Synchronous squamous esophageal carcinoma and urothelial renal cancer

I.D. Vilcea¹, I. Vasile¹, P. Tomescu¹, C. Mirea¹, A.M. Vilcea¹, L. Stoica¹, C. Mesina¹, T. Dumitrescu¹, M. Cheie¹, M.A. Enache²

¹IInd Surgical Clinic, University of Medicine and Pharmacy of Craiova
²Urology Clinic, University of Medicine and Pharmacy of Craiova
³Dermatology Clinic, University of Medicine and Pharmacy of Craiova

Abstract
Synchronous development of a second primary cancer in patients with esophageal squamous cell carcinoma was reported in 2.73%-11% of the cases. Although the synchronous association between esophageal and renal cancer is very rare, an increasingly number of cases is reported in medical literature. This study’s aim is to report a case of synchronous esophageal squamous cell carcinoma and an urothelial carcinoma of the right kidney. Patient G.D. was admitted in our clinic with esophageal cancer diagnosis; during the preoperative work-up protocol, an asymptomatic right renal mass was discovered. A nephroureteroscopy with biopsy was performed and the urothelial renal cancer diagnosis was established. The patient is proposed for seriate surgery: nephroureterectomy on the first stage, then esophagectomy with gastric reconstruction was performed. Postoperative evolution was unfavourable, patient being finally discharged, on his request, with severely altered status.

Key words: synchronous, esophageal cancer, renal urothelial cancer

Introduction
Squamous carcinoma of the esophagus is recognized for its frequent association with other primary malignancies, especially neck and head cancers, lung and stomach cancers; the incidence of multiple malignancies associated with esophageal cancer, as an index tumor, varies in different studies from 1.8% to 27% of cases. (1-5)

This variation is probably due to the variation between different types of cancer among patients of different nation-
alities. Anyway, the number of cases increases with the intensifying of screening and postoperative follow-up of patients with esophageal cancer. (2-5)

The risk of identifying a second malignancy in patients curatively operated for esophageal cancer, was estimated to be three-fold increased than in general population, with a calculated standardized incidence ratio of 1.28 (1.18-1.38). (1, 3)

Synchronous development of a second primary cancer in patients with esophageal squamous cell carcinoma was reported in 2.73%-11% of the cases. (2, 5) Although the synchronous association between esophageal and renal cancer is very rare, an increasingly number of cases is reported in medical literature; a metachronous development of an esophageal cancer, after a curatively treated renal cancer, was also reported. (6)

This study’s aim is to report a case of synchronous esophageal squamous cell carcinoma and an urothelial carcinoma of the right kidney.

**Case presentation**

Patient G.D., male, 56 years old, was admitted in our clinic (32196/28.06.2007) for total dysphagia and weight loss (15 kg) for 3 months. The patient is a heavy drinker and smoker. Blood tests revealed a slight anemia (11.4g%) and proteinemia (5.6g%); blood urea (27 mg%) and serum creatinine levels (0.9 mg%) were normal. A barium esophago-gastrography revealed a malignant stenosis, on the midthoracic esophagus, confirmed by the endoscopy with biopsy (squamocellular esophageal carcinoma); no other gastro-duodenal lesions were found. The spirometry revealed a slight decrease of the vital capacity (VC 4023 ml) and FEV1 (2672 ml), the report FEV1/VC being also slightly lowered (66.41%); plain chest X-ray and EKG were in normal limits. The routine abdominal ultrasound discovered an abnormal mass on the lower pole of the right kidney, 7 cm in diameter, with invasion of renal pelvis and perirenal fascia and fat. A thoraco-abdominal CT was performed and confirmed both esophageal and right renal tumors, radiologically operable (there seemed to be a cleavage plan between esophageal tumor, aorta and tracheal bifurcation); no enlarged lymph nodes, and no metastasis were found, both in the mediastinum and in the abdomen. The left kidney presented normal morphology and function on CT. A right retrograde ureterorenoscopy with biopsy was performed, the pathology report establishing the diagnosis of urothelial renal cancer.

With synchronous squamous T3N0M0 esophageal cancer and T3N0M0 urothelial cancer of the right kidney, the patient was proposed for seriate surgery.

Through a midline laparotomy, a right radical nephroureterectomy was performed and a jejunal feeding tube was inserted; no abdominal or retroperitoneal metastasis, neither enlarged lymph nodes were identified intraoperatively. The pathology confirmed the first result: right urothelial renal cancer pT3N0M0G3. (Fig. 1, 2)

After 2 weeks of normal postoperative evolution, with normal renal function (urine volume varied between 1200-1800 ml daily, normal blood urea and serum creatinine levels) and jejunal feeding, the patient was proposed for esophageal resection. Esophagectomy was performed through separate incisions: the right thoracic in the 5th interspace, abdominal and left cervical incisions. The esophagus was reconstructed with a gastric tube, preserving the right gastro-epiploic artery as the feeding vessel; the gastric substitute was ascended by the retrosternal route and a cervical, end-to-side hand-sewn eso-gastric anastomosis was performed. Many periesophageal and subtracheal small lymph nodes (<4-5 mm) were identified on mediastinal dissection, and a big tumor (over 6 cm height) (Fig. 3), which apparently invaded the entire esophageal wall. Histopathology diagnosis: pT3N1M0 squamocellular esophageal carcinoma.
cancer of the midthoracic esophagus (stage III). (Fig. 4)

The postoperative evolution was normal in the first 6 days after the second operation; on the 4th postoperative day, a control chest X-ray was made, and the thoracic drainage (serohematic) was suppressed; an anastomotic control X-ray (contrast: Ultravist), made on the 7th postoperative day, showed eso-gastric anastomosis apparently normal, without obvious leakage, hence, the patient started to be fed orally.

