discussion

DSVPTC of the thyroid gland is a rare malignant neoplasm [8,9]. Kwak et al [10] reported the histopathological features of DSVPTC as diffuse involvement of the thyroid gland with dense fibrosis, extensive squamous metaplasia, patchy lymphoid infiltration with germinal centers, psammoma bodies, and some areas within the smear showing typical papillary carcinoma.

Corresponding psammoma bodies are the round collections of calcium seen microscopically. They are associated with the papillary (nipple-like) histomorphology and are thought to arise from the infarction and calcification of papillae tips and calcification of intra-lymphatic tumor thrombi [11]. When degenerating changes occur in the papillae of papillary carcinoma they appear as laminated, basophilic, and stromal structures. They appear in about half of all papillary carcinomas, and the presence of psammoma bodies in the thyroid or a metastatic cervical lymph node is a strong evidence of papillary carcinoma. A large number of psammoma bodies in one or both lobes provide strong evidence for this variant. This variant is found in less than 4% of papillary carcinomas of the thyroid [2]. Many authors reported the clinical and cytopathological features of this entity [6,12,13]. Only a few case reports and small series regarding this entity correlating with imaging findings have been reported in the literature [10,14,15]. However, the report of sonographic features of this entity in larger series is rare. In our institution, the frequency of DSVPTC is extremely rare, accounting 0.5% of a total of 3,200 surgically proven thyroid cancers. Clinically, DSVPTC may mimic Hashimoto thyroiditis with characteristic presentation of rapid and diffuse thyroid enlargement in young women. Hence, the diagnosis is often delayed. When DSVPTC is diagnosed, almost all patients have associated metastasis in regional nodes. The
<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)/Sex</th>
<th>Location</th>
<th>Sonographic features*</th>
<th>Associated mass on sonograms</th>
<th>Lymphadenopathy</th>
<th>Adler score</th>
<th>Initial operation</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24/F</td>
<td>Right</td>
<td>No</td>
<td></td>
<td>+</td>
<td>I</td>
<td>Total thyroidectomy</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>49/F</td>
<td>Entire</td>
<td>No, but diffusely enlarged gland</td>
<td></td>
<td>+</td>
<td>III</td>
<td>Total thyroidectomy</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>46/F</td>
<td>Entire</td>
<td>Multiple-hypoechoic ill-defined nodules, each &lt;1.2 cm</td>
<td>++++</td>
<td>III</td>
<td>Total thyroidectomy</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>19/F</td>
<td>Right</td>
<td>No</td>
<td></td>
<td>−</td>
<td>III</td>
<td>Lobectomy</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>25/F</td>
<td>Both</td>
<td>Ill-defined hypoechoic mass, 2.5 cm</td>
<td>++++</td>
<td>I</td>
<td>Total thyroidectomy</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>21/F</td>
<td>Right</td>
<td>No</td>
<td></td>
<td>+</td>
<td>III</td>
<td>Total thyroidectomy</td>
<td>–</td>
</tr>
<tr>
<td>7</td>
<td>11/F</td>
<td>Right</td>
<td>Ill-defined hypoechoic mass, 0.5 cm</td>
<td>+</td>
<td>III</td>
<td>Total thyroidectomy</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>22/F</td>
<td>Left</td>
<td>Ill-defined hypoechoic mass, 1.5 cm</td>
<td>+</td>
<td>I</td>
<td>Total thyroidectomy</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>29/F</td>
<td>Both</td>
<td>Multiple hypoechoic ill-defined nodules on both sides, up to 1.7 cm on the left, 1.2 cm on the right</td>
<td>−</td>
<td>I</td>
<td>Near-total thyroidectomy</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>8/M</td>
<td>Right</td>
<td>Ill-defined hypoechoic mass, 1.5 cm</td>
<td>++++</td>
<td>III</td>
<td>Total thyroidectomy</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>38/F</td>
<td>Both</td>
<td>Ill-defined hypoechoic mass on the left, 0.9 cm</td>
<td>++++</td>
<td>III</td>
<td>Total thyroidectomy</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>12/M</td>
<td>Entire</td>
<td>Ill-defined hypoechoic mass on the left, 0.4 cm</td>
<td>+</td>
<td>0</td>
<td>Total thyroidectomy</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>20/M</td>
<td>Left</td>
<td>Multiple hypoechoic ill-defined masses, &lt;2.5 cm</td>
<td>++++</td>
<td>I</td>
<td>Total thyroidectomy</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>27/M</td>
<td>Left</td>
<td>Ill-defined hypoechoic calcified mass, 2.5 cm, extravasation of left upper capsule was seen</td>
<td>++++</td>
<td>II</td>
<td>Total thyroidectomy</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>17/F</td>
<td>Both</td>
<td>No</td>
<td></td>
<td>++++</td>
<td>III</td>
<td>Total thyroidectomy</td>
<td>–</td>
</tr>
<tr>
<td>16</td>
<td>23/M</td>
<td>Right and Isthmus</td>
<td>Ill-defined hypoechoic mass, 3.0 cm on the right</td>
<td>++++</td>
<td>0</td>
<td>Total thyroidectomy</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>24/F</td>
<td>Left lobe</td>
<td>Ill-defined hypoechoic mass, 4.5 cm</td>
<td>++++</td>
<td>II</td>
<td>Near-total thyroidectomy</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

* The echogenicity is heterogeneous and hypoechoic in all cases. None of the patients had metastasis and all are alive until now. The microcalcification on sonograms are diffusely scattered in all cases.

