Author's response to reviews

Title: Solitary Peutz-Jeghers-type hamartomatous polyp in the duodenum: Is it associated with a low risk of cancer?

Authors:

Yusuke Sekino (ysekino@yokohama-cu.ac.jp)
Masahiko Inamori (inamorim@med.yokohama-cu.ac.jp)
Mitsuru Hirai (mitshirai@yahoo.co.jp)
Kaori Suzuki (kaori.suzuki@hotmail.co.jp)
Kaoru Tsuzawa (kaotsuzawa@hotmail.co.jp)
Keiko Akimoto (kaotsuzawa@hotmail.co.jp)
Ayako Takahata (ayatomi@hotmail.co.jp)
Nobutaka Fujisawa (fujisawa-yokohama2640@hotmail.co.jp)
Kumiko Saito (kumikumi2003@hotmail.co.jp)
Akisa Tsunemi (akisamahot@gmail.com)
Michio Tanaka (m-tanaka@hiroo-hospital.metro.tokyo.jp)
Hiroshi Iida (iida-ham@umin.ne.jp)
Yasunari Sakamoto (ys1125@yokohama-cu.ac.jp)
Hirokazu Takahashi (hirokazu@med.yokohama-cu.ac.jp)
Tomo Koide (tomo-k57@fuku.hp.yokohama-cu.ac.jp)
Chikako Tokoro (chikako@fuku_hp.yokohama-cu.ac.jp)
Yasunobu Abe (a0121@yokohama-cu.ac.jp)
Atsushi Nakajima (nakajima-tky@umin.ac.jp)
Shin Maeda (shinmaeda2-gi@umin.ac.jp)
Shigeru Koyama (Shigeru_Koyama@member.metro.tokyo.jp)

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Author's response to reviews: see over
Reviewer’s report

Solitary Peutz-Jeghers-type hamartomatous polyp in the duodenum: Is it associated with a low risk of cancer? : a case report

Reviewer: Masayuki Ohta

Comments to authors:

1. This case report is well written except for the section of discussion. Therefore, the authors should add some comments about the strategy of diagnosis and treatment into the section.

Yes, as you pointed out, comments about the strategy of diagnosis and treatment should be added. The section of discussion have been revised as follows:

As compared with PJS, Peutz-Jeghers-type hamartomatous polyps are diagnosed at a more advanced age, in the absence of mutation of the STK11/LKB-1 gene, and without familial history and mucocutaneous pigmentation [5].

Previous reports showed that the areas of neoplastic change, such as adenomatous or carcinomatous change were 3-6% of the polyps in PJS [4-20]. Case reports up to July
2010 searched from the MEDLINE database, using the terms "hamartomatous polyp" and "duodenum", and from reference lists of published articles, including our cases, showed 27 patients of solitary Peutz-Jeghers-type hamartomatous polyp in the duodenum (Table 1). Although solitary Peutz-Jeghers-type hamartomatous polyps have been considered to show a lower potential for malignant transformation as compared to PJS, three cases (including ours) of solitary Peutz-Jeghers-type hamartomatous polyps with malignant component were reported since 2008, and the total malignant transformation rate of solitary Peutz-Jeghers-type hamartomatous polyp was 4/27 (14.8%). There were no significant tendencies of malignant transformation among the age, sex, location, size and endoscopic appearance.

The most serious problem in PJS is an increased risk for cancer in gastrointestinal tract. The percentage of cancer in the gastrointestinal tract has been reported in 20-25% of patients with PJS and the risk of cancer in other organs including ovary, breast, bladder, pancreas and thyroid has been also reported [20-23].

Previously, no patients with solitary Peutz-Jeghers-type hamartomatous polyps have been reported to have malignancy of other organs, and it is one of the reasons that solitary Peutz-Jeghers-type hamartomatous polyps have been considered as a separate clinical entity from PJS. However, case 2 in our report had duplicated malignancy in six
organs, and overlap between solitary Peutz-Jeghers-type hamartomatous polyps and PJS may need to be re-examined.

Our two cases were diagnosed at an old age similar to previous reports, but differ in malignant alteration of hamartomatous polyp and concomitant other cancers. Patients with duodenal Peutz-Jeghers-type hamartomatous polyps are encouraged to undergo colonoscopy and whole-body screening, duodenal solitary Peutz-Jeghers-type hamartomatous polyps are preferably treated by endoscopic or surgical resection.
Reviewer: Takashi Joh

Comments to authors:

1. You should provide the malignant transformation rate of solitary Peutz-Jehghers-type hamartomatous polyp and Peutz-Jehghers-Syndrome (PJS), and discuss about them.

Yes, as you pointed out, the malignant transformation rate of solitary Peutz-Jehghers-type hamartomatous polyp and Peutz-Jehghers-Syndrome (PJS) should be presented. The section of discussion have been revised as follows;

Previous reports showed that the areas of neoplastic change, such as adenomatous or carcinomatous change were 3-6% of the polyps in PJS [4-20]. Case reports up to July 2010 searched from the MEDLINE database, using the terms "hamartomatous polyp" and "duodenum", and from reference lists of published articles, including our cases, showed 27 patients of solitary Peutz-Jeghers-type hamartomatous polyp in the duodenum (Table 1). Although solitary Peutz-Jeghers-type hamartomatous polyps have been considered to show a lower potential for malignant transformation as compared to PJS, three cases (including ours) of solitary Peutz-Jeghers-type hamartomatous polyps with malignant component were reported since 2008, and the total malignant
transformation rate of solitary Peutz-Jehghers-type hamartomatous polyp was 4/27 (14.8%).

