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CLINICAL CASE

Respiratory failure and tracheoesophageal fistula due to mediastinal metastasis from cervical cancer: case report

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Abstract

Cervical cancer is relatively frequent in the world and Perú. Mediastinal metastasis is a rare occurrence, with few descriptions in the literature. We present the case of a woman with cervical cancer FIGO IVA, treated with curative intention, who developed dysphonia and dysphagia; she received external beam radiation therapy. Months later, she developed paraaortic node progression and severe dysphagia, resulting in a tracheoesophageal fistula, which caused aspiration pneumonia, sepsis, and death. Infrequent metastatic sites should be taken into account in the workup and treatment of systemic progression of cervical cancer. Proper treatment leads to clinic relief and impacts on quality of life.

Keywords: *Cervical. Cancer. Radiation. Therapy. Case report.*

Insuficiencia respiratoria y fístula traqueoesofágica debido a metástasis mediastina de cáncer de cérvix: reporte de caso

Resumen

El cancer de cérvix es relativamente frecuente en Perú y el mundo. Las metástasis mediastinales son una rara ocurrencia, poco descrita en la literatura. Se presenta el caso de una paciente con cáncer de cérvix IVA, tratada curativamente, que luego desarrolló disfonía y disfagia. Recibió radioterapia externa, con mejoría; luego presentó progresión paraaórtica, disfagia grave, desarrollando una fístula traqueoesofágica, neumonía por aspiración y muerte. Sitios infrecuentes de progresión deben de ser tomados en cuenta en el diagnóstico y la conducta terapeútica de la progresión sistémica del cáncer de cérvix. El tratamiento adecuado brinda alivio sintomático y calidad de vida.

Palabras clave: *Cáncer. Cérvix. Radioterapia. Terapia. Reporte de caso.*

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Introduction

Cervical cancer is the 2nd tumor site in incidence in Perú, and the fifth in the world, with 13.3 cases × 100000 women[1]. Most of those deaths happen in developing countries, where it is usual to find locally advanced or metastatic disease, the latter being easier to develop despite proper treatment.

In the setting of systemic progression in cervical cancer, mediastinal metastasis is a rare occurrence, with an airway obstruction due to it. We present the case of a 43-year-old woman, with clinical stage IVA cervical cancer, who received radiation therapy and posterior chemotherapy with complete response, showing later thoracic progression, with a mediastinum mass compressing the right bronchus, narrowing its lumen. She was treated with radiation therapy, showing improvement. Sometime later she developed dysphagia, tracheoesophageal fistula, and aspiration pneumonia, which caused her death.

