Carcinoid Tumors of the Appendix

Selected information concerning carcinoid tumors of the vermiform appendix is reviewed with the objective of identifying rational recommendations for treatment.

- Recognition of the carcinoid syndrome in the 1950s and development of the concept of APUD tumors in the 1960s stimulated intense and continuing interest in carcinoid tumors. Although the biologic commonalities of carcinoid tumors have been clarified, it has become apparent that there are important clinical differences in the behavior of carcinoid tumors arising in differing organ systems, and even in portions of the same organ system, e.g., the gastrointestinal tract.

It must be recognized that what is known about carcinoids of the appendix comes from retrospective analysis of institutional experiences. Because the tumors are uncommon, the analyses usually cover a considerable time span, and the follow-up of patients often is incomplete. Furthermore, most series are relatively small and there is little doubt that some, and perhaps many, of the conclusions

Figure 1—Gross appearance of typical carcinoid at the tip of the appendix.

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drawn will be proven by further experience to be incorrect.

The word "karzinoide" was first used by Oberndorfer (1907) in describing gastrointestinal tumors. Oberndorfer mentions that similar lesions had been described previously. The first description of a neoplasm of the appendix has been ascribed to Merling. The original report, published in 1838, cannot be located, but it was cited by Elting in 1903. Elting stated that the Merling report was a gross description only and considered the case more likely to be one of acute appendicitis with perforation. Similarly, Beger is often credited with describing the first carcinoid tumor of the appendix in 1882. The patient reported by Beger clearly had a malignant tumor of the appendix, but the microscopic description is meager and the clinical course and autopsy findings are more suggestive of mucinous adenocarcinoma of the appendix than carcinoid.

The affinity of cells of the carcinoid tumor for silver stain was reported by Gosset and Masson in 1914. The subject of argentaffin tumors of the appendix and small intestine was reviewed thoroughly by Forbus in 1925. Early discussions of the carcinoid syndrome emphasized the presence of liver metastases, although it is now known that liver metastases are not a prerequisite for developing the syndrome.

Pathology

It generally is agreed that carcinoid tumors arise from the Kulchitsky cell of the gastrointestinal tract. These cells are found in the crypts of Lieberkühn. The smallest tumors lie in the submucosa and encroach on both the lumen of the appendix and the muscularis as they enlarge. Extension into the muscularis is present in most carcinoids of the appendix, and extension through the muscularis to involve the serosa is common. The extent of in-

Figure 2—Fontana-Masson stain of carcinoid tumor of the appendix showing affinity for silver.
vasion of the appendiceal wall has not correlated with the behavior of the tumor. Extension into the mesoappendix has been described in 29% to 33% of appendiceal carcinoids. The possible significance of this finding will be discussed subsequently. Although the majority of carcinoids of the appendix are discrete mass lesions, a diffuse form involving up to the entire length of the appendix is recognized. Discrete tumors are firm, yellow masses, usually less than 1 cm in greatest diameter (Figure 1). They most commonly occur in the distal portion of the appendix. The midportion is a somewhat less common site of the discrete tumor, and involvement of the base of the appendix occurs in less than 10% of cases. Although carcinoids in other parts of the gastrointestinal tract tend to be multicentric in origin, multicentric carcinoids in the appendix are not common. In one series, 4% of appendiceal carcinoids were associated with carcinoids in other areas of the small intestine.

The microscopic appearance of carcinoid tumors usually is characteristic, the distinguishing feature being uniformity of size of cells and nuclei. Four microscopic patterns found in carcinoid tumors have been described by Soga and Tazawa, but to date this has not been helpful in predicting the behavior of the tumor. Silver stains may be useful in some instances (Figure 2). The goblet cell or mucinous cell carcinoid of the appendix is of some importance because it has microscopic features which may lead to diagnosis of carcinoma, although its behavior, and therefore its treatment, more closely resembles carcinoid tumor.

There is controversy concerning the incidence of lymphatic invasion by carci-

Figure 3—Photomicrograph of carcinoid tumor of the appendix. Shrinkage artifacts are clearly visible.
Carcinoid tumors of the appendix. Moertel et al., state that lymphatic invasion is almost invariable, while others feel that it is much less common and that the appearance is often an artifact (Figure 3). Metastasis to regional lymph nodes clearly occurs in a small percentage of carcinoids of the appendix. Whether carcinoid of the appendix can metastasize to distant organs or result in sufficient tumor mass to produce the carcinoid syndrome remains controversial. Cases in which this is thought to have occurred have been reported, but it is almost impossible to be certain that the appendix was the site of the original disease. It is reasonable to conclude from the present evidence that distant metastasis and carcinoid syndrome from carcinoid of the appendix are extremely rare.

