Int Surg 2015;**100**:365–369
DOI: 10.9738/INTSURG-D-13-00195.1

Case Report

Granular Cell Tumor of the Esophagus With Elevated Preoperative Serum Carbohydrate Antigen 19-9: A Case Report

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A 59-year-old Japanese man was admitted to our hospital for treatment of a submucosal tumor of the esophagus detected by upper gastrointestinal endoscopy and computed tomography (CT). Endoscopic examination revealed a submucosal tumor in the esophagus 35 cm from the incisor teeth. Biopsy of the lesions identified granular cell tumor. CT indicated a projecting and slightly enhanced homogenous mass measuring 2.0 × 1.5 cm in the esophagus below the tracheal bifurcation. Serum tumor marker studies revealed elevated carbohydrate antigen (CA) 19-9. Therefore, the tumor was considered to have malignant potential, and surgical resection was performed. The final pathologic diagnosis was a benign granular cell tumor, positive for S-100 protein. The patient was doing well with normal CA 19-9 levels and no recurrence more than 5 years after surgery. To the best of our knowledge, this is the first report of a granular cell tumor with elevated serum CA 19-9.

Key words: Granular cell tumor – Esophagus – Tumor-associated carbohydrate antigens

Granular cell tumor (GCT) is a comparatively rare lesion in clinical practice. It was first reported by Abrikossoff as myoblastoma in 1926.[1] Although the tumor cells were morphologically similar to myoblast cells, immunohistochemical studies for S-100 protein proved that this tumor originated from Schwann cells.[2] The tumors most often arise in skin or subcutaneous tissue, with 2.7%

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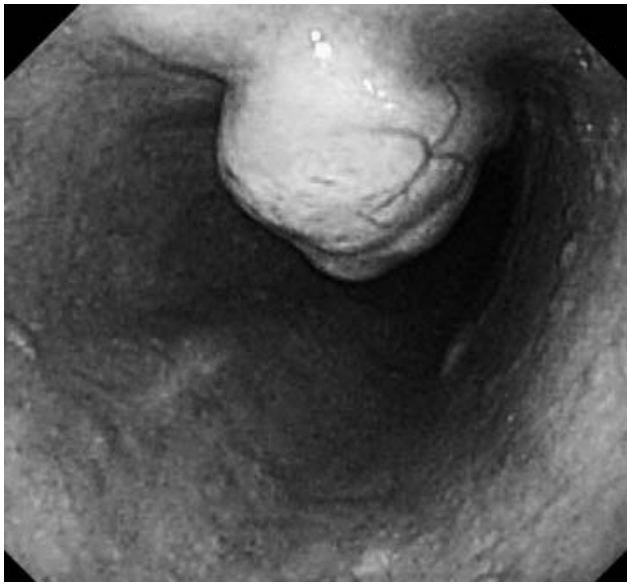

Fig. 1 Endoscopic examination showing a molar-shaped esophageal submucosal tumor covered with normal mucosa 35 cm from the incisor teeth.

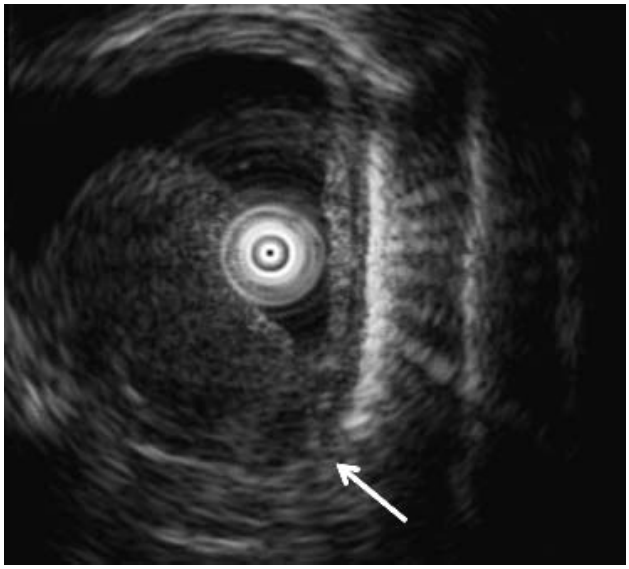

Fig. 2 Endoscopic ultrasonography showing that the tumor was a submucosal, solid, and relatively hypoechoic mass with a diameter of 2.0 cm. The tumor was located mainly in the third layer but may have extended into the border of the fourth layer (white arrow).

