Esophageal Cancer Initially Thought to be Accompanied by a Solitary Metastasis to an Intrathoracic Paraaortic Lymph Node

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Esophageal cancers usually exhibit lymph-node metastases. Although a solitary lymph-node metastasis is occasionally found, the involvement of an intrathoracic paraaortic node is rare. We present here an intrathoracic mid-esophageal cancer case in which an accompanying solitary retroaortic mass was found within the posterior mediastinum by integrated positron emission tomography/computed tomography. For diagnosis, thoracoscopic resection of the mass was performed from a left thoracic approach, and histology revealed it to be a squamous cell carcinoma metastasized from the esophageal cancer. Upon radical esophagectomy after neoadjuvant therapy as a T3N1M0 Stage IIIa (AJCC/UICC) cancer, the esophageal cancer was found to have invaded unexpectedly deeply in the vicinity of the descending aorta. Another lymph node within the paraaortic region was also involved (T4N1M0 Stage IIIc). The present case and other cases we review here inform our understanding of metastasis to intrathoracic paraaortic nodes as follows: 1) its existence may indicate extensive lymph-node metastasis or direct tumor invasion nearby, and 2) it may be accompanied by other lymph-node involvements in this region, even if it appears solitary upon preoperative investigation. Thus, for radical esophagectomy, sufficient lymph-node dissection is required, even at locations not reached by the usual right thoracic approach. Definitive chemoradiotherapy may be a better choice for preoperatively recognized T3 esophageal cancer when the cancer is accompanied by paraaortic lymph node metastasis.

Key words: esophageal cancer, intrathoracic paraaortic lymph node, solitary metastasis
heavy alcohol intake and smoking. He had suffered from epigastralgia for 2 months. Upon admission, his laboratory data were unremarkable, and the serum values of carcinoembryonic antigen, cytokeratin-19 fragment, and squamous cell carcinoma (SCC) antigen were each within the normal range. Both esophagography and upper endoscopy revealed a 5-cm Borrmann type-2 tumor within the mid-thoracic portion of the intrathoracic esophagus (Fig. 1A), and histology of biopsy samples taken from that tumor revealed SCC, G2. However, computed tomography (CT) of the chest displayed a mass behind the intrathoracic descending aorta, in addition to the predicted mid-thoracic esophageal cancer (Fig. 1B), while \(^{18}\)fluoro-deoxyglucose (FDG)-positron emission tomography (PET)/CT revealed abnormally high FDG uptakes at those sites (Fig. 1C). No abnormal FDG uptake values were observed at other sites.

We considered whether the retroaortic mass might be an ITPAN metastasis from the esophageal cancer, a benign granulomatous inflammation, or another entity, since a solitary ITPAN metastasis from an esophageal cancer is rare and an elevated FDG uptake does not necessarily indicate a malignancy [5]. A further problem was that the location of the mass meant that it could not easily be approached during the usual one-stage resection for a mass and a mid-esophageal cancer using a right thoracic approach. Thus, a 2-stage operation was planned, and for resection of the mass we selected thorascopic resection using a left thoracic approach as the first procedure, followed by esophagectomy using a right thoracic approach, since it would be less invasive. During the first procedure, the mass was found on the dorsal surface of the intrathoracic descending aorta at the 8th vertebral level (Fig. 2A). It was easy to detach from the aorta, and cancer invasion was indistinct there. Histology revealed the mass to be a destructured lymph node due to metastatic deposits of SCC (Fig. 2B), a finding consistent with a T3N1M0 Stage IIIa (AJCC/UICC

![Fig. 1 Imaging studies of the esophageal cancer and the paraaortic mass. A, Esophagography revealed an esophageal cancer forming an irregular crater within the intrathoracic mid-esophagus (arrows); B, Chest computed tomography displayed a mass (arrowheads) posterior to the descending aorta; C, \(^{18}\)Fluoro-deoxyglucose-positron emission tomography revealed an abnormally elevated uptake of fluoro-deoxyglucose at the site of the paraaortic mass (arrowhead) as well as at that of the esophageal cancer (arrow).]
esophageal cancer.

The patient received neoadjuvant therapy (2 cycles of cisplatin 80 mg/m² on day 1 and 5-fluorouracil 800 mg/m² on days 1–5, with a 4-week interval). However, imaging showed this to have caused only a minimal improvement in the esophageal cancer, which could not deny its periaortic invasion (Fig. 3). PET/CT was not performed at that time. A radical esophagectomy was performed using a right thoracic approach 8 weeks after termination of the neoadjuvant therapy. During the operation, the esophageal cancer was found to have extended into the periaortic tissue, where the tumor remained after the esophagectomy. In the resected specimen, an ulcerated tumor, sized 52 × 29 mm, was located within the mid-thoracic esophagus. Histology revealed a trabecular and nested proliferation of SCC cells. The tumor cells invaded the adventitia of the esophageal wall and were exposed at the detached surgical margin near the aorta. Lymphovascular invasion by tumor cells was observed at the primary site, and SCC deposits were observed within 2 upper paraesophageal lymph nodes and an ITPAN, which were all excised during the operation. The final diagnosis was G2 SCC, T4N1M0. The post-operative period was uneventful, and the patient has been followed up with chemotherapy. There has been no sign of either tumor regrowth or metastases in the 2 years since the operation.

