Introduction

Barrett’s metaplasia (BM) is the main risk factor for oesophageal adenocarcinoma, a cancer which carries a mortality of >50% at 12 months. Refluxate containing gastric and bile acids seems to be causative for inflammation at the lower oesophagus, but it is not known how this induces replacement of stratified squamous epithelium (SSQE) with columnar epithelium at a molecular level.

There is likely to be a progenitor cell population replacing denuded epithelium, although the origin of these cells has not been proven. Genes that play a role in gut tissue patterning during embryogenesis have received attention. One such transcription factor is demonstrable in BM, but not in normal SSQE in the oesophagus. At the GOJ, there was clear delineation between HNF4α positive nuclei in the columnar gastric cardia mucosa, and negative HNF4α staining of SSQE. In contrast, the columnar epithelial nuclei in BM were consistently positive.

 Methods

We optimised an immunohistochemistry protocol for demonstrating HNF4α on formalin-fixed paraffin-embedded slides of human tissue. This protocol was applied to forceps biopsy specimens of normal oesophagus, gastro-oesophageal junction (GOJ), stomach, ileum, colon and BM (UK REC reference: 13/YH/0197). Tissues were examined from at least 3 different patients per anatomical site.

Results

In healthy tissues, nuclear HNF4α positive immunostaining was demonstrated in stomach, ileum and colonic epithelium, but not in normal SSQE in the oesophagus. At the GOJ, HNF4α was insufficient to induce an intestinal phenotype, whereas HNF4α induced villin, K18, trefoil factor 3 and mucin 5AC. We propose a 2-hit hypothesis for the development of BM:

1. induction of HNF4α (which initially converts the oesophageal SSQE to columnar epithelium) and
2. Cdx2 (which causes intestinalisation of the columnar epithelium).

Results

46/71 referrals had either achalasia or dysphagia post-fundoplication. 30 (41%) had achalasia, 6 had prior Heller myotomy and 7 had prior Botulinum toxin. 16 (22%) patients had OGJ obstruction after fundoplication. 29/30 patients with achalasia underwent pneumatic dilatation, one bougie dilatation. Overall symptom response was inadequate in 5 (16) referred for surgery), satisfactory in 3 (11%) and good-excellent in 22 (73%). 14/16 patients with post fundoplication dysphagia had pneumatic balloon dilatation, 2 had bougie dilatation. Overall symptom response was inadequate in 7 (44% referred for surgery), satisfactory in 4 (25%) and good-excellent in 5 (31%). Complications from the both groups include chest pain (n = 2), chest infection (n = 1), reflux symptoms (n = 4 in each group) and minor bleeding. All resolved with conservative treatment.

Conclusion

Endoscopic dilatation is safe and effective treatment for patients with dysphagia related to achalasia and also OGJ obstruction post-fundoplication. A good-excellent symptom response was reported more often by achalasia patients (p = 0.010).

Disclosure of Interest

None Declared.