to 8.1% of GCTs occurring in the digestive tract.[3,4] One third of reported GCTs in the digestive tract originate in the esophagus.[4] Histologically, GCTs are usually located in the submucosal layer, but some GCTs are seen in the muscle or mucosal layer.[5] The histologic criteria for the diagnosis of a malignant GCT are based on the presence of mitotic activity and nuclear atypia.[6]

From a clinical perspective, the tumor's malignant potential must be determined prior to surgery. Evaluation of tumor serum markers can help with the diagnosis of malignant epithelial neoplasms, but the results may be unclear in the case of malignant nonepithelial neoplasms.[7] Some reports have described high carbohydrate antigen (CA) 19-9 levels in patients with uncommon diseases, such as, retrorectal cystic hamartoma, mediastinal mature teratoma, and splenic cyst.[8–10] To the best of our knowledge, ours is the first documented case of esophageal GCT with elevated serum CA 19-9.

Case Report

A 59-year-old Japanese man visited our hospital for investigation and treatment of a submucosal tumor of the esophagus in January 2008. At the time of diagnosis, he was completely asymptomatic. He had received treatment of oral medication for diabetes at 58 years of age, although he had no diabetic complications. The results of blood biochemical examinations were normal, but serum tumor marker studies revealed elevated CA 19-9 (90.7 U/mL; normal range, 0–36.9 U/mL). Endoscopic examination showed an esophageal submucosal molar-shaped tumor 35 cm from the incisor teeth (Fig. 1). Biopsy of the lesion identified a GCT. Endoscopic ultrasonography (EUS) identified a submucosal solid tumor with a diameter of 2.0 cm. The tumor was located mainly in the submucosal layer, but it was not clear whether the deep margin was separate from the adjacent muscle layer. The tumor was relatively hypoechoic, but hyperechoic compared with the adjacent muscle layer (Fig. 2). Computed tomography (CT) indicated a projecting and slightly enhanced homogenous mass of 2.0×1.5 cm in the esophagus below the tracheal bifurcation (Figs. 3A and 3B).

The tumor was not malignant based on the biopsy findings, but we could not exclude the existence of malignant potential because of the elevated CA 19-9. Because of the possibility that the tumor was located partially in the muscle layer based on EUS, we judged endoscopic resection too difficult. Therefore, we performed tumor enucleation via a mini-right thoracotomy in March 2008. Macroscopically, the resected tumor was a firm mass with a smooth surface measuring $2.0 \times 1.6 \times 1.3$ cm

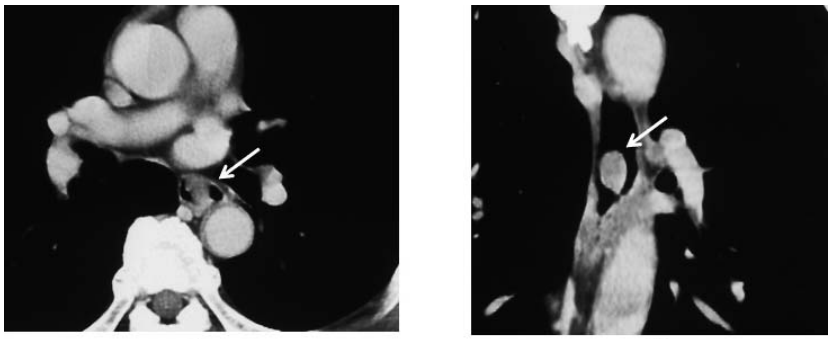

Fig. 3 CT findings. CT revealed a projecting and slightly enhanced homogenous mass measuring 2.0 × 1.5 cm in the esophagus below the tracheal bifurcation (white arrow). (A) Horizontal slice. (B) Coronal slice.