Case description

A 43-year-old woman presented with pelvic pain and vaginal blood discharge in February 2022. She had a history of two pregnancies, one miscarriage, and one liveborn by a cesarean section 9 years ago; she did not mention any history of cancer in the family, and she never did a Pap smear. A biopsy from the cervix showed squamous cell carcinoma, with a computed tomography (CT) scan showing a mediastinal lymph node of 14 × 6 mm, probably reactive. It also showed a cervical neoplasm measuring 52 mm in diameter, with vaginal extension (thickened anterior wall up to 17 mm) and partial loss of interphase with bladder and rectum. There were pelvic suspicious nodes. On pelvic examination, there was a tumor of 5 cm diameter, with parametrial and rectal invasion, and an inguinal node. Cytology was obtained for this node; she received chemotherapy for the first instance (carboplatin-paclitaxel) for four cycles (from March 2022 to June 2022) not being able to receive radiation therapy at the moment. The cytology from the inguinal node showed no malignancy. A pelvic magnetic resonance imaging, although deemed necessary, was not performed, as our institution lacked that technology at the time. Regardless of that, it was possible to stage the patient FIGO IVA, with an estimated 5-year survival of 15%. She started radiation therapy treatment in July 2022, receiving 39 Gy/13Fx plus weekly cisplatin 4 times finishing it, with 2nd degree of gastrointestinal toxicity according to common terminology criteria for adverse events, and no pain or bleeding. After treatment completion, a pelvic examination revealed infiltration to the upper third of the vagina, a small cervix with mild stiffness, and both parametria infiltrated left side to the external third and right side to the internal third. A pelvic ultrasound was performed which showed a complete response from lymph nodes. The patient received three high-dose-rate brachytherapy applications of 8 Gy each. A point dose A of 78.25 Gy was reached, with 64.3 Gy to the point bladder and 54.56 Gy to the point rectum. One month later pelvic examination revealed cervix with absence of neoplasm, both parametria free. Patients with clinical complete response started periodic controls with no disease for 9 months, returning with a bloody cough, and mild dysphonia. A CT scan of June 2023 showed a moderately suspicious mediastinal lymph node measuring 10 × 14 mm (Fig. 1). Another CT scan later that month showed a mass which encircles the carina and main right bronchium of 12 × 45 mm, it contacts the esophagus, seeming to lose its transition with it (Fig. 2); palliative external beam radiation therapy (EBRT) was prescribed. She received 39 Gy/13 Fx in August 2023 with 3D planning (Figs. 3 and 4), presenting 2nd degree emesis, and asthenia. Two months after treatment, the patient showed clinical improvement in respiratory failure but still with dysphonia. She referred at that time to feeling relieved of not feeling shortness of breath, and worried for the persistent dysphonia. A CT scan on October 2023 showed a 40% reduction of the mediastinal mass (18 × 11 mm) with necrosis in its center, involving the right main bronchium. There were retroperitoneal lymph nodes up to 18 × 12 mm EBRT initiated to paraaortic nodes, 45.9 Gy/27 Fx, from November 2023 to December 23. Upon EBRT completion, she complained of dysphagia. An X-ray scan on January 2024 showed middle-third esophageal stenosis. A CT scan later that month showed esophagus stenosis in a length of 33 mm and 15 mm diameter, some calcifications on upper esophagus walls, and no other findings. An esophagogastroduodenoscopy (EGD) was performed on January 26, 2024, showing stenosis at 30 cm. It was intended for her to start chemotherapy, but on February 2024 the patient presented to the emergency room, complaining of a 3-day cough, fever, and dyspnea. The EGD was repeated, showing a solution of continuity, beyond that there were three ways, to stop the procedure. With a diagnosis of tracheoesophagical fistula from the infiltrative process, she was admitted to oncology, with a CT scan which showed the same findings (Fig. 5), a gastrostomy was

