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Erradicación total de esófago de Barrett con displasia de bajo y alto grado por medio de terapia combinada con resección mucosa focal con Duette y ablación por radiofrecuencia: Reporte de caso y revisión de la literatura
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Complete cure of Barrett’s Esophagus with low and high grade dysplasia through a combination of Focal Duette® Endoscopic Mucosal Resection and Radiofrequency Ablation: Case report and literature review

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Abstract

The management of Barrett’s esophagus (BE) and dysplastic and neoplastic changes associated with it has changed with the recent advent of techniques such as endoscopic mucosal resection and radiofrequency ablation. These two techniques have been added to the repertoire for managing this complication of gastroesophageal reflux disease because of their high levels of safety combined with the rarity of complications resulting from them. We report a case of Barrett’s esophagus and associated dysplasia which was managed first with a sequence of mucosal resection of large lesions followed by radiofrequency ablation. Complete eradication of dysplasia and intestinal metaplasia was achieved.

Keywords

Barrett’s esophagus, radiofrequency ablation, endoscopic mucosal resection, treatment.

Since its initial description more than 60 years ago by the Australian surgeon Norman Rupert Barrett, Barrett’s esophagus has become one of the most fearful consequences of gastroesophageal reflux. This replacement of the columnar epithelium in the esophagus is confirmed when a biopsy finds the presence of intestinal metaplasia which has the risk of developing into adenocarcinoma. This condition remains a challenge for physicians and surgeons (1). Increased incidence esophageal adenocarcinoma of up to 400% has been reported. This finding has prompted development of multiple strategies to reduce the progression of this disease (2, 3). The risk of developing adenocarcinoma from Barrett’s epithelium is 0.5% per year, (4) but this to 1.6% per year for low grade dysplasia (5) up to 6% per year for high grade dysplasia (6). There is no doubt that this condition needs specific follow-up which is offered to patients according to initial endoscopic findings in order to monitor and characterize the appearance dysplasia and to determine the type of treatment (7). Traditionally, surgery has been considered the treatment of choice for high grade dysplasia, but the not insignificant morbidity and mortality rates have motivated investigation into new nonsurgical treatments that might be able to decrease the number of complications without endangering long time results for patients. The Duette Multiband Mucosectomy Kit (Cook Ireland Ltd, Limerick, Ireland) is easily applicable to esophageal dysplasia (Figure 1) and has minimal complications which have made this procedure increasingly popular (8). Radiofrequency ablation (RFA) is a technique which ablates the lesion by heating the tissues. It has the advantage of penetrating only through the mucosa because it is automatically controlled by an impedance based feedback loop (9).

The HALO system (BÂRRX Medical, Inc., Sunnyvale, CA) is composed of 2 different ablation systems. The HALO 360 performs circumferential radiofrequency ablation and the HALO 90 performs focal ablation which can
be used for primary treatment of short segments of EB or for secondary of focal residual lesions. The HALO 360 ablation catheter has a generator and a 3 cm bipolar electrode located in the external surface of a balloon which has 5 possible diameters (22 mm, 25 mm, 28 mm, 31 mm and 34 mm). The ablation catheter is inflated with a pedal while the radiofrequency is released by the electrode. For circumferential ablation, two applications of radiofrequency of 10-12 J/cm^2 and 40W/cm^2 are adequate for ablation of the thickness of the mucosa. The HALO 90 consists of an electrode with a 20 x 13mm surface attached over the end of the endoscope. The recommended potencies with this catheter are 2 applications of 12-15 J/cm^2 and 40W/cm^2. For the 2 types of catheters, the generator releases the radiofrequency at a predetermined density which reaches a uniform penetration in the tissue of 1000 microns that does not depend on the operator. With this method it is possible to destroy all epithelial layers, the lamina propria and part of the muscularis mucosae without damaging the submucosa (Figure 2) (9, 10).

We present the first case in our country of complete eradication of Barrett’s esophagus and high and low dysplasia with the treatments described above.