Discussion

Esophageal cancers usually exhibit lymph-node metastasis. In published autopsy series [7–9], about 60–70% of patients with esophageal cancer have dis-
played metastatic deposits within the lymph nodes. Although the location of the esophageal cancer within the esophagus (viz. upper, mid, or lower intrathoracic, or abdominal portion) tends to influence the site of lymph-node metastasis, extensive propagation can occur in esophageal cancer [10, 11]. Therefore, radical esophagectomy with 3-field (cervical, mediastinal, and abdominal) lymph-node dissection has been recommended for intrathoracic esophageal cancers [12]. However, it has been found that esophageal submucosal lymphatics drain longitudinally to perigastric and/or cervical (including recurrent nerve) lymph nodes, and that when tumors penetrate into the proper muscle layer or deeper, then paraesophageal lymph nodes will be involved segmentally [13, 14]. Thus, most instances of solitary lymph-node metastasis occur within the perigastric or cervical region [13]. In the present case, a single ITPAN (within the posterior mediastinum) was revealed to be swollen and positive by preoperative PET/CT. There have been only 3 published cases in which esophageal cancer was found to involve an ITPAN within the pre- or peri-operative period [3, 4]. From the rarity of such involvement, ITPANs are supposed not to receive drainage directly from the lymphatics embedded in the esophageal wall; that is to say, the Japanese guidelines for the clinical and pathologic aspects of esophageal carcinoma treat ITPANs as compartment 3 for intrathoracic mid-esophageal carcinoma [15]. ITPANs are nodes of the para-aorto-esophageal nodes that are located in the vicinity of the aorta and lie along the bilateral grooves formed between the esophagus and aorta [16]; The aortic wall is surrounded by a lymphatic meshwork that does not penetrate the aortic walls [17] and drains to the ITPANs; from there, the upper lymphatics seem to drain into the parabranchial lymph nodes and the lower ones to the thoracic duct or the cistern chylli [16].

In 2 of the 3 published surgical cases with ITPAN involvement (i.e., excluding the present case), metastasis to ITPAN was suspected preoperatively. The primary tumors were all located within the intrathoracic mid-esophagus, were SCC, showed lymphovascular invasion, and were considered to have infiltrated at the level of the proper muscle layer or adventitia of the esophageal wall (in one case, although the cancer invasion was reported to be limited to the level of the deep submucosal layer of the esophageal wall, it was accompanied by local cancer proliferation within the adventitial tissue [3]). Apart from ITPAN, these 3 cases exhibited relatively extensive or widely propagated lymph-node metastasis: one case involved cervical, recurrent nerve, and perigastric lymph nodes; the second case cervical; and the third case recurrent nerve, parastrachal, paraesophageal, and perigastric. An extensive tumor burden in the lymphatics (such as in certain autopsy cases and the above 3 cases) could be responsible for the findings of metastatic deposits within the ITPANs. However, the present case did not show such extensive lymph-node involvement, and the metastasis may have been due to the deep cancer invasion into the aortic wall.

From the above considerations, an extensive or widely propagated lymph-node involvement of the cancer or direct tumor invasion in the vicinity of the aorta was considered as the possible cause of the ITPAN metastases. Interestingly, in 2 of the 3 published cases, recurrence occurred within ITPANs. The present case also had an involvement of another ITPAN within the specimens resected during the operation. Excluding one case whose postoperative local status in the posterior mediastinum was not available [4], the other 2 published cases and the present case each had 2 or more involved lymph nodes within this paraaortic region. From this, we infer that ITPAN involvement in cases of esophageal cancer is likely not solitary, even if the involvement of other nodes is indistinct on imaging.

Whether or not this inference is always justified, we suggest that if radical cure is expected, sufficient lymph-node dissection should be carried out for an esophageal cancer that is accompanied by any ITPAN swelling. In the present case, we unfortunately selected thoracoscopic resection for the first stage of the two-stage operation, and therefore sufficient lymph-node dissection in the paraaortic region was not performed. Such dissection in the region of the posterior mediastinum requires operation from the left thoracic approach. However, this approach has limits for dissection of the neck or of the tissue in the vicinity of the right recurrent nerve or the right lung hilar lymph nodes. In one of the 3 previously reported cases with ITPAN involvement, an unusual operative approach was adopted [4]: namely, a left thoracic incision, accompanied by resection of the manubrium of the sternum and dislocation (turn) of the aortic arch, to
provide sufficiently wide operative fields for dissection of these regions. If the dissection were found to be unsatisfactory, a particularly careful follow-up would of course be required. Upon reflection, in the present case it might have been better to have considered definitive chemoradiotherapy instead of surgery-based therapy. In Japan, T3-Stage III patients are generally recommended to receive neoadjuvant chemotherapy plus surgery \[18\]. Definitive chemoradiotherapy remains an alternative treatment because of its late toxicity and because there is the possibility of salvage surgery \[18\]. Actually, with the inferences drawn from the previous ITPAN-positive cases, in which there was the possibility of either periaortic invasion or involvement of another ITPAN that would be difficult to dissect, definitive chemoradiotherapy might be the first-choice therapeutic modality in such cases.

In conclusion, we present here an esophageal cancer patient with ITPAN metastasis. Even if the ITPAN swelling initially appears to be solitary, such cases may have extensive lymph-node involvement or direct cancer invasion in the vicinity of the aorta. Sufficient lymph-node dissection, including this region, should be considered as an adjunct to the radical operation, and a therapeutic modality for T4 or stage IV esophageal cancer may be a suitable selection for such cases.

References