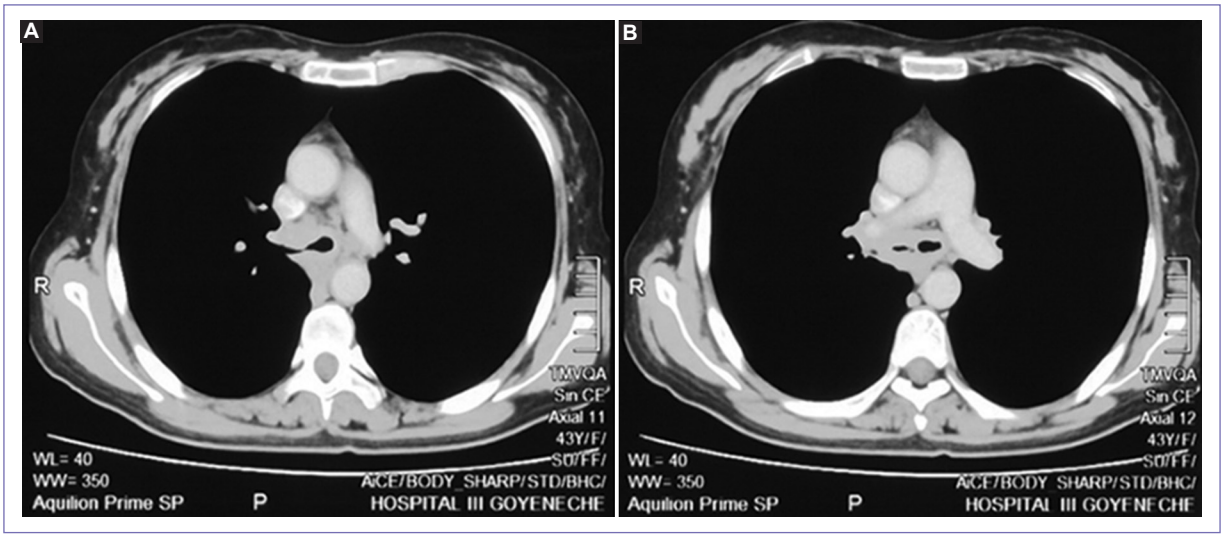

Figure 1. Chest computed tomography scan shows mediastinal lymph node, already encircling the right main bronchium, narrowing its lumen **A**: at the right pulmonary artery and **B**: at the pulmonary trunk.

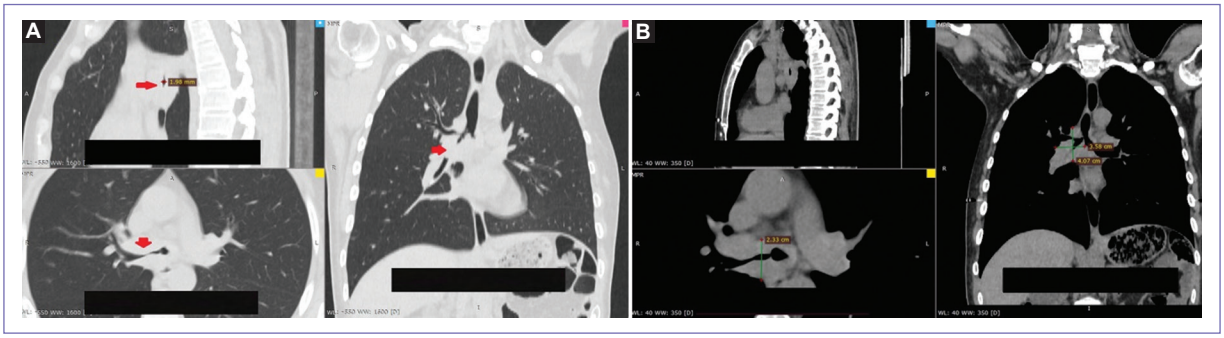

Figure 2. Chest computed tomography scan shows in axial, sagittal, and coronal views, mediastinal mass encircling the right main bronchium, narrowing its lumen, in contact with esophagus losing interphase with esophageal wall in **A**: pulmonary and **B**: mediastinal windows.

performed, and antibiotic therapy was initiated but despite that, the patient's condition got worse, and she died 2 weeks later.

Discussion

As medical science advances, treatments offering better chances of survival are given, and thus, the disease's natural history is modified. Hence, we start to see atypical, infrequent disease courses, such as rare metastatic sites. Mediastinal lymph metastasis occur in 1% of cervical cancer cases[2], with other sites such as lung and liver being much more frequent.

In a study, 137 patients from 2001 to 2013 from the University of Tokyo were assessed; 40% developed recurrence or progression, and only 5.1% of the total cohort developed lupus nephritis progression and were in common iliac, internal iliac, and obturator sites[3]. It is clear that mediastinal metastatic lymph nodes are a rare occurrence and are not in the scope of view of the physician in charge of controls post-treatment, until a distinctive symptom, such as cough, dysphagia, dysphonia, etc., makes them turn their heads.