**CASE REPORT**

The patient is a 58 year old man who had been an occasional smoker until 19 years ago. Patient is a social drinker who was diagnosed with grade B esophagitis and 7 cm (30 to 37 cm) Barrett’s esophagus in 2000. He had a 3 cm hiatal hernia associated with symptoms of pyrosis and intermittent hoarseness and coughing (Figure 3). Patient was treated with continuous administration of proton pump inhibitors to control symptoms and esophagitis. An endoscopic examination in 2002 identified Barrett’s esophagus without elevated or sunken lesions. Biopsies showed low grade dysplasia which persisted until March 2007. An examination in August 2007 showed grade CA dysplasia in situ. Patient was referred to one of the authors (M.R.F) who checked the histological slides with 3 pathologists to confirm the diagnosis of high grade dysplasia. In November 2007 endoscopy with magnification and NBI (Narrow Band Imaging) was performed with patient under deep sedation to take direct biopsies. Each centimeter of the metaplastic epithelium was evaluated in a helical form. Three areas of dysplasia were identified. One was a small modulated area of 1mm. Images were taken pictures of each suspicious area and of the biopsy sites. Biopsies were placed in separate flasks which were marked for identification with locations in centimeters and the time that the samples were taken. Three areas with low grade dysplasia were confirmed as lesions with neovascularization and mucosal dysplasia identified through endoscopic NBI. One area of high grade dysplasia was found in an elevated lesion of 1 mm (Figures 4-7). In February 2008 multiple mucosectomy with suction and elastic band ligation was performed together with resectioning using the Duette system to completely remove the lesions in six 1.2 cm diameter segments. Pathology results for all biopsies had negative margins (Figure 8, 9). One month later endoscopic examination showed adequate healing (Figure 10). Later examinations identified three islets of Barrett’s esophagus which progressed to low grade dysplasia over the next three years. In September 2011 a point focus of high grade dysplasia without elevated lesions was identified (Figures 11-14). On November 10, 2011 radiofrequency ablation using the HALO 360 degree system was performed with the patient under deep sedation. A 6 cm (33 to 40 cm) area of Barrett’s esophagus had been found in an esophagus that was 3.1 cm in diameter. A 28mm balloon was used for ablation since the 30 cm balloon would have extended to the gastric creases of the hernia. The fibrin was removed with a cup and then the device was used without complications (Figures 15 and 16). Patient was put on a liquid diet followed by a soft and analgesic treatment for 3 days. Since the procedure the patient has had follow-up examinations every 3 months at which the protocol calls for biopsies every 2 cm. 16 biopsies taken from the first follow-up and 12 biopsies taken from the second follow-up showed only mild esophagitis or normal mucosa thus confirming complete eradication of Barrett’s esophagus and both low and high grade dysplasia (Figures 17-19).
DISCUSSION

Barrett’s esophagus is considered to be a pre-malignant lesion. Patients have risks of 10 to 150 times that of the general population of developing esophageal cancer. Level of risk depends on whether or not dysplasia is present, and on the grade dysplasia (11-13). Current recommendations for patients with Barrett’s esophagus include esophagogastroduodenoscopy plus biopsies from 4 quadrants every 2 cm of the columnar epithelium every 3 to 5 years when dysplasia is absent. Biopsies should be taken every 6 to 12 months in cases with low grade dysplasia and every 3 months in cases of high grade dysplasia that have not been eradicated (7). Indisputably the treatment outlined above has important costs. This is also true for studies of biomarkers to improve diagnosis of low grade dysplasia and determine disease progression through estimation of aneuploidy although this method has not yet been approved for routine use (14).

