

Esophageal Stenosis: A Differential Diagnosis Between Esophageal Cancer and Metastasis from Other Neoplasia

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Abstract. *Background: The occurrence of radiological mediastinal lymphadenopathy as the only evidence of tumor recurrence of cervical carcinoma is very rare. We report on such a case with stenosis of the esophagus. Case Report: A 36-year-old Caucasian woman, without any relevant history of gynecological cancer, underwent a trans-vaginal ultrasound with evidence of any cervical lesion locally extended. After histologically-proven diagnosis of squamous cell carcinoma of the cervix uterine, the patient was treated by neoadjuvant chemoradiation, followed by total abdominal hysterectomy with bilateral salpingo-oophorectomy. A subsequent close follow-up was negative for recurrence of disease until December 2008, two years after diagnosis. At that period, the patient experienced cough and severe dysphagia and for this reason she underwent several examinations including esophagogastroduodenoscopy, whole-body computed tomographic scan and bronchoscopy with transbronchial needle aspiration. Histology led to diagnosis of recurrence of cervical cancer, HPV31-positive, in multiple mediastinal lymph nodes, with infiltration of the esophageal mucosa. Conclusion: Mediastinal lymphadenopathy in patients with a history of cervical carcinoma should be suspicious of metastatic disease, even if there is no radiological evidence of distant metastases.*

Cervical cancer ranks as the second most common malignancy in women worldwide, with the majority (80% of new cases) appearing in developing countries (1). Approximately 80% of primary cervical carcinomas arise from pre-existing squamous dysplasias (2). Despite aggressive local therapy leading to excellent local control, the incidence of distant metastases in patients with invasive

carcinoma of the uterine cervix is high (3). Approximately 70% of recurrences from cervical cancer are estimated to be distant or a combination of local and distant metastases (4). The incidence of metastases to other organs is 56%. The most frequent sites are the lung, abdominal cavity, liver, and gastrointestinal tract (3). Thoracic metastatic localization by cervical cancer includes lung parenchyma, pleura, bronchial tree, lymph nodes, lymphatics and chest wall (5). The incidence of clinically-apparent lymph node involvement is 22%, mainly to para-aortic, supraclavicular, and inguinal nodes (3). Few cases of isolated mediastinal lymph node metastases from cervical cancer have been reported in the literature (6-9), with no previous case describing an extensive infiltration of the esophagus by mediastinal lymph node metastases from cervical cancer recurrence. Distant metastases are detected in clinically-advanced stages with symptoms such as cough, hemoptysis, dysphagia and pain (10), mimicking other neoplastic disease.

Case Report

A 36-year-old Caucasian woman, without any personal clinical history of cancer, underwent a trans-vaginal ultrasound in May 2007 which showed cervix echotexture subverted by the presence of a polycyclic formation of 58×28×54 mm extending to the left side. To confirm the lesion, the patient underwent a pelvic magnetic resonance imaging (MRI) scan that documented an expansive lesion of the uterine cervix of 5×4 cm, with spiculated and polycyclic margins infiltrating the adipose tissue of both parametria. Below, the lesion extended into the vagina with involvement of the left fornix and, marginally, also of the right fornix. Abdominal computed tomography (CT) scan confirmed the expansive hypodense cervical lesion with a peripheral ring of contrast enhancement and cervical margins preserved; it also showed that the lesion displaced, without signs of infiltration, the fundus bladder and the right juxta-vesical urether. Endo-cervical biopsies of the lesion documented squamous cell carcinoma with stromal invasion. From June to July 2007 a neoadjuvant chemo-radiotherapy was

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Figure 1. Chest scan: stenotic esophagus.



Figure 2. Chest scan: mediastinal lymph node metastasis.

performed. Multimodal treatment was performed with intravenous cisplatin in continuous infusion. In August 2007, the patient was evaluated by a pelvic MRI that showed a size reduction of the lesion (25 mm vs. 50×40 mm) but the extension in adipose tissue was more evident in the left parametrium with vagina infiltration. Hysterectomy according to Piver III was performed with bilateral salpingectomy and bilateral pelvic lymphadenectomy. Histological examination documented the absence of residual tumor in both the left and right parametria, in fallopian tube and in all 15 lymph nodes removed, with free vaginal resection margins. Subsequent follow-up was negative until December 2008 (15 months from diagnosis), until the appearance of epigastric pain, orthodox dysphagia, cough, vomiting and weight loss of 8 kg in three weeks. Esophagogastroduodenoscopy showed gastroesophageal reflux disease that was treated with esomeprazole and domperidone without any clinical benefit. For this reason, in February 2009, the patient came to the emergency room of our hospital and was submitted to further esophagogastroduodenoscopy that showed stenosis at 34 cm from the dental arch. Staging with whole-body CT with contrast scan confirmed the presence of the hypodense esophageal tissue, with heterogeneous contrast enhancement in the middle third and lower third of the esophagus, for a cranio-caudal extension of about 10 cm. Critical stenosis determined dilatation of the first third of esophagus and loss of periesophageal planes of cleavage. Cleavage with the ascending aorta was preserved (Figure 1). CT scan showed subcentimetric lymph nodes in the right paratracheal and precarinal side, and lombo-aortic lymph nodes of about 20 mm (Figure 2). The patient underwent fibrobronchoscopy with transbronchial needle aspiration (TBNA) into retro-