In the assessment of mediastinal disease, positron emission tomography-CT (PET-CT) has shown a good performance in detecting recurrence or metastases in lymph nodes, irrespective of their size, but also with the presence of false negatives, and positives; the latter are frequent occurrence in mediastinum[4]. In CT, mediastinal nodes are a common occurrence, even in patients

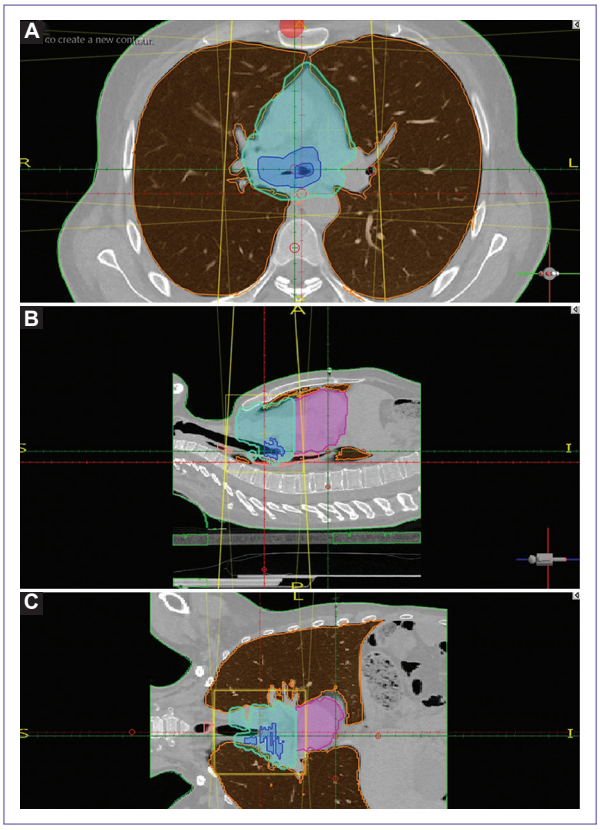

Figure 3. Radiation therapy planning – contouring in **A**: axial, **B**: sagittal, and **C**: coronal views.

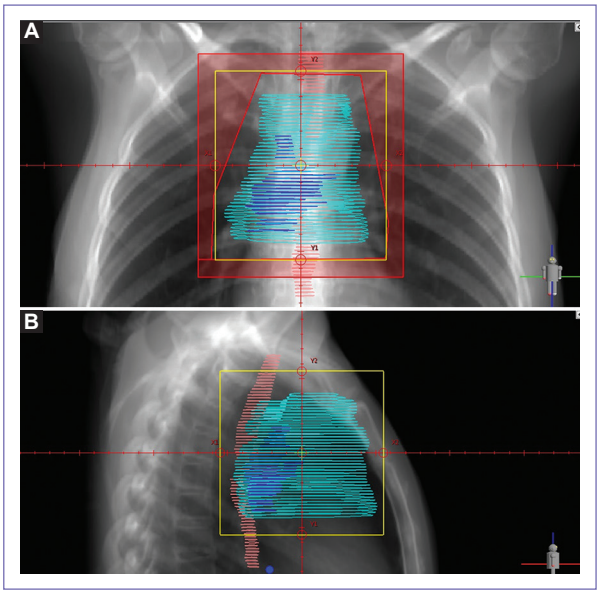

Figure 4. Radiation therapy- digitally reconstructed radiograph of **A**: anterior and **B**: right lateral fields.

without malignancy, making it a challenge to discern between a reactive lymph node and a malignant one; mediastinoscopy can be used as a tool to collect biopsies and obtain histological confirmation. Sometimes, the diagnosis is made for markers, such as Ca125[5] or squamous cell carcinoma (SCC). In a 2004 study[6], it was shown that the addition of PET-CT to a 2 times positive SCC-antigen test helped to determine which patients had a real recurrence, but in two cases, a false positive from mediastinal lymph nodes (due to anthracosis) was present. Sometimes, it is difficult to establish the diagnosis of mediastinal progression, not only by the rarity of but for the false positives. False negatives are present too; in a study of 2014[7], patients with a PET-CT positive recurrence went to a CT-guided biopsy that showed no neoplasm, and was only when an echoendoscopic guided biopsy was performed, that the diagnosis was made. It emphasizes an important point in the workup: surgical evaluation is required, as PET-CT can show up to 75% of false negatives[8].

