Anatomical analysis of distant lymph node metastasis from cancer of the uterine cervix: a case report and literature review

Mei Kang\(^1\), Liyang Zhu\(^1\), Yichun Wang\(^1\)

\(^1\)Department of Radiation Oncology, the First Affiliated Hospital of Anhui Medical University, No.218, Jixi Road, Hefei, 230022, Anhu, P. R. China

Summary

Lymph node metastasis (LNM) beyond the pelvis and paraaortic region is unusual for the uterine cervix cancer (CC). The mechanism of these distant lymph node metastasis is not clearly understood. We reported a case of cervix cancer with extensive distant lymph node metastasis, including in the inguinal region, celiac region, mediastinal region, bilateral lower neck and supraclavicular regions. The literature was reviewed and possible anatomical mechanism was analyzed. Retrograde lymphatic drainage through many routes may explain these distant lymph node metastasis. Except the insufficient valves of lateral branches of thoracic duct, the blockage and compression of the lymphatic vessels or thoracic duct may be reasons for the retrograde lymphatic drainage. However, the lymphatics are complex and variable between individuals. Further studies need to confirm these results.

Key words: Cervical cancer; Lymph nodes; Recurrence; Anatomy; Rhemoradiotherapy.

Introduction

Pelvic lymph node metastasis (LNM), which is an important prognostic factor [1], can be identified for some advanced cervix cancer (CC). The LNM beyond the pelvis is more likely to extend to the paraaortic and left supraclavicular regions. Many researchers reported mediastinal LNM from CC in a low incidence [2-4]. However, LNM elsewhere is rare. Patients with distant LNM are generally difficult to treat and associated with poor prognosis. Understanding the development of these diseases will provide better treatment for patients. However, the mechanism of distant LNM from CC is not clearly understood. In this study, we reported a patient of CC with extensive distant LNM, reviewed the literature to analyze the anatomical lymphatic drainage of these distant LNM.

Case Report

A 56-year-old woman was hospitalized in Dec 2017 with an irregular vaginal bleeding for more than one month. Gynecological examination revealed cauliflower-like neoplasm in her cervix and histopathological examination confirmed that it was a poorly differentiated squamous cell cancer. Pelvic and abdominal enhanced magnetic resonance images (MRI) was performed and the result showed the presence of a large mass in the uterine cervix involving the lower uterus body and the upper third of vagina, enlarged LNs near bilateral iliac blood vessels and in the retroperitoneal region (Figure 1). No evidence of metastasis in the supraclavicular region and thorax was noted on computed tomography (CT) images (Figure 2A). She was finally diagnosed with stage IIC2 CC according to the 2018 version staging system of FIGO.

After diagnosis, she received CRT. The treatment regimen was given as follow: External beam radiation therapy (EBRT) was delivered to the whole pelvis and paraaortic region, which encompassed the primary mass, entire uterus, vagina, paracervical, parametrial, and pelvic LNs, as well as paraaortic LNs. The total dose of EBRT was 50.4 Gy, consisting of 1.8 Gy fractions once day for 4-5 days per week. 192Ir High-dose-rate intra-cavitary irradiation was started after 15 days of EBRT was done and the total dose was 30 Gy, consisting of 6 Gy fractions once week for 5 weeks. The first cycle of chemotherapy using docetaxel 120 mg day1 plus cisplatinum (DDP) 30 mg day 1-4 was given 3 weeks before radiotherapy and only one cycle of the same chemotherapy regimen was concurrently carried out with radiotherapy due to the poor condition during the late course of radiotherapy. Three cycles of adjuvant chemotherapy using paclitaxel liposome 240 mg day1 plus DDP 20 mg day1-5 for every 4 weeks were performed after radiotherapy. The last cycle was finished at June 2018. CT images revealed suspicious LNM in the mediastinal region for the reexaminations at July 2018 (Figure 2B). This patient refused further examination and anti-tumor therapy. He returned to our hospital until Nov 2018 because of masses of her neck. MRI showed no evidence of tumor in the pelvis (Figure 3A), enlarged LNs behind head of the pancreas, around the celiac trunk, in the hepatogastric ligament, at the root of left gastric artery, and in the left groin (Figure 3B and 3C). Extensive mediastinal enlarged LNs were noted on CT images (Figure 2B and 2C). Multiple enlarged LNs were visible on MRI of the neck (Figure 3D). A right supraclavicular LN and an inguinal LN were confirmed as squamous cell cancer by cytology. There was no evidence of hematological metastasis in the neck, thorax, abdomen, and pelvis on CT images and MRI. She was proposed for systematic anti-tumor therapy and palliative radiotherapy. After radiotherapy with a total dose of 20Gy for 10 fractions, she gave up further treatment and died 3 months later.