2. The author should provide some features (endoscopic appearance and size, and so on) about Solitary Peutz-Jehghers-type hamartomatous polyp with malignant transformation.

Yes, as you pointed out, endoscopic findings of solitary Peutz-Jehghers-type hamartomatous polyp with malignant transformation should be added. The section of discussion and Table 1 have been revised as follows;

There were no significant tendencies of malignant transformation among the age, sex, location, size and endoscopic appearance.
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Number of patients</th>
<th>Age</th>
<th>Sex</th>
<th>Location</th>
<th>Surface</th>
<th>Size (mm)</th>
<th>Treatment</th>
<th>Malignant transformation</th>
</tr>
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<tbody>
<tr>
<td>Gannon [6]</td>
<td>1962</td>
<td>6</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>Smooth</td>
<td>NS</td>
<td>NS</td>
<td>No</td>
</tr>
<tr>
<td>Shiegel [7]</td>
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<td>1</td>
<td>75</td>
<td>NS</td>
<td>2nd</td>
<td>Smooth</td>
<td>NS</td>
<td>surgery</td>
<td>No</td>
</tr>
<tr>
<td>Ushijima [8]</td>
<td>1986</td>
<td>1</td>
<td>46</td>
<td>M</td>
<td>2nd</td>
<td>Lobulated</td>
<td>20x20x15</td>
<td>endoscopy</td>
<td>No</td>
</tr>
<tr>
<td>Bott [9]</td>
<td>1986</td>
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<td>23</td>
<td>M</td>
<td>4th</td>
<td>NS</td>
<td>50x40</td>
<td>surgery</td>
<td>No</td>
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<td>Naitoh [10]</td>
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<td>1</td>
<td>56</td>
<td>F</td>
<td>3rd</td>
<td>Smooth</td>
<td>30x15</td>
<td>endoscopy</td>
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<td>41</td>
<td>M</td>
<td>3rd</td>
<td>Lobulated</td>
<td>25x18</td>
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<td>Nebri [4]</td>
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<td>NS</td>
<td>50x35</td>
<td>surgery</td>
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<tr>
<td>Ichiyoshi [13]</td>
<td>1996</td>
<td>1</td>
<td>84</td>
<td>F</td>
<td>2nd</td>
<td>Lobulated</td>
<td>25x20</td>
<td>endoscopy</td>
<td>Yes</td>
</tr>
<tr>
<td>Oncel [14]</td>
<td>2003</td>
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<td>68</td>
<td>F</td>
<td>3rd</td>
<td>NS</td>
<td>15</td>
<td>endoscopy</td>
<td>No</td>
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<td>Kitaoka [5]</td>
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<td>22</td>
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<td>Lobulated</td>
<td>35x30x30</td>
<td>endoscopy</td>
<td>No</td>
</tr>
<tr>
<td>Itaba [15]</td>
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<td>87</td>
<td>F</td>
<td>2nd</td>
<td>NS</td>
<td>17</td>
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<td>Suzuki [16]</td>
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<td>59</td>
<td>F</td>
<td>2nd</td>
<td>Lobulated</td>
<td>15x15</td>
<td>surgery</td>
<td>No</td>
</tr>
<tr>
<td>Jamaludin [17]</td>
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<td>46</td>
<td>M</td>
<td>1st</td>
<td>Lobulated</td>
<td>70x40</td>
<td>surgery</td>
<td>Yes</td>
</tr>
<tr>
<td>Kantarcioğlu [18]</td>
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<td>28</td>
<td>M</td>
<td>2nd</td>
<td>Lobulated</td>
<td>25x15</td>
<td>endoscopy</td>
<td>No</td>
</tr>
<tr>
<td>Sekino: our report</td>
<td>2010</td>
<td>2</td>
<td>84</td>
<td>M</td>
<td>2nd</td>
<td>Lobulated</td>
<td>16x13</td>
<td>endoscopy</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>76</td>
<td>M</td>
<td>2nd</td>
<td>Lobulated</td>
<td></td>
<td>15</td>
<td>endoscopy</td>
<td>No</td>
</tr>
</tbody>
</table>

Table 1 Twenty-seven cases of solitary duodenal Peutz-Jeghers-type hamartomatous polyps. NS: not stated
3. Case 2 in this report have any cancers in the various organs. Please discuss about relations of Solitary Peutz-Jehghers-type hamartomatous polyp or PJS and duplicated cancer, based on the previous report.

Yes, following your recommendation, The section of discussion have been revised as follows;

The most serious problem in PJS is an increased risk for cancer in gastrointestinal tract. The percentage of cancer in the gastrointestinal tract has been reported in 20-25% of patients with PJS and the risk of cancer in other organs including ovary, breast, bladder pancreas and thyroid has been also reported. Previously, no patients with solitary Peutz-Jeghers-type hamartomatous polyps have been reported to have malignancy of other organs, and it is one of the reasons that solitary Peutz-Jeghers-type hamartomatous polyps have been considered as a separate clinical entity from PJS. However, case 2 in our report had duplicated malignancy in six organs, and overlap between solitary Peutz-Jeghers-type hamartomatous polyps and PJS may need to be re-examined.