Coexistence of subacute thyroiditis and renal cell carcinoma: a paraneoplastic syndrome

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Abstract

RENAL CELL CARCINOMA IS CHARACTERIZED by varied manifestations, which include unusual metastatic sites and paraneoplastic and vascular syndromes. We describe the case of a 57-year-old man who presented with high fever, weight loss, palpitations and a tender goitre. We suggest that, in this patient, subacute thyroiditis manifested as a paraneoplastic syndrome of renal cell carcinoma.

Case

A 57-year-old previously healthy man presented with a 1-month history of high fever, weight loss and palpitations. Physical examination revealed a tender goitre with a nodule on either side, about 3 cm in diameter and the other about 1 cm. Ultrasonography revealed that the thyroid gland had a heterogeneous echogenicity and there were nodules of 36 mm and 14 mm in diameter on the right and left sides, respectively. He had elevated levels of triiodothyronine and thyroxine and a suppressed level of thyrotropin (Table 1). His erythrocyte sedimentation rate was 68 mm/h, and the C-reactive protein level was greater than 206 mg/L. A thyroid scan revealed low radioiodine uptake (less than 1% in 24 hours). A fine-needle aspiration biopsy of thyroid tissue revealed numerous multinucleated histiocytic giant cells and scant epithelioid cells (Fig. 1), as well as degenerated follicular cells and scanty colloid. The cytoplasm of the histiocytic giant cells was syncytial and contained no phagocytosed material. Cytopathologic diagnosis was chronic granulomatous thyroiditis. In addition, the patient had high levels of alkaline phosphatase (1045 [normally < 270] U/L) and gamma-glutamyl transferase (219 [normally 6–49] U/L). A CT scan of the abdomen showed a mass of about 4 x 4 cm on the right kidney.

A right radical nephrectomy was performed. Pathologic examination revealed grade 2, stage I renal cell carcinoma and coexistent angiomyolipoma. Although the patient received no specific therapy for the thyroiditis, 1 month after the nephrectomy the nodules on the thyroid gland had disappeared, the patient was euthyroid and his erythrocyte sedimentation rate and C-reactive protein, alkaline phosphatase and gamma-glutamyl transferase levels were all normal (Table 1).

Comments

Subacute thyroiditis is an acute inflammatory disorder of the thyroid gland most likely due to viral infection. No association between subacute thyroiditis and renal cell carcinoma has been reported to date.

Among neoplastic diseases, renal cell carcinoma is recognized for its unpredictable various paraneoplastic syndromes. The biologic basis for these unusual features of renal cell carcinoma might be the mediation of effects by cytokines, such as interleukin-6 (IL-6), or growth factors produced by the tumour and immune mechanisms.

IL-6 has been shown to be involved in the pathophysiology of paraneoplastic syndromes, in particular the elevation of C-reactive protein and haptoglobin levels but also para-

Table 1: Laboratory values in a case of coexistent subacute thyroiditis and renal cell carcinoma

<table>
<thead>
<tr>
<th>Parameter (and normal range)</th>
<th>On admission (3 wk before nephrectomy)</th>
<th>Just before nephrectomy</th>
<th>4 wk after nephrectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyrotropin (0.4–4.0 mU/L)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>3.86</td>
</tr>
<tr>
<td>Triiodothyronine (2.5–7.2 nmol/L)</td>
<td>7.9</td>
<td>7.6</td>
<td>3.2</td>
</tr>
<tr>
<td>Thyroxine (10–23 pmol/L)</td>
<td>54</td>
<td>52</td>
<td>12</td>
</tr>
<tr>
<td>C-reactive protein (&lt; 5 mg/L)</td>
<td>&gt; 206</td>
<td>&gt; 206</td>
<td>8</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (&lt; 15 mm/h)</td>
<td>68</td>
<td>73</td>
<td>8</td>
</tr>
<tr>
<td>Alkaline phosphatase (&lt; 270 U/L)</td>
<td>1045</td>
<td>966</td>
<td>215</td>
</tr>
<tr>
<td>Gamma-glutamyl transferase (6–49 U/L)</td>
<td>219</td>
<td>234</td>
<td>16</td>
</tr>
</tbody>
</table>
neoplastic cholestasis (Stauffer syndrome), paraneoplastic thrombocytosis, neutrophilia and monocytosis. All of these paraneoplastic syndromes spontaneously regress after surgical remove of the neoplastic tissue.

Variations in serum IL-6 levels have also been reported in cases of thyroid dysfunction: increased levels have been found in patients with thyroidal destructive processes such as subacute thyroiditis and some forms of amiodarone-induced thyrotoxicosis, and after percutaneous ethanol injection into “hot” thyroid nodules.

In the past, high levels of IL-6 during the course of subacute thyroiditis was thought to be the result of cytokine release from the damaged thyrocyte. However, Yamada and colleagues showed that IL-6 levels do not fall along with other parameters of disease activity during treatment with corticosteroids. An alternative explanation may be that elevated IL-6 levels during the course of subacute thyroiditis are the cause, not the result, of the destructive process.

We did not measure the preoperative level of IL-6 in our patient, but his fever, the elevated C-reactive protein level and erythrocyte sedimentation rate, and the paraneoplastic cholestasis were clinical clues of high circulating IL-6 levels. We suggest that the destructive process in the thyroid that presented clinically as subacute thyroiditis may have been triggered by high levels of IL-6.

Resolution of the patient’s thyroiditis and its pathologic parameters was much faster than that in the average case of subacute thyroiditis. In addition, the common pathophyslogic influence of IL-6 in thyroiditis and renal cell carcinoma suggests that the subacute thyroiditis manifested as a paraneoplastic syndrome of the renal cell carcinoma.

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References

Contributors: All authors contributed equally to the writing and revising of the article and approved the final version.

This article has been peer reviewed.

Fig. 1: Numerous multinucleated histiocytic giant cells and scant epithelioid cells seen in thyroid tissue of man presenting with subacute thyroiditis (May–Grunwald–Giemsa stain; original magnification × 200, reduced by 30%).