Discussion

LNM is a key step for metastasis of CC. Previous studies revealed that the sentinel nodes were located in the pelvis, includ-
Figure 1. — Pelvic and abdominal MRI showed the neoplasm in cervix and the enlarged LNs before CRT (Dec 2017). A: Neoplasm in the cervix on the sagittal T₁-weighted enhancement image (red arrow); B Neoplasm in the cervix on the diffusion-weighted image (DWI) (red arrow); C and D: Pelvic enlarged LNs on DWI (blue arrows); E and F: Paraortic enlarged LNs on T₂-weighted images (blue arrows).

Figure 2. — Changes in the mediastinal regions before and after CRT on CT images. A: There were no evidence of metastasis before CRT (Dec 2017); B: Soft tissue shadows (blue arrows) were noted for the 1st reexamination after CRT (July 2018). C: Enlarged LNs (blue arrows) with increased sizes compared to the 1st reexamination in the right supraclavicular, right paratracheal, subcarinal, prevascular regions were noted after CRT (Nov 2018).
Figure 3. — Recurrence in the neck, abdomen and groin was shown on MRI after CRT (Nov 2018). A: Neoplasm in the cervix and enlarged LNs completely disappeared (T₁-weighted enhancement images); B and C: Enlarged LNs (blue arrows) in the inguinal, paraaortic and celiac regions on T₂-weighted images and DWI; D: Enlarged LNs in the neck and supraclavicular regions on T₂-weighted images. Pentagram indicated a possible cystadenoma in the right thyroid.

We found LNM in the left supraclavicular region occasionally for more advanced CC. Virchow’s nodes can explain this route of metastasis [9]. As shown in Figure 4B, the left supraclavicular LNs have communications with the terminal tributaries of TD [8, 10]. The retrograde lymphatic from TD can explain the left supraclavicular LNM. The terminal TD has many variations [8]. Sometimes it merges with the jugular lymph trunk and subclavian lymph trunk before emptying to the venous system. As a result, the retrograde lymphatic from TD to these trunks is also possible. LNM in the right supraclavicular region from CC is rare because of the absent of direct drainage and far retrograde lymphatic drainage from TD. There may be 3 routes, as shown in Figure 4B. First, the upward lymphatic drainage from mediastinum can reach to the bilateral supraclavicular LNs. Second, there are communications between the right and left cervical lymphatic plexus [10]. Third, hematological metastasis to the head and neck may cause LNM theoretically. For this patient, the right supraclavicular LNM were likely caused by the right upward paratracheal lymphatic drainage system according to the changes on CT images (Figure 2). Though it is uncommon, however, the TD connects to the right venous angle also exits [8].

Mediastinal LNM is uncommon for CC because the anterograde lymphatic drainage passes through the thorax by TD (Figure 3A). However, many researchers reported it usually at the hilar or upper mediastinal regions from CC or prostate cancer [2-4,
Figure 4. — Lymphatic drainage routes for CC. Red arrows indicate anterograde lymphatic drainage while blue arrows indicate retrograde lymphatic drainage. Ao aortic, Dia diaphragm, Eso esophagus, IVC inferior vena cava, L left, Lu lung, R right, SVC superior vena cava, TD thoracic duct, Tr trachea. A: The anterograde lymphatic drainage. Regional lymph nodes are in the box for CC. B: The retrograde lymphatic drainage near bilateral venous angels. C: The retrograde lymphatic drainage near the root of the thoracic duct. D: The mediastinal retrograde lymphatic drainage and anterograde lymphatic drainage from thoracic hematological metastases (black arrows).

