Cowden syndrome: gastrointestinal manifestations of an infrequent polyposis

A 58-year-old man, with a history of total thyroidectomy for papillary carcinoma in 2012, presented with rectal bleeding for the last 4 years, without other digestive symptoms or weight loss. His physical examination revealed macrocephaly (63-cm circumference), skin with multiple verrucous papules of 1–3 mm on the face and dorsum of his hands (which histologically were trichilemmomas), papules in the oral mucosa (hamartomatous papillomas), and a furrowed tongue. The rest of his physical examination and laboratory test results were normal. Colonoscopy showed more than 50 sessile hamartomatous polyps of 2–5 mm in the rectum and sigmoid colon. Upper gastrointestinal endoscopy showed flat whitish lesions of 3–7 mm in the distal esophagus (acanthosis glycogen). In the stomach, multiple sessile polyps of 3–5 mm (▶Fig. 1) were resected and histology revealed these to be hamartomas (▶Fig. 2). In the second portion of the duodenum, a few sessile polyps of 4–5 mm were resected (histology revealed normal mucosa). Small-bowel capsule endoscopy revealed multiple polyps of 1–3 mm in the duodenum, proximal jejunum (▶Fig. 3), and distal ileum (▶Video 1).

Cowden syndrome is a rare entity related to the PTEN gene. It is characterized by the presence of hamartomatous lesions in any location. The diagnostic criteria (International Cowden Consortium criteria) include major and minor criteria (▶Table 1). Major criteria include: multiple gastrointestinal hamartomas or ganglioneuromas, macrocephaly, macular pigmentation of glans penis, mucocu-
taneous lesions (trichilemmoma, palmo-plantar keratoses, oral mucosal papillomatosis, and cutaneous facial papules),

and breast, endometrial, or follicular thy-roid cancer. Because of the risk of colo-
rectal cancer, surveillance is recom-mended, with colonoscopy starting at age
35 or 10 years younger than the age of
the index relative. Intervals should be
based on the findings, with colonoscopy
every 1–2 years if multiple polyps or
adenomatous polyps are present, or ev-
every 3–5 years if polyps are sparse or no
polyps are found [1–4].

Table 1 Diagnostic criteria for Cowden syndrome (International Cowden Consortium criteria updated by the National Comprehensive Cancer Network 2018).

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
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<tr>
<td>Breast cancer</td>
<td>Autism spectrum disorder</td>
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<tr>
<td>Endometrial cancer</td>
<td>Colon cancer</td>
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<tr>
<td>Follicular thyroid cancer</td>
<td>≥ 3 esophageal glycogenic acanthoses</td>
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<td>Multiple gastrointestinal hamartomas or ganglioneuromas</td>
<td>Lipoma</td>
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<td>Macrocephaly (58 cm in adult women, 60 cm in adult men)</td>
<td>Intellectual disability (IQ ≤ 75)</td>
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<tr>
<td>Macular pigmentation of glans penis</td>
<td>Papillary or follicular variant of papillary thy-roid cancer</td>
</tr>
<tr>
<td>Mucocutaneous lesions:</td>
<td>Thyroid structural lesions (adenoma, nodules, goiter)</td>
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<td>- One biopsy-proven trichilemmoma</td>
<td>Renal cell carcinoma</td>
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<tr>
<td>- Multiple palmar-plantar keratoses</td>
<td>Single gastrointestinal hamartoma or ganglioneuroma</td>
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<tr>
<td>- Multifocal or extensive oral mucosal papillomatosis</td>
<td>Testicular lipomatosis</td>
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<tr>
<td>- Multiple cutaneous facial papules</td>
<td>Vascular anomalies (including multiple intra-cranial developmental venous anomalies)</td>
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</table>

Operational diagnosis in an individual (either of the following):
1. Three or more major criteria, but one must include macrocephaly, Lhermitte-Duclos disease, or GI hamartomas
2. Two major and three minor criteria

Operational diagnosis in a family where one individual meets the revised clinical diagnostic criteria for PTEN hamartoma tumor syndrome or has a PTEN mutation (one of the following):
1. Any two major criteria with or without minor criteria
2. One major and two minor criteria
3. Three minor criteria

Competing interests
None

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