Cervical lymphadenopathies signaling thyroid microcarcinoma. Case study and review of the literature

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Summary

Background: Some lateral cervical lymphadenopathies may lead to the discovery of papillary microcarcinomas (PMC) of the thyroid that are not radiologically apparent. This relatively rare clinical situation raises questions about the diagnostic approach to chronic cervical lymphadenopathy and the impact of lymph node metastasis on PMC prognosis.

Purpose of the article: To study the epidemiologic, clinical, and prognostic criteria of cases of lymphadenopathy that signaled PMC.

Patients and methods: A retrospective study of 167 consecutive cases of PMC compared with 13 cases where a cervical mass signaled other forms of PMC.

Results: The mean age was 48.5 years, the ratio of men to women was 5:8, and the mean PMC size was 5.5 mm. These data did not differently significantly from those of the other PMC cases. The preoperative imaging found fluid content in six cases, with microcalcifications in three cases. All cases were treated by modified radical neck dissection on the side with the lymphadenopathy and total thyroidectomy with central neck dissection. The lymphadenopathy included a ruptured capsule in five cases and was accompanied by central lymph node metastases in three cases. Thyroid capsule involvement was significantly more common in cases of PMC discovered due to lymphadenopathy than in other cases of PMC (69% versus 9.7%, respectively; p < 0.001). The mean follow-up was 7.3 years. There were no deaths due to PMC signaled by lymphadenopathy. Two cases of lymph node recurrence after 8 and 10 years were controlled by another surgery and radioactive iodine treatment.
Introduction

The incidence of thyroid cancer in France is 2.5 per 100,000 (Francim cancer network (http://www.invs.sante.fr/surveillance/cancers/surveillance_cancers.htm)). The incidence of clinical and/or radiological lymphadenopathy at the time of cancer diagnosis is estimated at 20 to 25% for all sizes of thyroid tumors combined [1,2]. In 7 to 13% of cases [3], cervical lymphadenopathies lead to the discovery of thyroid cancer that is not clinically or radiologically apparent. These lymph node metastases thus signal subclinical papillary microcarcinoma (PMC) (< 1 cm: pT1a, UICC 2002).

This relatively rare clinical situation raises questions about the diagnostic approach in cases of chronic cervical lymphadenopathy with no apparent primary tumor and the impact of lymph node metastasis on the prognosis of PMC.

The purpose of this article is therefore to study the epidemiologic, clinical, and prognostic criteria of cases of cervical lymphadenopathy that signal subclinical PMC.

Patients and methods

This single-center series of 342 cases of differentiated thyroid cancer of follicular cell origin, treated consecutively from 1985 to 2007, included 167 cases of microcarcinoma, defined as a papillary carcinoma less than or equal to 1 cm in size, according to the histopathology report. After excluding clinically suspected cases of thyroid tumor and those with a positive fine-needle aspiration biopsy, we found 15 cases of cervical lymphadenopathy with no suspicious thyroid nodule. In two cases, these were discovered histologically after lymph node dissection for another tumor, one epidermoid carcinoma of the floor of the mouth and one melanoma of the face. Because these two cases did not meet the criteria for this study, they too were excluded. This analysis thus includes 13 cases of lymphadenopathy that signaled subclinical thyroid cancer.

The epidemiological, clinical, and histopathological data were recorded and compared with those for the rest of the PMC population, i.e., 154 other cases.

The data were input and analyzed with Excel® software (Microsoft Corp., WA). The descriptive variables were expressed as means and their standard deviations. The parametric data were compared with Student’s t test, and the proportions with a chi-square test. A value of $p \leq 0.05$ was considered significant.

Results

Table 1 summarizes the comparison of the 13 cases of lymphadenopathy that signaled PMC with the other types of PMC.

