Synchronous gastrointestinal stromal tumors (GIST) and other primary cancers: Case series of a single institution experience

Sheila S. Ferreira a, Gustavo Werutsky a,⁎, Marcelo Garcia Toneto b, Jarcedy Machado Alves b, Christina Duarte Pianta b, Raquel Cristine Breunig a, Adriana Brondani da Rocha c, Ivana Grivicich c, Bernardo Garicochea a

a Department of Medical Oncology, Pontifical Catholic University of Rio Grande do Sul, São Lucas Hospital, 6690 Ipiranga av., 90610-000 Porto Alegre, Brazil
b Department of Surgery, Pontifical Catholic University of Rio Grande do Sul, São Lucas Hospital, 6690 Ipiranga av., 90610-000 Porto Alegre, Brazil
c Laboratory of Cell Stress Biomarkers, Medical Science Research Center, Luterana do Brasil University, 8001 Farroupilha av., 92425-900 Canoas, Brazil

Article info

Article history:
Received 12 March 2010
Accepted 29 March 2010
Available online 7 April 2010

Keywords:
Gastrointestinal stromal tumors
Synchronous neoplasms
Immunohistochemistry

Abstract

Background: Gastrointestinal stromal tumors (GISTs) are rare mesenchymal neoplasm affecting the gastrointestinal tract. The incidental occurrence of mesenchymal tumors and other primary tumors has not been well described in literature.

Objective: The aim of this study was to evaluate the clinical and pathologic features of GIST occurring synchronously with other primary tumors.

Methods: Forty-three patients with diagnosis of GIST treated surgically with curative intent at our institution from 1998 to 2006 were included. The patient clinical data and pathological reports were reviewed.

Results: Of the 43 patients, there were 6 (14%) cases of synchronous GIST and other primary tumors discovered as coincidental findings. The synchronous GISTs analyzed were located in the stomach (50%) and small intestine (50%), size ranging from 0.7 to 7.6 cm (median 3.35 cm). Five (83%) of the concurrent primary tumors were from gastrointestinal origin and only one (17%) patient presented with concurrent breast cancer and GIST. The synchronous GISTs immunofenotype shows positivity for CD117 and CD34 (100%), smooth-muscle actin (SMA) (67%), S100 (50%) and desmin (33%). Whereas staining for cytokeratin AE1/AE3 and PDGF were all negative. According to GIST risk category for aggressive behavior three were classified as very low, one intermediate and two high.

Conclusions: The synchronous occurrence of GISTs and other primary neoplasm is not an uncommon entity however such occurrence has been more frequently described in literature mainly in form of single case reports.5−10 KIT and PDGFRA activating mutations are the oncogenic mechanisms in most sporadic and inherited GISTs. Little is known about the possible mechanisms involved in synchronous GIST and other neoplasms, some syndromic or familial disease are suspected in the presence of second primary tumor and C-KIT and PDGFRA negative GIST patients.19 Synchronous occurrence of GIST and other tumors are almost always discovered incidentally as during surgery or staging exams of the primary disease.

In this study, we introduce a series of six patients, from a single institution, with GIST and a second primary neoplasm occurring synchronously. The aim of this study was to evaluate the clinical and pathologic features of GISTs occurring synchronously with other primary tumors.
In our study, GIST occurred synchronously with other neoplasm in 6 (14%) patients. The concomitant cases were primary tumors and during the planned treatment, such as CT scanning or surgery, GIST was discovered as an incidental finding. From the synchronous neoplasms, five (83%) had gastrointestinal origin and only one (17%) presented with breast cancer. With the exception of the breast cancer patient all others GISTs were an incidental finding during the surgery for other primary tumors, where 50% of these were located in the stomach and other 50% were in the small intestine. The clinical characteristics of patients with synchronous tumors are shown in Table 1.

The synchronous GISTs analyzed were located in the stomach (50%) and small intestine (50%), size ranging from 0.7 to 7.6 cm (median 3.35 cm). The pathologic features of synchronous GISTs and other primary tumors are summarized in Table 2.

Regarding the treatment, GISTs were resected by enterectomies (n = 3) in 2 cases discovered during colectomy for colorectal cancer and 1 case found incidentally in an abdominal Computed Tomography (CT) for breast cancer staging. Partial and total gastrectomy (n = 2) was performed for gastric cancer and in this case GIST was discovered during the histopathological examination. Esophagogastrectomy (n = 1) was the treatment for esophageal cancer and concomitant GIST in the stomach diagnosed by esophagogastroendoscopy. Macroscopically all GISTs presented as nodular mass and were dissected with clear margins.

All synchronous GISTs were uniformly CD117 and CD34 positive. Smooth-muscle actin (SMA) was detected in four (67%) cases, S100 in three (50%) and desmin in two cases (33%). Whereas staining for cytokeratin AE1/AE3 and PDGF were negative for all GISTs studied. In addition to the immunophenotype, the tumor size and mitotic index reveal that the synchronous GISTs could be classified as very low (n = 3), intermediate (n = 1) and high (n = 2) risk of aggressive behavior. The histopathologic features of the synchronous GISTs are shown in Table 3.