+++ = Presence of metastases in supraclavicular, infraclavicular, and cervical lymph nodes; ++ = Presence of metastases in cervical lymph nodes; + = No abnormal lymphadenopathy; − = Normal.
F = female; M = male.
Histological criteria for diagnosing DSVTPC have been clearly defined, but the sonographic features of this entity have received much less attention. Kwak et al [10] reported sonographic features of six cases of DSVPTC in 2007. In this study, the patients’ ages ranged from 22 years to 49 years, with five women. These five (83.3%) cases showed diffused and scattered microcalcifications on sonograms. Kwak reported that when US reveals a diffusely enlarged thyroid gland with multiple scattered microcalcifications in a young women, DSVPC should be included in the differential diagnosis.

In this study, all 17 cases showed diffused and scattered microcalcifications on sonograms and 70% (12 of 17) of the cases had underlying associated mass. Lam et al [6] reviewed 150 cases of this variant of papillary carcinoma in 2006. The mean age reported for this variant (in series of more than five patients) ranged from 19.5 years to 34.7 years. The youngest patient reported was 9 years old and the oldest reported was 67 years old. In our series, the ages ranged from 8 years to 49 years and 12 were female. Young women in the third decade were more commonly affected. Compared with classical papillary thyroid carcinoma this variant is characterized by higher incidence of regional lymph node and pulmonary metastasis and higher prevalence in young women and larger tumor size [5,6,9,14]. In our study, 15 of 17 (88%) cases had regional lymph node metastasis, a finding that is consistent with previous studies [5,6,9,14]. Nine of 17 cases had supra/infracavicular and cervical lymph node metastasis. Six cases had only cervical lymph node metastasis (Table 1) whereas in two cases no metastatic lymph nodes were seen on sonogram. In this series none of the patients had distant metastasis. Only four cases had cervical lymph node recurrence, after near or total thyroidectomy.

In a case report by Kobayashi et al [14], moderate blood flow was seen in the diseased area. In this study, flow...
signals were observed in 15 of 17 cases with Adler Score III in eight cases; Score II in two cases and Score I in five cases (Fig. 1C and Fig. 2C).

US-guided FNAB of thyroid nodules has been proven to be sensitive, specific, and well tolerated by patients because of minimal discomfort and complications [16]. In this series, five cases with absence of underlying associated masses on diseased thyroid gland had US-guided FNAB (Fig. 3). FNAB revealed the presence of abundant psammoma bodies with features of papillary carcinoma on smears. The sensitivity of US-guided FNAB for the diagnosis of this variant in our study was 100%. The presence of numerous psammoma bodies in the aspirate may help to identify the variant of papillary thyroid carcinoma. Early diagnosis of this locally aggressive disease has both clinical and surgical importance.

Recent studies revealed that patients with DSVPTC have similar prognosis to patients with classical papillary thyroid carcinoma [5,6]. None of our patients have current metastasis, and all are still alive despite cervical lymphadenopathies in four cases. The limitation of the present study is that the follow-up period of 2.0 years to 9.1 years (mean 5.2 years) is not long enough. During the study period, we tried to contact all the patients.

In conclusion, our study highlights the sonographic features of DSVPTC, a disease that is very rare but more common in young women. Diffusely enlarged thyroid gland, hypoechoic heterogeneity with or without associated underlying mass, scattered microcalcifications, and regional lymphadenopathy are the sonographic features of this entity. On color Doppler US, mild to profuse blood flow

Fig. 2. A 22-year-old young woman with diffuse sclerosing variant of thyroid papillary carcinoma. (A) Longitudinal sonogram of right thyroid revealed diffused and scattered microcalcification on entire thyroid lobe without associated underlying mass. (B) Histopathological examination showed psammoma bodies (white arrow). (Hematoxylin and eosin, 100×). (C) Color Doppler sonogram shows profuse blood flow of the lesion with Adler Score 3.

Fig. 3. A 17-year-old young female with diffuse sclerosing variant of papillary thyroid carcinoma. A transverse sonogram of the right lobe of thyroid shows the ultrasound-guided fine needle (black arrow).

Fig. 4. A 25-year-old woman with recurrent lymph node seen on right supraclavicular region after 9 months of near-total thyroidectomy. The calcified nodes corresponded to psammoma bodies on histopathology.
pattern is seen. Preoperative US-guided FNAB would be of
great clinical and surgical value. The presence of numerous
psammoma bodies in the aspirate may also help to identify
this variant of papillary thyroid carcinoma.

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