11, 12. The intrathoracic lymphatic drainage for CC is complex and not well understood. There may be many routes, as shown in Figure 4C and 4D. First, at the root of TD, there are some tributaries connected to the lower mediastinal lymphatics (i.e. the pulmonary ligament lymphatic plexus) through the diaphragmatic aortic hiatus or esophageal hiatus (Figure 4C) [13-15]. As a result, the retrograde mediastinal LNM is possible through these tributaries. What is more, these lymphatic plexus can relay with the intraabdominal LNs before joining to the TD [14]. This may be a major reason for the retrograde LNM from thoracic cancers and should explain the celiac LNM for this patient. Second, the intrathoracic tributaries of TD can communicate with thoracic organs (lung, esophagus, heart, etc.) and thoracic LNs (subcarinal LNs, paracheal LNs, main bronchus LNs, and paratracheal LNs, etc.) [16, 17]. The insufficient valves of lateral branches of TD or the change of the liquid pressures in the TD may lead to mediastinal LNM from CC, as shown in Figure 4D. Third, the hematological metastasis of thoracic organs (lung, pleura, thoracic wall, etc.) from CC may also lead to mediastinal LNM (Figure 4D). For our patient, the hematological metastasis was not found on CT images and MRI. Therefore, the mediastinal LNM should be caused by the former two routes. The phrenic lymphatic chain in the anterior mediastinum can also communicate with lymphatic vessels near the venous angle. This route should be another reason for retrograde LNM in the anterior mediastinum (Figure 4B) [10].

The inguinal LNs usually receive lymphatic drainage from the lower limb, lower abdominal wall, groin, penile, vulvar, and anus [18, 19]. Inguinal LNM can be found for CC involving the lower third of the vagina or perineum while it is uncommon for other CC [20]. Our patient had a left superficial inguinal LNM (Figure 3B and 3C) which may be also caused by the retrograde lymphatic flow. After CRT, disorder of lymphatic drainage is common for CC.

Conclusions

The retrograde lymphatic drainage through many routes may explain these distant LNM for this patient. Though the insufficient valves of lateral branches of TD may be a reason for the retrograde lymphatic drainage, they were uncommon. For this patient with extensive distant LNM, many other reasons should be considered. For example, the blockage and compression of the lymphatic vessels or TD may lead to retrograde lymphatic drainage because of the change of fluid pressure. Additionally, the anatomy of the lymphatics is complex and variable among people. We need further studies to clarify these results.

Abbreviations

CC: cervical cancer; CRT: chemoradiotherapy; CT: computed tomography; DDP: cisplatinum; EBRT: external beam radiation therapy; FIGO: the Federation of Gynecology and obstetrics; IMRT: intensity modified radiation therapy; LNM: lymph node metastases; LNs: lymph nodes; MRI: magnetic resonance images; TD: thoracic duct.

Authors’ contributions

LYZ and MK collected the data and wrote the manuscript. YCW designed the idea, interpreted data, draw the pictures and revised the manuscript. All authors read and approved the manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.
Availability of data and materials

The datasets used during the current study available from the corresponding author on reasonable request.

Acknowledgments

The authors would like to thank the patient’s family for giving consent.

Conflict of interest

The authors have stated that they have no conflict of interest.

Submitted: August 10, 2019
Accepted: October 30, 2019
Published: December 15, 2020

