Endometrial Polyps with Predominant Stromal Component Are Characterized by a t(6;14)(p21;q24) Translocation

Roberta Vanni,1 Susanna Marras, Marcello Andria, and Gavino Faa
Istituto di Biologia Generale [R. V., S. M.], Via Ospedale, 119 09124 Cagliari (Sardinia), Italy, Dipartimento di Citomorfologia, Sezione di Anatomia Patologica [G. F.], and Divisione Ostetrica e Ginecologica USL 21 [M. A.], Cagliari, Italy

Abstract

Cytogenetic investigation of endometrial polyps revealed the presence of a t(6;14)(p21;q24) as the sole abnormality in three cases. All tumors showed a histopathological pattern of predominant stromal hyperplasia with scarce representation of glandular elements, suggesting that a cytogenetic subgroup characterized by the t(6;14) translocation can be associated with endometrial polyps with a preponderant component of mesenchymal origin.

Introduction

Endometrial polyps are common nonmalignant pedunculated or sessile nodules protruding into the uterine cavity. They originate as focal hyperplasia of the basalis and develop into benign, localized overgrowths of endometrial tissue covered by epithelium and containing variable amounts of glands, stroma, and blood vessels (1). Recurrence as carcinoma has been reported in <0.5% of benign polyps (2), although they are present in 12–34% of the uteri containing endometrial carcinoma (3).

Cytogenetic investigations of these types of proliferations have demonstrated the presence of nonrandom structural changes, found in eight cases (4–8), mainly involving chromosome 6p and 12q. The hypothesis that endometrial polyps, like a number of other benign tumors, may be cytogenetically dissected into different subgroups has been suggested (8).

We report the observation of a t(6;14)(p21;q24) in three clinically defined endometrial polyps, with a histological pattern showing a diffuse stromal hyperplasia and with an in vitro cell growth pattern of mesenchymal origin.

Materials and Methods

Case Reports

Case 1. A 43-year-old woman (gravida 3, para 3) was examined for abnormal bleeding. Diagnostic endocervical and endometrial curetage was performed. During the procedure a polyp was found, measuring 20 × 6 × 5 mm. Histological examination revealed an endometrial polyp with few endometrial glands, mostly pushed toward the periphery, and dense stromal hyperplasia.

Case 2. A 41-year-old woman (gravida 4, para 3) sought medical attention for abnormal bleeding and was found to have uterine fibromatosis. Laparohysterectomy revealed the presence of a polyp in the fundus measuring 23 × 10 × 8 mm. On histological examination an endometrial polyp with a preponderant stromal component was diagnosed.

Case 3. A 54-year-old woman (gravida 3, para 3) was seen for postmenopausal bleeding. Total hysterectomy was performed. At gross examination, a polyp in the fundus was found measuring 15 × 8 × 6 mm. The histology...
Table 1 Summary of clinical and cytogenetic data

| Case | Age (yr) | Size (mm) | Histology of the polyps          | Karyotype
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (380/93)</td>
<td>43</td>
<td>20 × 6 × 5</td>
<td>Abundant stromal hyperplasia</td>
<td>46,XX,t(6;14)(p21;q24) [10]</td>
</tr>
<tr>
<td>2 (449/94)</td>
<td>41</td>
<td>23 × 10 × 8</td>
<td>Abundant stromal hyperplasia</td>
<td>46,XX,t(6;14)(p21;q24) [14]</td>
</tr>
<tr>
<td>3 (460/94)</td>
<td>54</td>
<td>15 × 8 × 6</td>
<td>Abundant stromal hyperplasia</td>
<td>46,XX,t(6;14)(p21;q24) [11]/idem,add(1)(p33-34) [3]</td>
</tr>
</tbody>
</table>

a Karyotypes are expressed according to the Guidelines for Cancer Cytogenetics (9): numbers in brackets, number of cells constituting the clone(s); in case 3 a subclone was found with the same (idem) karyotype of the main clone, except for additional unknown material (add) on the short arm of chromosome 1.

b Number in parentheses, laboratory code.

Fig. 3. Metaphase spreads from cases 1 (A), 2 (B), and 3 (C), treated with biotinylated cocktail to chromosome 14. Large arrowheads, normal chromosome 14; medium arrowheads, chromosome der(14)t(6;14) with extra-chromosome 14 material (dull telomere); small arrowheads, der(6)t(6;14) with chromosome 14 material (bright telomere).
revealed an endometrial polyp with strong stromal hyperplasia with few endometrial glands.