On the 11th postoperative day, the patient presented fever (38.6°C) and slight dyspnoea with tachypnoea; the thoracic X-ray diagnosed a pyothorax, which required pleural drainage to be reinstated, evacuating 400 ml of pus and discrete bilious aspect. On the same time, the patient developed redness on the cervical postoperative wound and, after instrumental exploration, an anastomotic leakage was diagnosed.

The oral intake was stopped and the patient received again enteral nutrition through the jejunostomy tube; antibiotherapy was also started.

The patient continued to present intermittent fever and, on the 17th postoperative day, a pulmonary abscess was diagnosed on thoracic X-ray. In spite of the intensive care, antibiotic therapy, and thoracic drainage, on the 28th postoperative day, the patient developed a right latero-thoracic parietitis, involving the postoperative thoracic wound, which required incision and debridement, but the patient refused and requested to be discharged. On the 29th postoperative day, the patient was discharged, on his and his family’s request, with severely altered general status, cervical anastomotic leakage, pyothorax and latero-thoracic fasciitis.

Discussion

Although the incidence of multiple primary malignancies with esophageal carcinoma is high, synchronous development of an esophageal carcinoma and a renal carcinoma is very rare. Chuang et col., on 13 studied cancers registries, found this association in only 0.078% of esophageal cancer operated cases, corresponding to a 1.88 (1.18-2.85) standardized incidence ratio; de Hingh and col., found an incidence of 2.1% synchronous renal cancers in 192 patients with esophageal cancer who underwent abdominal CT scan on the workup protocol. (1, 7)

This association creates difficult problems of diagnosis and therapeutic strategy, as concluded by all authors that have reported such synchronous lesions. (7-9)

In this case, initial diagnostic difficulties were correlated with the lack of symptoms from renal cancer, the renal tumor being identified as an incidentaloma, on routine abdominal ultrasound examination; still, this is not a surprise since Poon and col., found a 28% asymptomatic association between esophageal cancer and synchronous tumor. (4, 7-9)

An even bigger incidence of associated malignancy may be obtained if a more intense preoperative evaluation is performed, with modern investigational technique (18F-FDG PET), but such investigation often lacks in daily practice, in many medical centers (high costs, technique unavailability). (5)

An intense postoperative follow-up of esophageal cancer operated patients may also be very useful in order to diagnose the second malignancy into an early, curable stage, but this is highly dependent on the patient’s long term survival and cooperation with the follow-up program. (2, 3)

Anyway, the discovery of this association is very rare, knowing the fact that the urothelial cancer represents only 10% of the renal malignant tumors; this association is
probably due to some genetic disturbances (aldehyde dehydrogenase-2 genotype, molecular instability), but also other environmental or habitual risk factors (as smoking and drinking) may be involved as well. In fact, in all the reported cases, the renal lesion was, histologically, a Gravitz tumor, hence, this is the first reported case of urothelial renal carcinoma associated with squamous esophageal carcinoma. However, the association between urothelial carcinoma of the bladder and esophageal carcinoma has already been described. (2-4, 7, 10)

The discovery of a synchronous renal tumor with an esophageal cancer raised at least two main problems: to avoid esophageal or renal cancer upstaging (considering one of the tumors a metastasis), and establish the best suitable therapeutic strategy for this patient.

Establishing whether one of the tumors is a metastasis of the other, or a second primary cancer, has represented the first challenge in this case. It is clinically difficult, even impossible to be sure if whichever of the tumors represents a primary second malignancy or a metastasis from the other site. It is known that the kidney and the bladder may represent a metastatic site of an esophageal cancer; on the other hand, it has been reported secondary esophageal cancer with primary site in a renal cancer. In both such cases, the patient’s prognosis is poor, the presence of metastasis being an indicative of advanced disease. (7, 11-15)

On the other hand, if the tumors represent two separate malignancies, the patient’s prognosis appears to be similar to those of the patients’ with unique esophageal malignant tumor. In fact, the 5-year-survival rate of curatively operated esophageal cancer, synchronously with other primary cancers, was similar with the 5-year-survival rate of the patients with unique esophageal tumors (around 46% in Japan), and it is largely dependent on the esophageal cancer’s stage in the moment of diagnosis. (2-4)

Therefore, what must be avoided is mistakenly upstaging of esophageal cancer, hence refusing the resection and, consequently, the only chance for cure in these patients. (5) In order to do so, it is mandatory to obtain a pathologic specimen of the second cancer, at least in apparently curatively esophageal cancer. In case of an inoperable esophageal cancer, this may be considered unnecessary since the inoperable metastatic esophageal cancer has a very bad prognosis, and, practically, dictates the patient’s prognosis over the associated second malignancy. (3, 4)

In our case, we need to be sure that the renal tumor was not a metastasis of the esophageal cancer, knowing that the prognosis of the metastatic esophageal cancer is very poor (a mean survival period of only 6 month), thus avoiding major surgery related to esophagectomy. (16)

We were sure that the renal tumor was not a metastasis, only after the retrograde ureterorenoscopy with biopsy and histopathology reports, which demonstrated the structure of the urothelial renal cancer; at the same time, the esophageal tumor’s biopsy clearly demonstrated the squamous cell cancer characteristics.