Clinical presentation

The mean age of these patients was 48.5 years (13—76 years). The ratio of men to women was 5:8. A fine-needle aspiration biopsy was done in three cases and was positive in one case, negative in one, and ambiguous in the other. Thyroglobulin assays of the aspirated material were never requested. There were no clinical signs of dysthyroidism or thyroid autoimmunity. The ultrasound (performed in 11 of 13 cases) showed a mass that was totally cystic in two cases, of mixed content in four cases (Fig. 1), and solid in five cases. There were microcalcifications in three cases. A CT scan with contrast was requested in three cases (Figs. 2 and 3) and an MRI in one case of a totally cystic mass (Fig. 3).

The lymphadenopathy was mapped at level III in five cases, IIa in six, and IV in two.

The mean lymph node progression time could not be determined.

Initial treatment

All cases underwent an exploratory cervicotomy with intraoperative pathological examination. In three cases the...
Table 1  Clinical and pathology data from cases of PMC signaled by LAP and other cases of PMC.

<table>
<thead>
<tr>
<th></th>
<th>Subclinical PMC discovered due to LAP n = 13</th>
<th>Other microcarcinoma n = 154</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>48.5 years</td>
<td>41.1 years</td>
<td>&gt; 0.1</td>
</tr>
<tr>
<td>Sex ratio</td>
<td>0.62</td>
<td>0.45</td>
<td>&gt; 0.1</td>
</tr>
<tr>
<td>Size of PMC</td>
<td>5.5 mm</td>
<td>5.9 mm</td>
<td>&gt; 0.1</td>
</tr>
<tr>
<td>Thyroid capsule involvement</td>
<td>9/13 (69%)</td>
<td>15/154 (9.7%)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Multifocal</td>
<td>2/13 (15.3)</td>
<td>20/154 (12.9%)</td>
<td>&gt; 0.1</td>
</tr>
<tr>
<td>Lymph node recurrence</td>
<td>2 cases</td>
<td>1 case</td>
<td>&gt; 0.1</td>
</tr>
</tbody>
</table>

immediate pathology of the cervical mass was inconclusive and the thyroidectomy was performed after conclusive testing. In 10 cases, the thyroidectomy was done at the same time as the lymph node surgery. All cases were ultimately treated by total thyroidectomy, central neck dissection, and lateral dissection on the side with the signal lymph node. For six patients, only the lateral compartment was involved, while three had an associated lymphadenopathy of the central compartment. The lymph node capsule ruptured in five patients.

The mean size of the PMC foci (largest focus in multifocal cases) was 5.5 mm (standard deviation = 2.7 mm, range: 2—7 mm). The primary tumors were unifocal unilobar, except in two cases — one bifocal unilobar and one bilobar (3 foci). Mapping showed PMC by the upper pole in six cases, the lower pole in one, and in the central lobe in five more.

In one case, no neoplastic focus could be found in the thyroid. The thyroid capsule was penetrated in eight of 13 cases, and infiltrated but not penetrated in one other case, for capsular involvement in nine of 13 cases (69.2%). Tumor encapsulation was not studied due to lack of details in the oldest histopathology reports.

The tumor subtype was papillary in six cases, mixed papillary-follicular in six cases, and no tumor in one case.

Adjuvant treatment and outcome

Postoperative treatment included radioactive iodine treatment in all cases, twice in two cases and three times in another. The follow-up time was 7.3 years (standard deviation = 5.6). There were two cases of lymph node recurrence, 2 and 12 years after the initial treatment. The first patient required a repeat dissection and 1 radioactive iodine treatment, and the second two radioactive iodine treatments.
These two patients were followed for 8 and 10 years, respectively, after the recurrence. The other patients had no local/regional or remote relapses after a mean follow-up of 8 years (standard deviation = 7.9 years).