### 4. Discussion

GIST is a rare neoplasm that represents about 0.1—1.0% of all malignant neoplasms of the gastrointestinal tract. Most GISTs arise from the stomach (50—62%), the small intestine (20—30%), the colon (11%) and the rectum (7%), while the esophagus is rarely involved (0.6—1%). They also have been found in others locations such as the omentum, mesentery and retroperitoneum. In our series, there were 14% (6/43) cases of synchronous occurrence of GIST and other gastrointestinal malignancies, which is in the average incidence of 10 to 35% described in the literature. GISTs have been reported to occur synchronously mostly with adenocarcinoma, in our series 83% (5/6) had this histology, nevertheless there are reports of synchronicity with lymphomas and carcinoid tumors. We also observed such high frequency of gastrointestinal epithelial tumors being diagnosed simultaneously with GIST, actually one in every 8 patients with GIST in our series presented a synchronous epithelial tumor, most of them in the stomach, colon and esophagus.

### Table 1

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age</th>
<th>Gender</th>
<th>Synchronous primary tumor localization</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36</td>
<td>F</td>
<td>Colon</td>
</tr>
<tr>
<td>2</td>
<td>52</td>
<td>M</td>
<td>Gastric</td>
</tr>
<tr>
<td>3</td>
<td>65</td>
<td>F</td>
<td>Gastric</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>F</td>
<td>Esophagus</td>
</tr>
<tr>
<td>5</td>
<td>69</td>
<td>F</td>
<td>Colon</td>
</tr>
<tr>
<td>6</td>
<td>79</td>
<td>F</td>
<td>Breast</td>
</tr>
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### Table 2

<table>
<thead>
<tr>
<th>Patient number</th>
<th>GIST Localization</th>
<th>Synchronous primary tumor Type</th>
<th>Localization</th>
<th>Size (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Small intestine</td>
<td>Adenocarcinoma (T3N0M0)</td>
<td>Colon</td>
<td>5.5</td>
</tr>
<tr>
<td>2</td>
<td>Gastric</td>
<td>Adenocarcinoma (T3N1M0)</td>
<td>Gastric</td>
<td>10.2</td>
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<tr>
<td>3</td>
<td>Gastric</td>
<td>Adenocarcinoma (T3N1M0)</td>
<td>Gastric</td>
<td>4.8</td>
</tr>
<tr>
<td>4</td>
<td>Gastric</td>
<td>Carcinoma epidermoid (T3N2M0)</td>
<td>Esophagus</td>
<td>4.6</td>
</tr>
<tr>
<td>5</td>
<td>Small intestine</td>
<td>Adenocarcinoma (T3N0M0)</td>
<td>Colon</td>
<td>5.8</td>
</tr>
<tr>
<td>6</td>
<td>Small intestine</td>
<td>Invasive ductal carcinoma (T3N1M0)</td>
<td>Breast</td>
<td>6.2</td>
</tr>
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</table>
The most important markers for defining GISTs are CD117 (c-kit protein) and CD34 (hematopoietic cell progenitor antigen). The majority of GISTs are usually positive for CD117 (near 95% of cases) and CD34 (positive in 40% of cases). Few cases present positivity for S-100 (positive near 5% of cases) and desmin (positive in approximately 2% of cases). Simultaneous detection of CD117/CD34 is not a feature observed in the majority of GIST tumors, but curiously, in all of our six patients with synchronous tumors the immunohistochemical staining for CD117 and CD34 proteins was positive. Another interesting observation regards to the independence of the stage of the disease and synchronicity. In our series, synchronicity was not related to the aggressiveness of GIST even low grade cases were found with synchronous tumors in our group of patients suggesting that the development of a second neoplasia (being GIST or carcinoma) can be a very early event in these individuals. The high frequency of synchronous GIST and adenocarcinoma rises some questions in regard to the origin of both neoplasias. It is conceivable that at least some cases of GIST arise from a progenitor cell capable to differentiate either to mesenchymal and epithelial lineages. It is interesting to observe that all patients with synchronous GIST in our series expressed CD34, a well-known marker of precursor cells. Another possibility to explain synchronicity is that the environmental carcinogens might affect molecular pathways that are shared by mesenchymal and epithelial cells of the digestive tract.

In summary, the synchronous occurrence of GISTs and other primary tumors is more common than it has been considered and usually they are discovered incidentally during the surgery performed because of the other malignancy. More assertive search for GIST in the digestive tract of patients with adenocarcinoma may reveal an even larger number of cases. Further studies are required to clarify the molecular and genetic mechanisms of carcinogenesis and progression associating GIST and synchronous tumors.

### Table 3

<table>
<thead>
<tr>
<th>Patient number</th>
<th>CD117</th>
<th>CD34</th>
<th>S-100</th>
<th>SMA</th>
<th>Desmin</th>
<th>AE1/AE3</th>
<th>PDCD</th>
<th>Tumor size (cm)</th>
<th>Mitotic index (x/50 hpf)</th>
<th>Risk category for malignant behavior</th>
</tr>
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<tr>
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<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>&gt;20</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>&lt;5</td>
<td>Very low</td>
</tr>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>−</td>
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<td>−</td>
<td>&lt;5</td>
<td>Very low</td>
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<td>+</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>&lt;5</td>
<td>Very low</td>
</tr>
<tr>
<td>5</td>
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<td>−</td>
<td>−</td>
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<td>−</td>
<td>−</td>
<td>&gt;20</td>
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<tr>
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<td>−</td>
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<td>−</td>
<td>−</td>
<td>&lt;5</td>
<td>Intermediate</td>
</tr>
</tbody>
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### References


### Conflict of interest

None.

### Funding

None.

### Ethical approval

None. Not needed for retrospective observational research in our institution.


