

Surgical Treatment of Zollinger-Ellison Syndrome

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Gastrinomas are functional endocrine duodenopancreatic tumors and are responsible for the Zollinger-Ellison-syndrome (ZES). Although most gastrinomas grow slowly, 60–90% are malignant [1]. The natural course of sporadic ZES is more aggressive than of MEN1-ZES with 15 years survival rates of 70–80 and 100% [2]. Patients with metastatic sporadic gastrinoma have 5-year survival rates of only 20–38%. Surgery is the only way to cure ZES. In this editorial the surgical management of sporadic and MEN-1 associated gastrinomas will be discussed.

Sporadic Gastrinomas

Most gastrinomas are located in the 'gastrinoma triangle', which comprises the head of the pancreas, and the first and second parts of the duodenum. As with all PNETs, the only chance of complete cure of gastrinoma is surgical resection. This is achieved in approximately 26–100% of patients [1]. Resection reduces the rate of hepatic metastases. One study compared 160 patients with ZES undergoing resection with 35 patients who had a similar stage of disease but did not undergo surgical exploration [3]. After a follow-up period of 12 years, 41% of patients were cured with surgery. Significantly more patients developed liver metastases with conservative treatment (29 versus 5%; $P < 0.001$). The 15-year disease-related survival was 98% after surgery and 74% after medical treatment ($P < 0.001$). These results demonstrate that routine surgical exploration increases survival in patients with ZES by increasing disease-related survival and reducing the rate of advanced disease [3]. Therefore, routine surgical exploration should be performed in all patients with sporadic gastrinomas without evidence of diffuse hepatic metastases or concurrent illness limiting life expectancy.

Pancreatic gastrinomas are usually larger than 2 cm in diameter and can be readily identified at exploration that includes palpation of the pancreas and IOUS [1]. This leads to distal pancreatic resection, splenectomy and peripancreatic lymph-node dissection when gastrinomas are in the pancreatic body and tail. Although enucleation with peripancreatic lymph-node dissection is the procedure of choice, pylorus-preserving pancreaticoduodenectomy (PPPD) is justified for large pancreatic head gastrinomas or when the tumor is close to the main pancreatic duct.

Because 50–70% of sporadic gastrinomas are found in the duodenum, duodenotomy should be performed routinely for all patients with ZES without any pancreatic tumors. These small tumors are usually located in the submucosal layer of the proximal duodenum and more than half of them are malignant [4]. Before a duodenotomy is performed, the duodenum should be carefully palpated from the pylorus to the level of the superior mesenteric vein. Then, a vertical duodenotomy centered in the second portion of the duodenum should be performed. After inspection and finger palpation, a small submucosal lesion can usually be identified. It seems that periduodenal lymph-node metastases can grow faster than their duodenal primary tumors and thus may form large tumors that are easily recognized, compared with the duodenal primary tumors [4]. Therefore, a regional lymph-node dissection should be performed.

MEN1 Gastrinomas

The management of MEN1-ZES is controversial [2]. Some have advocated a non-operative approach to MEN1-ZES and recommend control of the effects of hypergastrinemia with PPIs [1]. Some recommend an operative approach if the tumor reaches 2–3 cm in size, because the risk of liver metastases increases significantly [4]. Liver metastases occur in only 3–5% of patients with ZES managed surgically compared with 23–29% of those managed conservatively [3]. Therefore, duodenopancreatic resection is advocated in patients with MEN1 who have biochemical evidence of ZES. The aim of this approach is to remove potentially malignant tumors before liver metastases develop.

Apart from the timing of surgery, another controversial issue is the extent of surgery in MEN1-ZES. Several groups have suggested that gastrinomas should be enucleated or resected with the surrounding tissues [1]. The complete operation includes duodenotomy, enucleation of any head or uncinate tumors, peripancreatic lymph-node dissection and a distal pancreatectomy. However, it was noted that only one-third of patients submitted to this procedure had a negative secretin stimulation test after operation [2]. Therefore, a pylorus-preserving pancreaticoduodenectomy (PPPD) as the first-line procedure can be favoured, if the gastrin source can be regionalized to the pancreatic head before operation by selective arterial secretin injection. The rationale for this approach is that over 90% of MEN1-gastrinomas occur in the duodenum and so recurrence is impossible if the organ of origin is removed. Tonelli et al. [2,5] and our group reported a 77–85% biochemical cure rate after PD for MEN1-related gastrinoma.

Conclusion

Zollinger-Ellison syndrome must be managed to avoid life-threatening complications by the gastric acid hypersecretion, and an indolent, but malignant tumor. Careful management of each of these aspects will lead to long-term survival for most patients with this disease.

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