Although esophagectomies are commonly accepted for management of patients with both high grade dysplasia and Barrett’s esophagus, they have a 50% morbidity rate and 5% surgical mortality rate even at medical centers with great amounts of experience in this type of procedures (15,16). The most recent reports show that only 12% of these surgical specimens have invasive adenocarcinoma while it has also been demonstrated that surgical treatment and endoscopic treatment of this type of patients have the same survival rates (17,18). Since ml and m2 intramucosal lesions in these patients have no possibility of lymph node involvement, since m3 lesions involve the lymph nodes in only 4% of cases, less invasive endoscopic resection could be a valid alternative for treatment of this condition (19).

Focal endoscopic resection of the mucosa has obtained complete remission in 97% to 100% of patients with high grade dysplasia and carcinoma in situ with 5 year survival rates of 84% to 98% (20-22). Recurrences or meta-chronic lesions reported in 21.5% of these patients can also be managed this way (23). Management of metaplastic esophageal mucosa through circumference resection has achieved complete eradication in up to 97.5% of cases (24, 25). Even though endoscopic resection of the submucosa has shown better data than conventional mucosal resection techniques with respect to margins free of metaplastic tissue, endoscopic resection is a technically demanding
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Figure 5. Endoscopic view with NBI (Narrow Band Imaging) of Barrett’s esophagus with low grade dysplasia.

Figure 6. Endoscopic view with NBI of low grade dysplasia with neovascularization.

Figure 7. Endoscopic view with magnification and NBI that shows elevated 1mm lesion with high grade dysplasia.

Figure 8. Endoscopic view with biopsy of elevated lesion.

Figure 9. Endoscopic view with positioning of multiband mucosectomy with Duette.

Figure 10. Final endoscopic view after resection of macroscopic lesions through multiple mucosectomy with Duette.
technique which presents frequent major complications when used for the eradication of Barrett’s esophagus. The principal disadvantages of circumferential resections or those covering more than 75% of the diameter are high frequency of stenosis which require dilatation, bleeding, and in the case of submucosal endoscopic resections a higher incidence of perforations with low applicability in the west (26-28).

Ablation has a demonstrated impact on the development of adenocarcinoma avoiding 1 case out of every 20 patients with high grade dysplasia (29). The use of the Nd-YAG (neodymium-doped yttrium aluminum garnet) lasers, photodynamic therapy and cryotherapy have demonstrated their capacity to eliminate dysplastic mucosa as well as remaining metaplastic mucosa in BE, but they have two undesirable effects. The first is the impossibility of collec-
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Figure 15. Endoscopic view of zone with low grade dysplasia.

Figure 16. Endoscopic view of radiofrequency ablation in proximal Barrett’s Esophagus.

Figure 17. Endoscopic view of radiofrequency ablation in distal Barrett’s Esophagus.

Figure 18. Endoscopic view 1 month after radiofrequency ablation.

tion of tissue which has the consequence of preventing oncological confirmation. The second is the high incidence of stenoses subsequent to treatment (30, 31). In addition there can be complications such as photosensitization and development of metaplasia with dysplasia under the regenerated epithelium (32).

La ARF ha demostrado ser un método efectivo erradicando la mucosa pre-maligna con una duración sostenida en el tiempo (2 a 5 años) y escasa presentación de metaplasia bajo el epitelio regenerado, así mismo ha mostrado tener una baja frecuencia de complicaciones como estenosis o sangrado e incluso ya se cuenta con estudios que sugieren dicho procedimiento como costo-efectivo al compararlo con el seguimiento endoscópico en pacientes seleccionados (33-39).

Radiofrequency ablation has demonstrated itself to be an effective method for eradicating the pre-malign mucosa for sustained periods of two to five years with limited occu-
rences of metaplasia under the regenerated epithelium. Similarly, it has shown a low frequency of complications such as stenosis or bleeding. There are even studies that suggest that this procedure is more cost-effective than endoscopic follow-up for selected patients (33-39).

This has motivated the development of a technique combining resection of focal mucosa with the Duette type device followed by radiofrequency ablation of BE (40). This offers benefits similar to surgical management for eradication of metaplastic tissue, eliminating the possibility of metachronic lesions and avoiding wide resection of the mucosa. It has good results in terms of long term disappearance of the metaplastic mucosa (23, 26, 35, 36, 41-44).