Discussion

A lateral cervical mass should always suggest the possibility of lymph node metastasis of, firstly and depending on the alcohol and tobacco use, epidermoid carcinoma of the upper GI and respiratory tracts. The second most common form is thyroid cancer [4,5], particularly in subjects under 40 years of age with no other risk factor, especially in cases of a cystic cervical mass. In that situation, a clinical presentation of the second branchial cleft cyst leads to a diagnosis of cystic metastasis of thyroid cancer in one of 10 cases [6]. Such cystic metastases were reported in a population with a mean age of 30 years [7], versus 48 years in our series. The course of the disease is usually long — from several months to a few years, with cases reported at up to 14 years (cystic form) [8].

There is usually a single lymph node mass, mapped predominantly in the superior and median cervical levels IIa and III [2,6,9]. Involvement of the external jugular group dominantly in the superior and median cervical levels IIa is very suggestive, together with cortical heterogeneity and multiple cystic areas [12]. In predominantly cystic forms, the presence of intracystic hyperechoic elements [13,14] is consistently reported, as described here (Fig. 1). The CT scan with contrast also provides specific signs, including central necrosis, a cystic component, peripheral contrast uptake greater than in the muscle, and calcifications (Som's criteria) [15]. Based on an analysis of these criteria, Ahn et al. report that such CT has 100% sensitivity and 90% specificity, compared with 80% for ultrasound [1]. The MRI shows a T2 hyperintense signal, indicating content rich in thyroglobulin [16]. The sensitivity of fine-needle aspiration biopsy was 66% [17]. The specific cytological signs are presence of papillae, nuclear grooves, intranuclear cytoplasmic inclusions, and psammoma bodies [18]. The sensitivity of the thyroglobulin assay of the fine needle aspiration fluid is close to 100% [19–22].

In an initial lymph node metastasis situation, thyroid abnormalities are discovered during the workup in 75% of cases, primarily by ultrasound [2]. This is thus an essential test in a workup for chronic lymphadenopathy in young adults.

However, as presented in this series, the workup as a whole may be negative. It is in that particular situation, after fully informing the patient, that an exploratory cervicotomy with an immediate pathological examination may be done. The diagnosis of lymph node metastasis suggested by the fine needle aspiration biopsy and the dark blue color of the mass [7] is confirmed by immediate pathologic evaluation (74% in this series). Thus a complete lateral and central dissection is performed along with a total thyroidectomy [17]. The histological form most commonly found in the thyroidectomy specimen is papillary carcinoma of follicular origin. Rare cases of medullary (C cell) carcinoma have been reported [23,24]. The size of the primary tumor is small — between 2 and 8 mm (mean = 3.6 mm) [10], 5.5 mm in our series. In the literature, there is nothing specific about the number of tumor foci or the localization in the thyroid. There was a single focus in the vast majority of cases [10]. Compartmental involvement is found in nearly one of two cases according to Monchik et al. [7] (seven of 13 cases in this series). When no definitive diagnosis can be made based on the histopathology, the procedure is limited to a lymphadenectomy and then completed in a second procedure. 131I remnant ablation is the rule [25]. Prognosis seems controversial: Coleman reports a good prognosis [17], while others report a 28% rate of lateral lymph node recurrence after dissection [7]. In our series, two patients experienced a cervical lymph node recurrence at level IVb in one case and Iib in another, both with initial capsule rupture — a potentially poor prognostic factor. However, patients should be followed for more than 20 years, since recurrences sometimes occur very late.

Conclusion

When there is a lateral cervical cystic mass in a subject under 40 years of age who has no other risk factor, a thyroid origin should be considered. A fine-needle aspiration biopsy of the mass should be done, and possibly a thyroglobulin assay.

Immediate pathologic examination, while difficult, does provide a diagnosis. In that specific situation, in a duly informed patient, a total thyroidectomy with central and homolateral cervical lymph node dissection is recommended. Radiosotope remnant ablation makes it possible to properly monitor tumor progression by post-ablation scintigraphy, together with Tg levels and anti-Tg antibody titers. The prognosis is usually favorable, except in a few cases where a lymph node recurrence may occur, even more than 10 years after treatment, particularly in patients with an initial cervical lymph node rupture.

Conflict of interest statement

The author declare no conflict of interest.

References

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