Establishing the best fitted treatment strategy represents another challenge in this case. Some years ago, the detection of a second tumor (metastasis or primary malignancy, as well) synchronous with esophageal carcinoma would have represented a counter indication of esophagectomy. Nowadays, due to the progress in surgery, anesthesiology and intensive care, and especially in oncologic therapies, the survival of the esophageal cancer patients, bearing a second primary malignant tumor or even a single metastasis, does not differ significantly from that of the patients with unique esophageal tumor; hence, the esophageal resection no longer represents a counter indication in these cases. (2)

Practically, the discovery of the renal tumor puts us in front of the following therapeutic possibilities:
- resection of both tumors, since both seem to be resectable on CT scan, in the same operative session or into a staged procedures;
- palliative surgery for esophageal cancer (gastrostomy, thus avoiding major surgery), followed by oncologic therapy, since the renal cancer was asymptomatic, and long term survival is dependent mainly on the esophageal cancer.

Because both the renal and the esophageal tumors seem to be resectable, we choose the first option, surgery being the only chance for cure for this patient. Although some authors (7-9) had good results with one stage operation (nephrectomy, esophagectomy and reconstruction at the same time), the patient’s general status impaired by a long period of dysphagia and important weight loss, anemia and hypoproteinemia, made us choose the seriate surgery.

Despite the fact that esophageal cancer represents “index tumor”, dictating the patient’s prognosis, we considered too risky to perform an esophageal resection with reconstruction in the first stage, on a frail patient. On the first laparotomy, our primary objective was to establish an enteral nutritional pathway, and to seek for the evidence of cancer dissemination (peritoneal, liver or nodal metastasis), who have had counter indicate resections. Since, we did not discover other abdominal lesions, we performed nephroureterectomy for renal tumor (17, 18) and jejunostomy as an enteral nutritional pathway.

The postoperative evolution was favorable, with good left kidney function. Two weeks later, period in which the patient benefited of enteral nutrition, we performed subtotal esophagectomy and gastric reconstruction, by thoraco-abdomino-cervical approach.

After esophageal resection, the postoperative evolution was difficult, the patient developed an eso-gastric anastomotic leakage, followed by pyothorax and pulmonary abscess in the right lung, leading to a progressively impairment of the patient’s general condition. On the 28th postoperative day, the patient developed a latero-thoracic fascitis (probably related to purulent pleural drainage), but he refused any other therapeutic measures and was discharged with severely altered status, on his request.

Even though some authors (7-9) had good postoperative outcome, resecting both esophageal and renal tumors, sequentially, or in the same surgical session, inevitably performing two major resections in a frail patient, led to an increased
operative risk. The second surgery had also added an important risk factor, which may explain the failure of our therapeutic approach in this case.

Another important conclusion of this case is related to cervical anastomotic dehiscence after esophageal resection and reconstruction; also, considered benign comparative to the thoracic anastomosis, cervical anastomotic leakage can lead to a mediastinal or pleural collection, with the same gravity as a thoracic leakage, and performing a cervical anastomosis does not always avoid such severe complications. (19)

Not the least, a particular conclusion is related to the renal tumor: a relatively big tumor, invading the renal pelvis and parenchyma, and surrounding fat tissue, but still asymptomatic. This emphasizes the importance of the careful preoperative examination in the esophageal cancer, looking extensively for metastasis or another tumor in any abdominal or retroperitoneal organs, not only in the usual site (lung, liver or lymph nodes). The most common investigation for this purpose is thoracic and abdominal CT, even if this imaging technique failed to identify small regional lymph nodes in this case. (7, 16)

Retrograde renoureteroscopy allowed us the diagnosis of urothelial carcinoma; knowing the multifocality of this type of cancer, we could perform a nephroureterectomy (without bladder cuff), thus avoiding an incomplete resection of renal cancer. (17,18)

Conclusions
1. Synchronous development of esophageal and renal carcinoma is a rare event, which lead to difficult problems of therapeutic strategy.
2. In order to avoid upstaging of whichever of the tumors, preoperative biopsy of both tumors is mandatory, especially in potentially curative cases.
3. Resection of both tumors is the only chance for cure, in resectable cases, but it is associated with an increased risk of postoperative morbidity and mortality.
4. In addition, there are difficult to established “the best fitted” therapeutic strategy in these cases, especially due to the small number of cases reported in medical literature.

References