carinal lymph node then cytological examination documented neoplastic cells from cervix uterine neoplasm positive for Human Papilloma Virus-31 (HPV31) (Figures 3-4). Because of clinical worsening in dysphagia and cough, the patient was submitted to Savary dilatation with esophageal stenting. Moreover the patient was subjected to first-line chemotherapy with cisplatin 75 mg/m² on day 1 and vinorelbine 25 mg/m² on day 1 and 8, every 21 days, for two courses with good tolerance to treatment. In April 2009 (one year and eleven months after diagnosis), the patient came to our attention with fever (38.5°C) and persistent productive cough. The CT scan documented alveolar filling areas diffuse and widely confluent with aspects of 'tree in bud' compatible with bronchopulmonary inflammation and the presence of metastatic lymph nodes infiltrating the carina with diameter of 2.5 mm, the paraesophageal area, the right principal bronchus with 2.6 mm diameter. Considering this pneumonia, the patient underwent antibiotic therapy with improvement of the clinical status and CT scan. The third cycle of chemotherapy was infused with a 25% dose reduction for the altered performance status of patient. The patient was evaluated with a whole-body CT scan after the third cycle of chemotherapy. Staging of disease demonstrated reduction of the flogistic areas in the right lower lobe, with progressive disease in lymph nodes (17 mm) at the hepatic hilum. The patient died one year after diagnosis of thoracic recurrence.

Conclusion

The peculiarity of this case is associated with the pattern of recurrence of cervical uterine cancer. Despite regular follow-up, the patient experienced distant recurrence of disease that

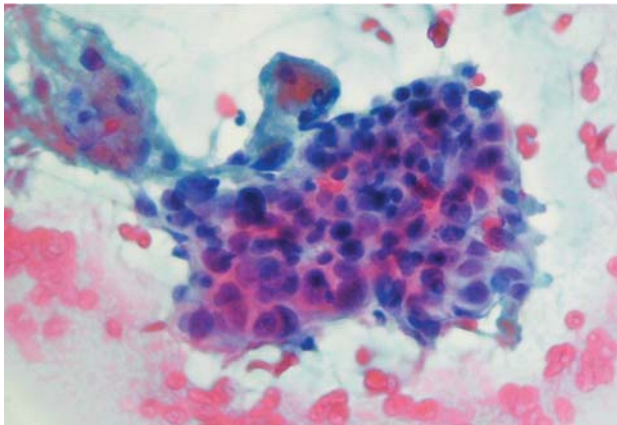


Figure 3. Diff Quick stain ($\times 40$): This fast stain is performed during the rapid on site cytology evaluation (ROSE) to assess immediately cytological sample quality and quantity. In this field, neoplastic cells are arranged singularly, showing a marked nuclear pleomorphism with chromatin clumping.

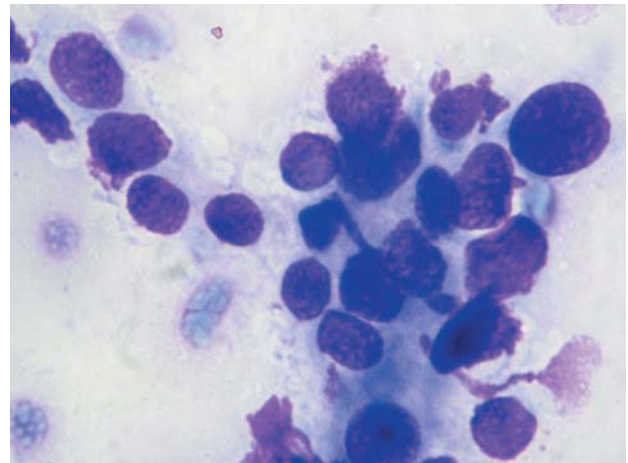


Figure 4. Papanicolaou stain ($\times 40$): Neoplastic cells are arranged in a syncytial mass in which they have indistinct boundaries. Cells appear highly pleomorphic with marked change of nuclear size and shape.

occurred with an important lesion determining severe symptoms. Most recurrences from cervical cancer are detected within 18 months after diagnosis, and the peak period of detection is, generally, 9-12 months after diagnosis (10). For this reason, it is very important to identify low- and high-risk patients. In patients with early-stage cervical cancer treated with radical surgery, adverse pathological factors, in addition to nodal metastases, include larger tumour size, deep cervical-stromal invasion, lymphovascular space involvement, and extension to the vagina or parametria (11, 12). Large tumours are related to an higher risk of extrapelvic disease, as well as to central recurrence after treatment (13). Therefore, in our opinion, high-risk patients should be accurately investigated with annual positron-emission tomography (PET) with 18-F-fluorodeoxyglucose (FDG), a technique that can detect early local or distant recurrence (14-16). The importance of PET-FDG is provided in current NCCN guidelines (2013). Moreover, the gastrointestinal tract is a common site for both primary and metastatic carcinomas and the differential diagnosis can be hard to achieve, particularly when a metastatic tumor involves the mucosal surface (17). Some studies have demonstrated a correlation between the pathogenesis of squamous cell carcinoma of the esophagus, head and neck cancer and HPV infection (18, 19), but in this case, TBNA of the lymph node showed that the cytological architecture in metastasis was similar to the cellular architecture of the primary tumor both positive for HPV31, suggesting a lymphatic metastatic spread with esophageal infiltration. Macroscopic evaluation during esophagogastroduodenoscopy, showed a normal mucosa in the esophagus with *ab estrinseco*

infiltration. In conclusion, mediastinal lymphadenopathy in patients with a history of cervical carcinoma should be considered suspicious for metastatic disease until proven otherwise, even if there is no radiological evidence of other distant metastases.

Conflicts of Interest

The Authors declare that they have no competing interests.

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