The chances of treatment and subsequent secondary effects are described in the literature. In one study, patients with oligometastatic disease received definitive radiation therapy, and radiation therapy (RT) to their metastatic sites; of 41 patients, 10 (12%) were mediastinal metastases, which received a dose above 50.4 Gy (median biologic effective dose [BED] 72 Gy-59 to 81 Gy range-), which was well tolerated[9]. In the case of our patient, she presented with a frail state, and a hipofractionation with a BED 50.7 Gy was delivered, which improved her clinical condition. Some studies showed that definitive irradiation in gynecological cancers[9,10] led to a disease-free survival of up to 50%. Chemotherapy is used too, alone[11], or concurrent with RT.

Tracheoesophageal fistula is a complication that is described in the literature, in the setting of irradiation for lung or esophageal cancer; the use of bevacizumab seems to increase its frequency. No biopsy was obtained from the fistula site, although there was a UDE performed, based on the frail state of the patient. The outcome could have been due to the dose, which allowed to palliate symptoms but not enough to eradicate the tumor, or due to complete response and subsequent destruction of fragile scar tissue, as seen in other cases[12].

Conclusion

This case illustrates the need for communication of rare occurrences, to establish more effective therapeutic approaches. It also points out that patients with

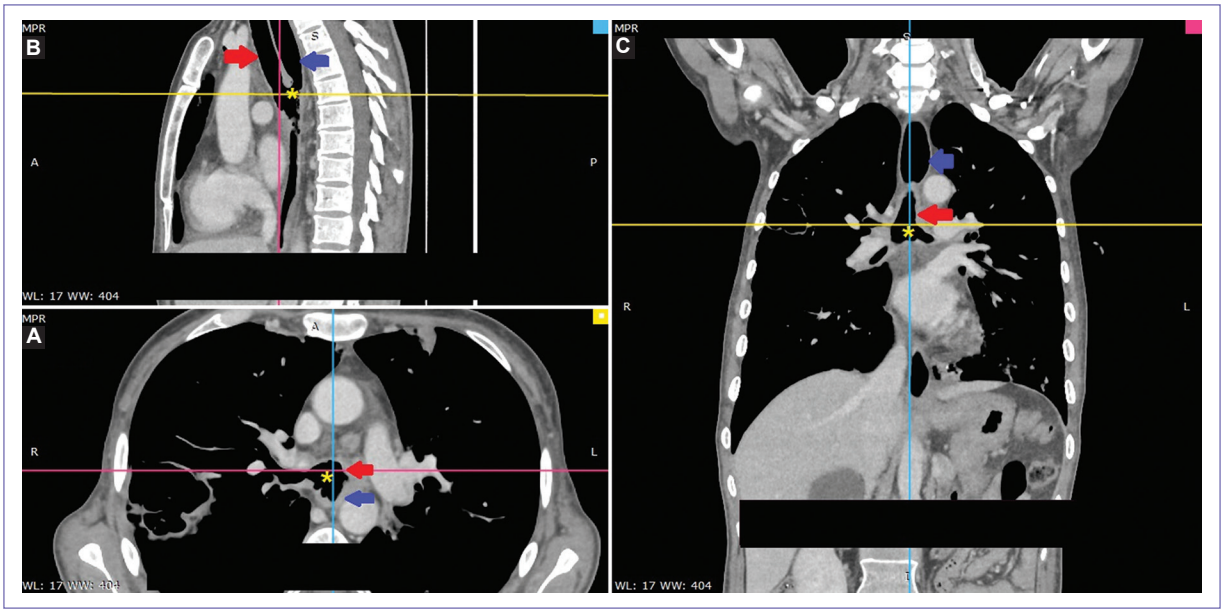

Figure 5. Chest computed tomography scan shows fistula in **A**: axial, **B**: sagittal, and **C**: coronal views, showing tracheoesophageal fistula (*), trachea (red arrow), and esophagus (blue arrow).

mediastinal metastases should be closely watched, before, during, and after the treatment.

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Conflicts of interest

The author declares having no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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