CASE STUDY

Thyroid Nodule as a First Sign of Progression in Uterine Cervical Carcinoma

Nódulo tiroideo como primer signo de progresión de carcinoma de cervix uterino

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Received 8 April 2014; accepted 20 April 2014

A 36 year-old woman, who consulted due to a thyroid nodule which had developed over one month. Computerised axial tomography (CAT) showed an irregular nodule measuring 5 cm that occupied a large part of the right thyroid lobe (Fig. 1). Fine needle aspiration (FNA) was used to obtain a population of hardly differentiated malign cells with an irregular clear nucleus, a clear nucleolus and little cytoplasm (Fig. 2A). Immunohistochemical studies in the cell block show that the cells stain focally with cytokeratin (CK) AE1/AE3 (Fig. 2B) and display patchy positivity for vimentin and epithelial membrane antigen. CK8 is slightly positive and focal. The following immunohistochemical markers are negative: thyroglobulin, PAX-8, CK19, CK7, synaptophysin, chromogranin, CD45, CD30, desmin, alpha actin and S100. The clinical history of the patient showed the previous case of a hardly differentiated stage IA uterine cervix carcinoma treated radically with brachytherapy and chemotherapy one year ago. Study of the previous biopsy of the cervical carcinoma shows cytological and immunohistochemical findings identical to those of the thyroid lesion (Fig. 2C and D). Study by polymerase chain reaction (PCR) for the human papillomavirus (HPV) using the Cobas® 4800 HPV test (Roche Molecular Systems, Pleasanton, CA, USA), shows positivity for HPV-16 in both 2 lesions. CAT was indicated, which showed metastasis in the right suprarenal gland and in the cervical and retroperitoneal lymphatic ganglia. Based on these results diagnosis was of thyroid metastasis of hardly differentiated cervical carcinoma. The patient received palliative treatment with radiotherapy and chemotherapy. Six months after the metastasis the patient died.

Discussion

Metastasis in the thyroid is extremely rare, although in recent years this organ has increasingly been reported to be the site of metastasis, probably due to its dense vascularisation. In the autopsy series the incidence of metastasis in the thyroid runs from 1.25% in cases with no previous
A history of neoplasia and 24% in those cases where there was a previous history of malignancy. The biopsy series shows a lower incidence, of 1.5%–8.5%.

The most common original sites of metastasis in the thyroid are the breasts, lungs, kidneys and skin melanoma. Some authors state that the kidneys are the most common origin, although others state that it is the breast. Carcinoma of the cervix rarely develops in the thyroid, and we only found 8 published cases. Six squamous carcinomas, one neuroendocrine carcinoma and one endocervical adenocarcinoma (Table 1).

Differential diagnosis of metastasis to the thyroid must chiefly be made against anaplastic thyroid carcinoma, for which immunohistochemical and molecular biology techniques are highly useful. The immunohistochemical markers thyroglobulin and PAX-8 may also help, although the first of these is the most specific for the thyroid, and it is only positive in 20%–30% of anaplastic carcinomas.

Given the nature of the primary carcinoma in our case and the high prevalence of HPV, the determination and genotyping of this virus were highly useful, given that there is a strong correlation between the genotype found in the primary tumour and its metastasis.

Metastasis must be considered in differential diagnosis whenever there is a previous malignancy. Nor does the time passed following treatment of the primary tumour make it possible to rule metastasis out, as it has been found in the thyroid up to 19 years after the primary tumour, as shown in the literature.

Treatment for metastatic lesions in the thyroid is usually palliative, with radiotherapy and chemotherapy, given that at the moment of diagnosis there is usually neoplastic dissemination, as there was in our case. Nevertheless, if there is a unique lesion then exeresis of the nodule may be performed with the intention to cure.

Lastly, the value of FNA should be underlined in the diagnosis of thyroid lesions. This simple procedure makes it possible to establish the definitive diagnosis or at least the suspicion of malignancy in the majority of patients, thereby avoiding the use of more invasive techniques and/or surgery that is not indicated.

Figure 1 The arrow indicates an irregular nodular lesion of approx. 5 cm, occupying the right lobe of the thyroid.

Figure 2 (A) Cell block from fine needle aspiration of the thyroid nodule. Pleomorphic and irregular nuclei, some clear and others with an obvious nucleolus. There are no residues of thyroid parenchyma, H&E 20×. (B) Intense and patchy positivity for cytokeratin AE1/AE3 in the thyroid nodule, immunoperoxidase 10×. (C) Biopsy of the uterine cervix showing cells identical to those in the thyroid. (D) Patchy staining for cytokeratin AE1/AE3.
Table 1  Carcinoma of the Neck of the Uterus Which Developed Metastasis to the Thyroid.

<table>
<thead>
<tr>
<th>References</th>
<th>Age</th>
<th>Histol. s.</th>
<th>Dis.-free interv. (months)</th>
<th>Metastasis to other locations</th>
<th>Survival (months)</th>
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<td>Karapanagiotou E</td>
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<td>Suprarenal. Neck and retroperitoneal LG</td>
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ADC: adenocarcinoma; SCE: squamous cell carcinoma; NC: neuroendocrine carcinoma; PDC: poorly differentiated carcinoma; LG: lymphatic ganglia; Dis. free interv: disease-free interval; Histol s.: histological subtype.

Conflict of Interest

They authors declare they have no conflict of interest.

References