(Fig. 4). Histologically, the tumor was located in the submucosal layer and showed no nuclear atypia with eosinophilic cytoplasm and a granular appearance (Fig. 5A). Immunohistochemical staining revealed that the tumor was positive for S-100 protein (Fig. 5B). The final pathologic finding was a benign GCT. The postoperative course was uneventful, and the patient was discharged 14 days after surgery. The patient was doing well with no recurrence more than 5 years after surgery. Also, the serum CA 19-9 level normalized postoperatively and remained normal as of the most recent follow-up (Fig. 6).

Discussion

GCTs are uncommon tumors in the digestive tract; although, nearly one third occur in the esophagus.[3,4] Most esophageal GCTs are found incidentally during upper gastrointestinal endoscopy performed for other reasons. A GCT is usually asymptomatic; however, when the tumor diameter is larger than 1.0 cm, it may cause dysphagia.[5] In our case, the tumor had a diameter of 2.0 cm without causing dysphagia.

Although the natural history of this tumor type is unclear, most esophageal GCTs have a benign clinical course. However, approximately 1.5% to 2.7% of GCTs are diagnosed as malignant variants.[11,12] Malignant GCTs are classified into 2 types[13,14]: the first is histologically and clinically malignant, and the second is histologically benign but clinically malignant. The infiltrative growth pattern and the presence of metastases are important features when differentiating malignant and benign tumors because they may be of very similar appearance histologically. The features associated with malignancy include local recurrence, rapid growth to a size greater than 4 cm, tumor necrosis, increased cellularity, nuclear atypia, and mitotic activity of greater than 2 mitoses per high power field.[6,15]

The optimum treatment for GCTs remains controversial, but the current treatment options are a conservative approach with regular endoscopic follow-up for tumors <10 mm in diameter without evidence of malignant change,[16] and surgical excision for tumors >20 mm in diameter, benign GCTs causing symptoms, or when malignancy is suspected.[17] However, sufficient follow-up for GCTs is necessary, even when they are histologically diagnosed as benign after resection. A previously reported case had no mitotic activity or other nuclear atypia present in the original resected

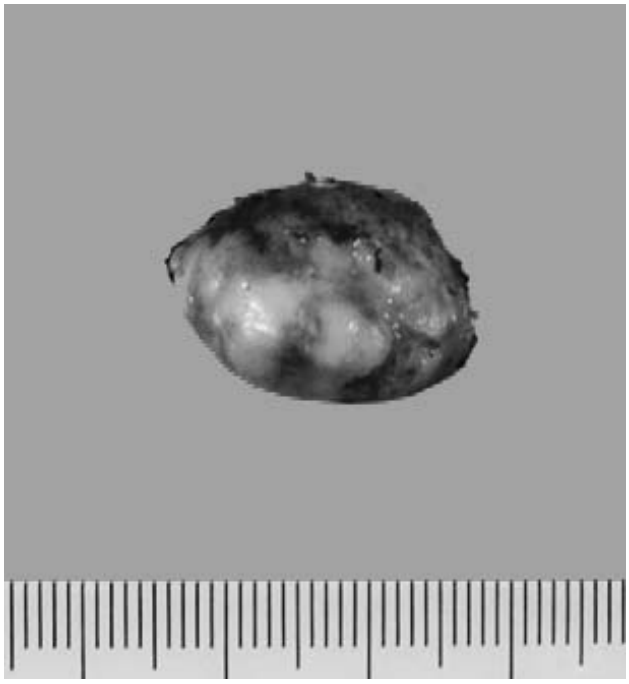

Fig. 4 Surgical specimens. The esophageal tumor was a firm mass with a smooth surface measuring 2.0 × 1.6 × 1.3 cm.

