INTRODUCTION

Brunner’s glands are typically present in the submucosa (although may focally extend into the mucosa) of the duodenum in mammals, extending variable distances distally (depending on the species) from the level of the pylorus. These glands normally comprise mucous-producing epithelial cells arranged around ducts that empty into duodenal crypts and produce alkaline secretion (and epidermal growth factor; “urogastrone”) to protect the mucosa from acid chyme produced in the stomach.2,3

Brunner’s gland hyperplasia (BGH) was first reported by Feyrter (1934)4 as a description of nodular hyperplasia of the Brunner’s glands. It was historically characterised by either circumscribed nodular hyperplasia, diffuse nodular hyperplasia or more “tumour-like” adenomatous hyperplasia.5 Although the exact pathogenesis is not clear in many cases, it is now generally accepted to be a functional response to chronic gastric acid hypersecretion (and not a neoplasm), resulting in Brunner’s gland proliferation.5,6 It can be associated with a range of conditions resulting from acid hypersecretion including gastric erosions and duodenal ulcers.6 It has also been suggested that Helicobacter pylori infection may be involved in the pathogenesis, although there is no clear causation.7,8 Despite benign duodenal tumours being rare in humans (incidence < 0.01%), BGH comprises 10.6% of these tumours.8

In humans, BGH is usually reported in adults (typically in the fifth or sixth decade of life). In most cases, the condition is asymptomatic and is considered incidental. Uncommonly, it can cause pyloric outflow obstruction10,11 and rarely results in more severe complications, for example, intussusception12 and severe gastrointestinal bleeding leading to haemorrhagic shock.8 Similar lesions to BGH have been reported in non-primate species, including sand rats (Psammomys obesus)13 and a horse.14

In non-human primates (NHPs), tumours of Brunner’s glands, in general, are very rarely reported. Multiple adenomas (described as “adenomatosis”) have been previously reported in a 44-year-old chimpanzee (Pan troglodytes),15 and a Brunner’s gland adenocarcinoma has been reported in a baboon (Papio cynocephalus).16 BGH has only been listed as an incidental gross finding in a chimpanzee with a leiomyoma at the gastro-oesophageal junction17 and diagnosed in a single case in a meeting report detailing a series of various spontaneous lesions in NHPs used in drug safety studies.18 However, the gross and histopathological features of this lesion in a NHP have not been described in detail. In this report, we describe BGH in a geriatric chimpanzee (P. troglodytes) and distinguish it from similar neoplastic changes.
A post-mortem examination of a 65-year-old, female chimpanzee was performed at Easter Bush Pathology, University of Edinburgh, UK. The chimpanzee was previously housed at Blair Drummond Safari and Adventure Park (Stirling, UK) and was euthanased due to an unrelated condition (severe, chronic, degenerative joint disease in multiple joints). Multiple incidental findings were noted including a subcutaneous lipoma in the region of the left mammary gland, a uterine leiomyoma, aortic atherosclerosis and mild, myocardial fibrosis (previously published in a case series of idiopathic myocardial fibrosis in captive chimpanzees\(^{19}\)). It was noted that the duodenal luminal surface had numerous, multifocal to coalescing, 3 to 15 mm diameter, raised to pedunculated nodules, for a length ~15 cm distal to the pylorus (Figure 1). Occasional serosal adhesions were present in the peritoneal cavity, but these were considered incidental and reflective of a non-active (resolved) process. The remainder of the gastrointestinal tract was considered to be macroscopically normal.

In histological sections of the duodenum, there was moderate to marked hyperplasia of the Brunner’s glands. Lobules of Brunner’s glands extended from the submucosa deep into the mucosa, ranging in distribution/morphology from regionally extensive to nodular to discrete exophytic and pedunculated masses (Figure 2). The cells formed tubuloalveolar structures and were cuboidal to columnar, with basal nuclei and a moderate amount of pale-eosinophilic, slightly floccular cytoplasm. There was no evidence of marked nuclear or cellular atypia, nor invasion of the basement membrane. The lobules of hyperplastic tissue were usually supported by fine trabeculae of fibrous stroma, although this was multifocally, variably increased in prominence. The surrounding mucosa/submucosa was slightly thickened.

**FIGURE 1** Proximal duodenal mucosal surface, showing the gross appearance of regionally extensive, Brunner’s gland hyperplasia. There are multifocal to sometimes coalescent, raised nodules; the surfaces of some nodules are hyperaemic. The tissue was moderately autolytic. Scale bar represents 1 cm

**FIGURE 2** Histological sections of Brunner’s gland hyperplasia in the proximal duodenum of a chimpanzee (Pan troglodytes), demonstrating various morphologies including coalescent mucosal nodules (A), an exophytic, pedunculated nodule (B) and plaque-like thickening of the mucosa (C). D. The hyperplastic Brunner’s glands extend above the muscularis mucosae (arrowhead) and expand into the mid-level mucosa, distorting the overlying villous architecture. E. The glandular tissue generally comprises well-differentiated and organised cuboidal to columnar cells, arranged in tubuloalveolar structures, with basal nuclei and a moderate amount of pale-staining, slightly floccular cytoplasm (mucin). In this section, there is a moderate increase in fibrous connective tissue and moderate infiltrates of lymphocytes, plasma cells and fewer eosinophils. Scale bars represent 1 mm (panels A to C), 250 μm (panel D) and 50 μm (panel E)
not compressed by the hyperplastic glandular tissue, but there was mild, multifocal, oedema in the lamina propria. Within the pre-existing mucosa and hyperplastic tissue, there were aggregates of variably dense (mild to marked) inflammatory infiltrates (duodenitis), predominately comprising lymphocytes, plasma cells and fewer eosinophils (Figure 2). The duodenal villous structures were infrequently fused and “club-shaped.” There were rare luminal organisms resembling ciliated alveolates, which were considered incidental.

3 | DISCUSSION

The nomenclature and diagnostic criteria for BGH have not been clearly standardised in medical texts. In human clinical literature, the term has apparently been used synonymously with “adenoma” and “hamartoma.” The use of the term “Brunner’s gland hyperplasia” in humans beings should refer to multifocal, relatively small, nodular and polypoid masses in the duodenum, histologically composed of hyperplastic Brunner’s glands supported and separated by a variably extensive, fibrous stroma. In previous reports, nodular duodenal lesions with a diameter less than 1 cm have been classified as “hyperplasia,” whereas foci greater than 1 cm have been classified as an adenoma. There was no evidence of basement membrane invasion (precluding a diagnosis of a malignant tumour) and no evidence of marked compression of the surrounding mucosa or encapsulation (precluding a diagnosis of an adenoma). In this chimpanzee, the lesions were most consistent with “hyperplasia”; larger nodules (up to 15 mm diameter) were deemed a result of multiple coalescing hyperplastic nodules, rather than a single compressive focus.

Although there is no widespread agreement on a suitable “cut-off value” for the size of Brunner’s gland tumours, this description should serve as a suitable guide to diagnose BGH in NHPs. Practically, the clinical distinction between adenoma and hyperplasia may be somewhat subjective; it is more important to distinguish these benign tumours from a malignant process carrying a poorer prognosis. Adenocarcinomas can be more easily recognised by histological invasion of neoplastic cells through the basement membrane. In this case, the BGH was asymptomatic, which it often is in humans. However, as some BGHs may cause obstruction or upper gastrointestinal haemorrhage, it is important to recognise it, even when identified as an incidental finding in aged NHPs.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ETHICAL APPROVAL

The authors confirm that the ethical policies of the journal, as noted on the journal’s author guidelines page, have been adhered to. Ethical approval was not required because no animals were used for research in this study.

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