**Cytogenetics and in Situ Hybridization**

In all cases the specimens were divided into two parts: one for histological examination and the other for cytogenetic investigation. Tissue for cytogenetic analysis was mechanically and enzymatically disaggregated by incubation with collagenase 500 units/ml at 37°C in 5% CO₂ for 12-24 h. The resulting cell suspension was seeded into glass chamber slides containing RPMI 1640 medium supplemented with 16% FCS, L-glutamine 2 mM, penicillin (100 IU/ml), and streptomycin (100 μg/ml). Short-term (3 days) cultures were incubated with colcemid (0.03 μg/ml) for 16 h and harvested in situ by hypotonic treatment (tri-sodium citrate, 0.5%) for 45 min, and fixed with three changes of methanol:acetic acid (3:1).

In order to obtain G bands, slides were aged at 100°C for 20 min and treated with Wright’s stain. Chromosome analysis followed the ISCN (1991) recommendations (9). FISH was carried out using the chromosome 14-specific library (biotinylated probe cocktail; Oncor, Gaithersburg, MD) according to the manufacturer’s protocols. Probe detection was obtained with subsequent incubations of FITC-labeled antibodies, and chromosomes were counterstained with propidium iodide.

**Results and Discussion**

All of the endometrial polyps were classical pedunculated nodules protruding into the uterine cavity. The histopathological examination of all specimens revealed a dense stromal hyperplasia consisting of spindle fibroblast-like cells and abundant collagen fibers in which endometrial glands were underrepresented and pushed toward the periphery of the lesion (Fig. 1). Stromal cells appeared to be inactive with very few mitotic figures.

A summary of cytogenetic and clinical data of the cases is reported in Table 1. The t(6;14)(p21;q24) was found in all examined metaphases of the three cases (Fig. 2). In cases 1 and 2 no other subclones were found, whereas in case 3 a clonal evolution leading to a side clone with 46,XX,add(1)(p33-34),t(6;14)(p21;q24) karyotype was identified. FISH, utilizing the chromosome 14-specific library resulted in the following hybridization pattern: a D group chromosome (namely, chromosome 14) showed bright hybridization signals along the entire length of the chromosome. Another D group chromosome [namely, the der(14)t(6;14)] appeared dull in the distal part of the long arm, while the rest of the chromosome fluoresced with bright hybridization signals. A C group chromosome showed bright hybridization signals along the distal part of the short arm: namely, the region q24 from chromosome 14 replaced the reciprocal chromosome 6 material in the region p21 (Fig. 3). FISH results confirmed the cytogenetic interpretation given by chromosomal G-banding. Examination of cell cultures by a phase-contrast inverted microscope revealed that about 95% of colonies consisted of fibroblast-like cells (a pattern compatible with the use of collagenase dissociation of a tissue containing a low percentage of epithelial cells).

Presence of a certain degree of cytogenetic heterogeneity in endometrial polyps has been documented on the basis of cases showing rearrangements of 6p21, due to inversions, duplications, and translocations, and cases showing rearrangements of 12q13–15, due to inversions (4–8). These findings, consisting of eight reported abnormal cases, suggest that at least two abnormal cytogenetic subgroups, one characterized by rearrangements of 6p21 and another of 12q13–15, may be associated with endometrial polyps. The present observation of a seemingly identical t(6;14) translocation as the sole abnormality in three cases represents the first report of such a translocation in endometrial polyps, as well as the first observation of chromosome 14 involvement in such a benign tumor. This translocation seems to identify the most frequently recurrent primary change in endometrial polyp, since the 6p21 breakpoint consistently recombines with the same chromosomal partner. Interestingly, the histological pattern of these three polyps is very similar: in fact the glandular component of these cases was underrepresented, resulting in the cell outgrowth predominantly represented by stromal cells.

By using combined cytogenetic and immunohistochemical techniques on cultured cells from an endometrial polyp composed of both glandular and stromal elements, Fletcher et al. (10) demonstrated that the presence of 6p21 changes was restricted to the mesenchymal component. In our cases, indirect indications that cells bearing these chromosome changes could belong to the mesenchymal component are based on both the type of histopathological pattern (stromal hyperplasia) and the type of in vitro cell growth pattern (fibroblast-like).

On the other hand, an apparently identical translocation t(6;14) has been observed in the mesenchymal component of pulmonary chondroid hamartoma (11). Hence endometrial polyp is the second neoplasm in which this translocation occurs, and in which it is possibly associated with a peculiar histological type with preponderant stromal outgrowth.

**Acknowledgments**

We thank Dr. C. Hilliker for helpful discussion and Dr. G. Pichiri for technical assistance.

**References**

Endometrial Polyps with Predominant Stromal Component Are Characterized by a t(6;14)(p21;q24) Translocation

Roberta Vanni, Susanna Marras, Marcello Andria, et al.


**Updated version**
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/55/1/31

**E-mail alerts**
Sign up to receive free email-alerts related to this article or journal.

**Reprints and Subscriptions**
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

**Permissions**
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.