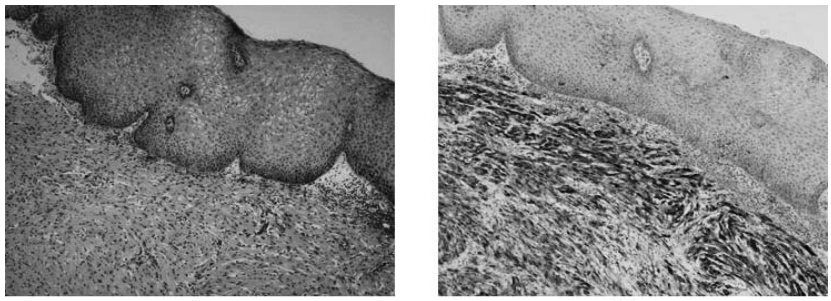

Fig. 5 Macroscopic examination. (A) The submucosal tumor showed no nuclear atypia with granular, eosinophilic cytoplasm (H&E ×40). (B) A strong, diffuse, positive immunohistochemical reaction for S-100 protein occurred in the tumor cells (H&E ×40).

specimen but showed malignant features such as nuclear atypia in the recurrent tumor.[18]

CA 19-9 is a tumor marker that can be detected by a monoclonal antibody that recognizes the sialyl Lewis A carbohydrate chain. Sialyl Lewis A is secreted into the serum and is elevated in patients with adenocarcinoma of the digestive tract, particularly pancreatic cancer, biliary tract cancer, and advanced digestive tract cancer. This antigen is also detected in epithelial tissues of the salivary gland, biliary system, and pancreatic duct system in normal fetuses and adults. In addition, high levels of CA 19-9 are seen in inflammatory diseases such as benign hepatobiliary and pancreatic conditions. In our case, no abnormalities of the biliary system or pancreatic duct system were seen on preoperative magnetic resonance imaging (MRI) (data not shown).

To our knowledge, our case is the first report of a benign esophageal GCT associated with an elevated CA 19-9 level. In our case, immunohistochemical staining of the resected tumor revealed that it was negative for CA 19-9 (data not shown), and serum levels normalized after tumor resection. In a previous report, we described falsely elevated CA 19-9 levels related to a benign gastric schwannoma with negative staining for CA 19-9. In the current case, the high CA 19-9 level also appeared to be a false elevation but was at least partly associated with the esophageal GCT. Other reports of diseases with elevated CA 19-9 levels have not discussed the mechanisms involved, and it is unknown whether these diseases actually induce production of CA 19-9.[19–21] The association between elevated serum CA 19-9 and esophageal GCT remains unclear.

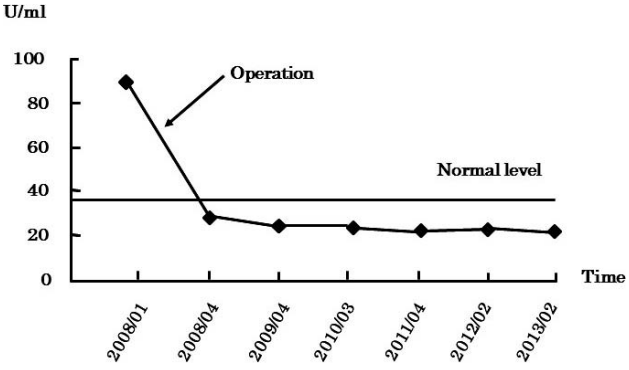

Fig. 6 Follow-up measurement of the serum CA 19-9 levels. The levels of serum CA 19-9 decreased postoperatively and remained normal as of the most recent follow-up.

In conclusion, we report a case of esophageal GCT with elevated serum CA 19-9. The tumor was considered to have malignant potential because of the high CA 19-9 level, and surgical resection was therefore performed. However, the histologic diagnosis of the resected specimen revealed a benign GCT. The patient was doing well, with normal CA 19-9 levels and no recurrence more than 5 years after surgery. This case may be valuable in examining the malignant potential of GCT, although the association between the elevated serum CA 19-9 level and esophageal GCT could not be conclusively proven.

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