Colonic ganglioneuromatosis in a Shih tzu

Anya C. Hawthorn, MS, DVM
Tanya LeRoith, DVM, PhD, DACVP
Michael Leib, DVM, MS, DACVIM
History

• 7 year old female spayed Shih tzu
• Presented April of ‘07 for chronic, mixed bowel diarrhea of 2 years duration
  – Multicentric, infiltrative ganglioneuroma diagnosed by endoscopic biopsy
• Rectal mass found 3 weeks later
  – low grade adenocarcinoma and ganglioneuroma
• Second rectal mass in March of ‘09
Neuron Specific Enolase
Ganglioneuroma

- Composed of mature ganglion cells, nerve fibers and supporting elements (Schwann cells, fibroblasts)
- May be focal, polypoid ganglioneuromatosis, or diffuse ganglioneuromatosis
- Diffuse may be transmural or mucosal, and may create strictures; often congenital
- Associated with NF-1, MEN type IIB
- Human cases reported associated with colonic adenocarcinoma, carcinoids or adenomatous polyps.
Ganglioneuroma

- Ganglioneuroma reported in dogs, F344 rats, horses, cattle, pigs, cockatiels and humans.
- Clinical signs: diarrhea, constipation or obstruction, occasionally intussception.
- Diffuse type with increased expression of glial-derived neurotrophic factor and neurturin (human).
- TEM; hyperplasia of parasympathetic fibers and neurons, multiple neurotransmitters.
- This case may represent hamartomatous overgrowth.
<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Gene(s)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial adenomatosis polyposis</td>
<td>APC</td>
<td>Numerous colonic adenomatous polyps progressing to carcinoma</td>
</tr>
<tr>
<td>Juvenile polyposis syndrome</td>
<td>SMAD4, BMPR1A</td>
<td>Hamartomatous (juvenile) polyps in the GI tract, progression to malignancy</td>
</tr>
<tr>
<td>Peutz-Jeghers syndrome</td>
<td>LKB1</td>
<td>Intestinal hamartomatous polyps with mucocutaneous melanocytic macules, progression to malignancy</td>
</tr>
<tr>
<td>Cowden syndrome</td>
<td>PTEN</td>
<td>Hamartomatous polyps of mucosal membranes (mouth, nose and GI), increased risk of breast, thyroid and uterine cancer</td>
</tr>
<tr>
<td>MEN</td>
<td>RET</td>
<td>Mucosal neuromas, ganglioneuromatosis, pheochromocytoma</td>
</tr>
<tr>
<td>NF1</td>
<td>NF1</td>
<td>Multiple cutaneous neurofibromas, café au lait spots, MPNST, Lisch nodules, mesodermal dysplasia</td>
</tr>
</tbody>
</table>

- RET, NF1 and PTEN all have overlapping signaling through Akt and mTOR
References

• Masashi et al. 2007. Multiple rectal carcinoids with diffuse ganglioneuromatosis. World Journal of Surgical oncology. 5(19) Http://www.wsjo.com/content/5/1/19
• Owen, TM & Haghhighi. 2006. Hamartomatous polyps of the colon; Ganglioneuromatous, stromal and lipomatous. Archives in Pathology and Laboratory medicine. 130, Oct.
Acknowledgments

• All the pathologists who have examined this case:
  – G. Saunders DVM, MS, DACVP
  – D.P Sponenberg, DVM, PhD
  – B. Jortner, VMD, MS, DACVP
  – J. Robertson DVM, PhD

• Our Histology lab:
  – Luther Vest
  – Barbara Wheeler
  – Jill Songer