The Length of the Barrett’s Mucosa in Baboons, Revisited

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Abstract. Background: Chewing of regurgitated food with rumination elicits, gastroesophageal reflux (GER) in baboons. Protracted reflux transforms the distal multilayer squamous cell-lined epithelium into columnar-lined mucosa, with mucus-producing glands having interspersed oxyntic glands. In humans, this histological constellation is called Barrett’s mucosa type 2 (BMT2). Materials and Methods: The distal esophagus together with the proximal stomach was removed en bloc, at autopsy, from 35 adult baboons. Longitudinal sections were stained with toluidine blue, a stain that permits easy discrimination between parietal and chief gastric glands. Using a calibrated ocular scale, the length of the BMT2 was assessed in all 35 baboons. Results: The mean length of the BMT2 was 9.80 mm (range 1.0 mm-40.2 mm). Conclusion: BMT2 in baboons is an integrated part of the natural phenomenon of mucosal adaptation to daily regurgitation of gastric acid into the distal esophagus (natural GER), whereas BMT2 in humans might reflect an evolutionary atavism in the esophagus, triggered by a non-physiological disorder (pathological GER). The baboon offers a suitable model to monitor the series of histological events that take place in the distal esophagus under the influence of protracted GER.

Following chewing of regurgitated food with rumination, baboons develop after birth, daily gastro-esophageal reflux (GER) (1, 2). Regurgitation with rumination apparently occurs not only in baboons (3), but also in other non-human primates (NHP), such as chimpanzees (4, 5) and gorillas (6, 7). Protracted, life-long physiological reflux transforms the distal multilayered squamous cell-lined epithelium into columnar-lined mucosa with mucus-producing glands of pyloric phenotype having interspersed glands of oxyntic type (8). This columnar-lined mucosa mimics Barrett’s mucosa type 2 (BMT2) in humans (8-10). In this respect, The British Society of Gastroenterology (BSG) (11) defines Barrett’s esophagus as a columnar-lined esophageal mucosa, found in biopsies taken from endoscopical areas, suggestive of Barrett’s esophagus. The accompanying glands can be of mucus, oxyntic and/or intestinal metaplastic phenotype. This new definition has gained acceptance both in Europe and in Asia (12,13). As in baboons, the function of the Barrett’s mucosa in humans is to buffer the gastric acid entering the esophagus during reflux.

In a previous study (8), the length of the columnar-lined metaplastic mucosa of the esophagus of adult baboons was assessed in hematoxylin-eosin (H&E) sections by measuring the distance between the most distal portion of the stratified epithelium of the esophagus and the first oxyntic gland found. Recently, it was realized that this method was inaccurate as BMT2 was not included. In a recent study of gastric biopsies in humans (14) it was found that discrimination between parietal and chief glands was easier in sections stained with toluidine blue than with H&E stain. Therefore, sections having both the esophagus and the stomach in baboons were stained here with toluidine blue stain. The aim was to measure the length of the columnar-lined mucosa intercalated between the outermost distal part of the stratified squamous epithelium of the esophagus and the innermost proximal portion of the fundic mucosa.

Materials and Methods

The distal esophagus together with the proximal stomach was removed en bloc at autopsy in 35 adult baboons (Papio spp.) dying from natural causes. The baboons were members of colonies at the Southwest National Primate Research Center, Southwest Foundation for Biomedical Research. The conditions of animal housing have been reported elsewhere (8). Briefly, the baboons were housed in metal and concrete indoor-outdoor cages and were fed commercial monkey diets, occasionally supplemented with a variety of fruit and vegetables. Water was available ad libitum.

Longitudinal blocks, obtained from the esophagus and the stomach were fixed in 10% neutral buffered formalin, processed conventionally, embedded in paraffin, cut at 5 μm, stained with HE and with toluidine
blue, and evaluated with a conventional microscope using a 10 x objective. All procedures were carried out in accordance with the Institutional Animal Care and Use Committee guidelines.

Definitions

**Esophagus:** i) **Stratified squamous-cell mucosa.** The esophagus is covered by stratified squamous epithelium showing discrete papillae having one layer of basal cells, with or without occasional intraepithelial lymphocytes (15).

ii) **Columnar-lined metaplastic mucosa.** The distal esophagus is covered with metaplastic columnar epithelium (Figure 1) having accessory mucus-producing glands with interspersed oxyntic glands. This histological constellation in baboons will be referred here as BMT2 (Figures 2 and 3).

**Stomach:** i) **Fundic mucosa.** The fundic mucosa in baboons exhibits, at the top, a parietal (oxyntic) cell domain, followed by a neck region with mucin-producing neck cells (containing occasional parietal and/or chief cells) and at the bottom, chief (zymogenic) glands (16) (Figure 4). The fundic mucosa does not include mucus-producing glands having intercalated oxyntic glands.

**Assessment of the length of the BMT2 of the esophagus.** Toluidine blue stain permitted the easy identification of a parietal cell domain and a chief gland domain. By the aid of a calibrated ocular scale, the distance between the outermost distal end of the stratified squamous epithelium of the esophagus and the innermost proximal end of the fundic mucosa was recorded (in millimeters).

**Statistical analysis.** Data was analyzed by the Mann-Whitney U non-parametric test. Statistical significance was defined as p<0.05.

**Results**

**Frequency of BMT2.** All 35 animals exhibited Barrett’s mucosa in the esophagus, with accessory oxyntic glands interspersed between pyloric mucus (metaplastic) glands.

**The length of the BMT2.** The mean length of the BMT2 in this cohort of 35 baboons was 9.80 mm (range 1.0 mm-40.2 mm).

**The length of the BMT2 and gender.** Out of the 35 baboons, 14 were males and the remaining 21, females. The mean length of the BMT2 in males was 11.14 mm (range 2.0-20.2 mm) and in females 8.9 mm (range 1.0-40.2 mm). The difference in BMT2 length between males and females was non-significant (NS).

**The length of the BMT2 and age.** The only baboon of 2-months-old had a BMT2 length of 20.2 mm. Animals of one year to more than 26 years of age, had a BMT2 length of 5 mm or less. There was no apparent difference between the size of the BMT2 according to the age of the animals (NS).

**Discussion**

BMT2 occurred in all 35 (100%) consecutive esophagi from baboons investigated. The length of the BMT2 varied considerably, from 1.0 mm to 40.2 mm. These variations occurred independently of the age and gender of the animals.
mucosa in these animals (17). In the Barrett’s mucosa in humans, sialomucins are found in goblet cells and, occasionally, in columnar cells. The bulk of these secretions appear, however, insufficient to buffer the acidic fluid entering the esophagus, as Barrett’s esophagus in humans is a disease that requires long-lasting anti-acid medication and may precede esophageal adenocarcinoma (9, 11, 13).

In conclusion, BMT2 in baboons is an integrated part of the natural phenomenon of mucosal adaptation to daily regurgitation of gastric acid into the distal esophagus (natural GER), whereas BMT2 in humans might reflect an evolutionary atavism conveyed by a non-physiological disorder (pathological GER).

The results of this investigation strengthen the conviction that the baboon might be an excellent model to monitor the series of histological events that take place in the distal esophagus, under the influence of protracted GER.

Acknowledgements

Thanks are due to the staff of the Histology Laboratory and to Priscilla Williams, Data Management, Biostatistics and Scientific Computing, at the Southwest Foundation for Biomedical Research, San Antonio, Texas, for their invaluable help.

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