The case reported herein is the first in our country with endoscopic and pathological demonstration of 7 cm BE with both high and low grade dysplasia. Both types of dysplasia were completely eradicated as confirmed by normal esophageal mucosa found in follow-up examinations which once again confirms the favorability of this combined approach.

R.E. Pouw’s retrospective study of 169 patients with average 32 months follow up showed the superiority of combined management for resection of visible lesions associated with RFA for complete eradication of Barrett’s mucosa. The study showed absence of Barrett’s mucosa in the short and medium term and a low recurrence rate of 6% in cases of BE without dysplasia. The study showed a complete response in 100% of cases of carcinoma in situ (35). In addition this technique resulted in a lower frequency of complications such as perforations and stenosis than did circumferential mucosal resections.

All of the above points toward taking combined therapy into consideration for multiple reasons. First, focal mucosal resection of visible lesions provides a surgical piece which is evaluable to the pathologist and which provides the security of correct oncological management. Second, it avoids complications derived from extensive circumferential mucosal resections and the complication of stenosis with respect to the submucosa. Third, the incidence of Barrett’s mucosa under the regenerated epithelium is practically nonexistent, unlike for other ablative therapies. Fourth, it offers the possibility of eradicating all Barrett’s epithelium thus limiting the appearance of synchronous or metachronous lesions and providing for integral management of the situation. Studies of RFA combined with mucosal resection prior to appearance of visible lesions have shown this technique to be safe and efficient. Follow-up periods up to 60 months have shown eradication rates of intestinal metaplasia of 54% to 100%, eradication of dysplasia from 79% to 100%, frequency of buried glands from 0% to 5.1% and frequency of stenosis from 0% to 14% subsequent to this type of treatment (Table 1).

Table 1. Summary of studies that include endoscopic resection combined with radiofrequency ablation.

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients (Combined therapy)</th>
<th>Average follow-up (months)</th>
<th>CR-IM</th>
<th>CR-D</th>
<th>CR-HGD</th>
<th>Buried glands</th>
<th>Patients with stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ganz, 2008</td>
<td>142 (24)</td>
<td>12</td>
<td>54%</td>
<td>80%</td>
<td>90%</td>
<td>0%</td>
<td>1</td>
</tr>
<tr>
<td>Sharma, 2009</td>
<td>63 (5)</td>
<td>24</td>
<td>79%</td>
<td>95%</td>
<td>79%</td>
<td>0%</td>
<td>1</td>
</tr>
<tr>
<td>Pouw, 2010</td>
<td>24 (24)</td>
<td>22</td>
<td>96%</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
<td>1</td>
</tr>
<tr>
<td>Van Vilsteren, 2011</td>
<td>47 (22)</td>
<td>24</td>
<td>96%</td>
<td>96%</td>
<td>NR</td>
<td>0%</td>
<td>3</td>
</tr>
<tr>
<td>Okoro, 2012</td>
<td>90 (44)</td>
<td>20</td>
<td>43%</td>
<td>76%</td>
<td>NR</td>
<td>NR</td>
<td>6</td>
</tr>
</tbody>
</table>


Figure 19. Endoscopic follow-up six months after treatment biopsies taken every 2 centimeters showing resolution of both Barrett’s Esophagus and dysplasia.
esophagus associated with high grade dysplasia, we ask ourselves whether we should continue waiting in the face of this cancer precursor, or if to the contrary – we should remember our experience with resection of colorectal polyps and use this type of management for select patients with Barrett’s esophagus and low grade dysplasia. If we do we will avoid complications derived from circumferential mucosal resections including the risk of future development of synchronous and metachronous lesions in the premalignant epithelium in cases when eradication is incomplete and including performing radical surgery required when there is a diagnosis of reappearance of neoplasia.

REFERENCES


