Use of a Novel FISH Assay as an Adjunct to Diagnosis of Dermatofibrosarcoma Protuberans and Giant Cell Fibroblastoma

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Abstract

Background: DFSP and GCF are characterized by a COL1A1/PDGFB fusion ([17;22](q22;q113) identification of this characteristic fusion may be especially useful when confronting with DFS/GCF lesions arising in uncommon sites, deviating from the classic histologic appearance, or exhibiting fibrosarcomatous transformation. As a diagnostic aid, we constructed FISH probe sets that: 1) can be performed on paraffin-embedded, formalin-fixed tissue; 2) identify potential unusual variant translocations or cryptic rearrangements; and 3) assess individual histologic components such as fibrosarcomatous areas in DFSP.

Methods

Tumor Samples

In total, 39 samples including 17 DFSP specimens, 3 GCFs, 3 fibrosarcomatous DFSP variants, 4 dermatofibromas and 3 pathologically unremarkable skin specimens were evaluated by conventional cytogenetic analysis, RT-PCR, and/or FISH (Figure 2). All tumors were diagnosed according to the WHO histological criteria (1). The clinicopathologic features are listed in Table 1.

Cytogenetic Analysis

Cytogenetic analysis was performed on six DFSps (cases 1-3, 11-12, 16) and one fibrosarcomatous DFSP variant (case 23) according to standard procedure (2).

Reverse Transcription – Polymerase Chain Reaction (RT-PCR)

RT-PCR for the COL1A1-PDGFB fusion transcript was performed as previously described (3).

Fluorescence in situ Hybridization (FISH)

The COL1A1 (17q21) and PDGFB (22q13) loci were investigated using combinations of probe sets designed to identify potential unusual variant translocations or cryptic rearrangements, characterizing complex rearrangements and potentially identifying variant translocations.

Results

Cytogenetic Analysis

Global karyotypic abnormalities were detected in all seven specimens analyzed (Figure 1). Table 1. Reverse transcription – polymerase chain reaction (RT-PCR)

RT-PCR analysis of Case 1 demonstrated a COL1A1-PDGFB fusion transcript composed of an in-frame fusion of COL1A1 exon 26 with PDGFB exon 2.

Fluorescence in situ Hybridization (FISH)

FISH studies were positive for a fusion of COL1A1 and PDGFB probe signals in 15 of 16 successfully analyzed DFSps, all three fibrosarcomatous DFSP variants and all three GCFs (Table 1). Importantly, the FISH findings were concordant in all DFSps that also had informative conventional karyotyping or RT-PCR results.

Conclusions

1. FISH analysis with these newly designed probe sets is a reliable and specific method of detecting cryptic translocations, characterizing complex rearrangements and potentially identifying variant translocations.

2. FISH analysis for t(17;22) can be used successfully in routinely processed tissue (including paraffin-embedded, formalin-fixed tissue).

3. FISH may serve as a useful diagnostic aid in DFSP/GCF cases with unusual histopathologic features (myxoid DFSP, DFSP with fibrosarcomatous transformation) or atypical clinical presentations (uterus DFSP).

References


Acknowledgements: The authors would like to thank Drs. Lilia Debbache, St Jude Hospital; Cristina Antinucci, Memorial Sloan-Kettering Cancer Center; Alexandre Benitah and Andrew Wagner, Brigham and Women’s Hospital; and Thomas Roux, University of Chicago Medical Center for submission of valuable case material.

Table 1. Clinicopathologic and Molecular Pathologic Data

<table>
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<tr>
<th>Diagnosis</th>
<th>Age/G = Sex</th>
<th>Clinical Site</th>
<th>Size (cm)</th>
<th>Karyotype</th>
<th>FISH</th>
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<td>3.1</td>
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<td>Back</td>
<td>4.5</td>
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</tr>
<tr>
<td>DFSP</td>
<td>11/M</td>
<td>Back</td>
<td>NA</td>
<td>17;22 rearranged</td>
<td>–</td>
</tr>
<tr>
<td>DFSP</td>
<td>61/F</td>
<td>Abdominal</td>
<td>2.3</td>
<td>49,XX,+16,+21,+22,+der(22)t(17;22)(q21;q13)x2[5]/46,XX[11] +</td>
<td>–</td>
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<td>56/F</td>
<td>Back</td>
<td>2.3</td>
<td>51/X, del(4)(q32), add(5)(q23), del(17)(p11.2), der(17)t(17;22)(q21;q13), +19, +ider(22)t(17;22), +mar[6]</td>
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<tr>
<td>GCF</td>
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<td>Abdominal</td>
<td>2.3</td>
<td>49,XX,+16,+21,+22,+der(22)t(17;22)(q21;q13)x2[5]/46,XX[11] +</td>
<td>–</td>
</tr>
</tbody>
</table>

Figure 1: Upper left: Case 11 exhibiting a supervenous ring chromosome (arrow) shown to be composed of part of COL1A1 and PDGFB. Upper right: Case 12 exhibiting the following abnormal complement 45.XX,del(4)(q32),add(5)(q23), del(17)(p11.2), der(17)t(17;22)(q21;q13), +19, +ider(22)t(17;22), +mar[6].

Figure 2: Upper left: DFSP with classic honeycomb infiltration into subcutaneous fat (Case 12). Upper right: DFSP infiltrating into wall of fallopian tube (Case 1). Lower left: DFSP with myxoid change (Case 17). Lower right: Fibrosarcomatous variant of DFSP characterized by a hypercellular, desmoplastic growth pattern (lower portion of the photo). (Case 23).