**Clinical Features**

Carcinoid tumors of the appendix are discovered incidentally at operation or autopsy. In all hospital series, a significant number of carcinoids were found in appendices removed for acute appendicitis. It is not clear whether this relationship is coincidental or whether occlusion of the appendiceal lumen by the carcinoid can cause acute appendicitis. Moertel et al., assumed this to be true, but the subject does not appear to have been studied carefully. Carcinoid tumors may be removed because the surgeon sees or feels the lesion or by incidental appendectomy. Pathologists discover carcinoids either in surgical pathology material or at autopsy. It is of interest that the incidence of discovered carcinoids goes up significantly when routine histologic sections of appendices are performed. Because the majority of appendiceal carcinoids are less than 1 cm in diameter, it seems unlikely that the imaging techniques will lead to preoperative diagnosis.

**Surgical Treatment**

The recognition of the malignant potential of carcinoid tumors, the demonstration of regional node metastases from carcinoid of the appendix, and the minimum risk and physiologic effect of right colectomy have led to the suggestion that right colectomy with ileotransverse colostomy be considered in treating appendiceal carcinoids. On the other hand, follow-up of patients with appendiceal carcinoids who have been treated by simple appendectomy suggests that recurrence is very rare. The following factors have been suggested as being of importance in making the decision to perform simple appendectomy or radical right colectomy.

**Presence of Suspicious Regional Lymph Nodes:** When a carcinoid of the appendix is identified at operation, the mesentery and pericecal area should be explored for the presence of suspicious nodes. Since the majority of nodal metastases are microscopic and since sizable lymph nodes frequently are encountered in this area, the determination of clinically significant nodes may be difficult or impossible. If nodal involvement is suspected or proven by frozen section, right colectomy is probably indicated. It should be recognized that there is no available proof that involved nodes will become clinically significant.

**Involvement of the Base of the Appendix:** If the base of the appendix (the junction of the appendix and cecum) is involved by either discrete or diffuse tumor so that appendectomy with gross removal of the lesion is not possible, right colectomy should be considered. The same is true if the surgical margins after appendectomy are proven on pathological examination to be involved with tumor. A single patient reported by Ponka remained symptom-free for 17 years after what the surgical pathologist called incomplete removal of an appendiceal carcinoid tumor, suggesting that this indication for right colectomy also is equivocal.

**Gross Size of Tumor:** In 1976, Moertel et al., described the experience of the Mayo Clinic with appendiceal carcinoids and reviewed the available literature. They state that “there seems to be one
common denominator among reported cases of metastatic carcinoid tumor of the appendix, the size of the primary lesion. 17 Where metastatic disease was present, in all instances in which the tumor size was recorded, it was greater than 2 cm. Of the 144 cases from the Mayo experience, only 3 carcinoid tumors were greater than 2 cm in diameter and, in 2 of these, there was proven lymph node metastasis. On these rather tenuous bases, the recommendation was made that right colectomy be considered in all instances of appendiceal carcinoid in which the tumor measures more than 2 cm in diameter. Dent et al., reported experience with 29 patients with carcinoid tumors. 8 Eight hemicolectomies were performed in this series, and six showed no evidence of residual or metastatic tumors. In two patients, metastatic disease in regional nodes was found at the time of hemicolectomy and, in one of these, there was residual tumor in the appendiceal stump. It is of interest that these were the two largest carcinoids in the series, both measuring more than 1 cm. On the basis of this experience, the authors suggested that the indications for right colectomy include carcinoids greater than 1 cm in diameter or the presence of positive nodes.

Invasion of the Mesoappendix: The significance of microscopic invasion of the mesoappendix by carcinoid was emphasized by Syracuse et al., in 1979.20 Ninety-two cases having an appendiceal carcinoid were reviewed. The mesoappendix was invaded in 13 instances. Two of these patients underwent a subsequent right colectomy and both were found to have metastatic disease in the resected lymph nodes. In both patients, the primary tumor was larger than 1 cm in diameter. Both patients were followed for a relatively short period of time (four years) without evidence of recurrence. No follow-up of the remaining 11 patients with mesoappendiceal invasion is mentioned. The authors state that their policy is to perform ileocolonectomy in the presence of mesoappendiceal invasion. Although this ultimately may prove to be correct, the current supporting evidence is not overwhelming.

Summary

Although unusual, carcinoid tumors of the appendix will be encountered by most general surgeons. Appendectomy is the treatment of choice in the vast majority of instances. Distant metastasis and the development of the carcinoid syndrome from carcinoid tumors of the appendix are rare, if they occur at all. On the basis of scanty and incomplete data, right hemicolectomy for carcinoid of the appendix should be considered in the presence of lymph node metastases, when the carcinoid tumor exceeds 1 cm in greatest diameter and when the lesion cannot be removed grossly by appendectomy alone.

References