References

[1] Brotons M.L., Bolca C., Freechette E., Deslauriers J.: “Anatomy and physiology of the thoracic lymphatic system”. Thorac. Surg. Clin., 2012, 22, 139.
[2] Cesmebasi A., Baker A., Du Plessis M., Matusz P., Shane Tubbs R., Loukas M.; “The surgical anatomy of the inguinal lymphatics”. The American Surgeon., 2015, 81, 365.
[3] Chaddha U., Patil P.D., English R., Panchabhai T.S.; “An unusual presentation of cervical carcinoma metastasis as mediastinal adenopathy”. J. Bronchology. Interv. Pulmonol., 2017, 24, 61.
[4] Chausse G., Niaz T., Abikhzer G.S., Probst S.M.; “Biopsy-proven diffuse mediastinal prostate cancer metastases negative on 18F-Fluorocholine, diagnosed on 18F-Ga-PSMA and 18F-PSMA PET/CT”. Clin. Nucl. Med., 2017, 42, 801.
[5] Cheng-Yen Lai J., Lai K.J., Yi-Yung Yu E., Hung S.T., Chu C.Y., Wang K.L.; “Sentinel lymphatic mapping among women with early-stage cervical cancer: A systematic review”. Taiwan. J. Obstet. Gynecol., 2018, 57, 636.
[6] de Foucher T., Bendifallah S., Ouldamer L., Bricou A., Lavoue V., Varinot J., et al.; “Patterns of recurrence and prognosis in locally advanced FIGO stage IB2 to IIB cervical cancer: Retrospective multi-centre study from the FRANCOGYN group”. Eur. J. Surg. Oncol., 2019, 45, 659.
[7] Fagundes H., Perez C.A., Grigsby P.W., Lockett M.A.; “Distant metastases after irradiation alone in carcinoma of the uterine cervix”. Int. J. Radiat. Oncol. Biol. Phys., 1992, 24, 197.
[8] Hematti H., Mehran R.J.; “Anatomy of the thoracic duct”. Thorac. Surg. Clin., 2011, 21, 229.
[9] Kim H.S., Kim T., Lee E.S., Kim H.J., Chung H.H., Kim J.W., et al.; “Impact of Chemoradiation on Prognosis in Stage IVB Cervical Cancer with Distant Lymphatic Metastasis”. Cancer Res. Treat., 2013, 45, 193.
[10] Kim J.Y., Kim J.Y., Kim J.H., Yoon M.S., Kim J., Kim Y.S.; “Curative chemoradiotherapy in patients with stage IVB cervical cancer presenting with paraaortic and left supraclavicular lymph node metastases”. Int. J. Radiat. Oncol. Biol. Phys., 2012, 84, 741.
[11] Liu B., Gao S., Li S.; “A comprehensive comparison of CT, MRI, positron emission tomography or positron emission tomography/CT, and diffusion weighted imaging-MRI for detecting the lymph nodes metastases in patients with cervical cancer: A meta-analysis based on 67 studies”. Gynecol. Obstet. Invest., 2017, 82, 209.
[12] Mizutani M., Nawata S Fau - Hirai I, Hirai I Fau - Murakami G, Murakami G Fau - Kimura W, Kimura W.; “Anatomy and histology of Virchow’s node”. Anat. Sc. Int., 2005, 80, 193.
[13] Murakami G., Sato T., Takiguchi T.; “Topographical anatomy of the bronchomediatinal lymph vessels: Their relationships and formation of the collecting trunks”. Arch. Histol. Cytol., 1990, 53, 219.
[14] Ning M.S., Ahobila V., Jhingran A., Stecklein S.R., Frumovitz M., Schmeler K.M., et al.; “Outcomes and patterns of relapse after definitive radiation therapy for oligometastatic cervical cancer”. Gynecol. Oncol., 2018, 148,132.
[15] O’Boyle J.D., Coleman R.L., Bernstein S.G., Lifshitz S., Muller C.Y., Miller D.S.; “Intraoperative lymphatic mapping in cervix cancer patients undergoing radical hysterectomy: A pilot study”. Gynecol. Oncol., 2000, 79, 238.
[16] Pinaquy J.B., Fernandez P., Fau - Pasticier G., Pasticier G., Fau - Parrens M., Parrens M., et al.; “mimicking mediastinal lymph node metastases with 18F-FCholine in high-risk prostate cancer”. Clin. Nucl. Med., 2015, 40, 253.
[17] Riquet M.; “Anatomic basis of lymphatic spread from carcinoma of the lung to the mediastinum: surgical and prognostic implications”. Surg. Radiol. Anat., 1993, 15, 271.
[18] Riquet M.; “Bronchial arteries and lymphatics of the lung”. Thorac. Surg. Clin., 2007, 17, 619.
[19] Riquet M., Le Pimpec Barthes F., Souilamas R., Hidden G.; “Thoracic duct tributaries from intrathoracic organs”. Ann. Thorac. Surg., 2002, 73, 892.
[20] Scaglioni M.F., Suami H.; “Lymphatic anatomy of the inguinal lymphatic drainage”. Ann. Plast. Surg., 1995, 30, 724.
[21] Skandalakis J.E., Skandalakis L.J., Skandalakis P.N.; “Anatomy of the lymphatics”. Surg. Oncol. Clin. N. Am., 2007, 16, 1.
[22] Wang Y., Zhu L., Xia W., Wang F.; “Anatomy of lymphatic drainage of the esophagus and lymph node metastasis of thoracic esophageal cancer”. Cancer Management and Research., 2018, 10, 6295.

Corresponding Author:
YICHUN WANG, M.D.
Department of Radiation Oncology,
the First Affiliated Hospital of Anhui Medical University,
No.218, Jixi Road, Hefei, 230022, Anhui (China).
E-mail: wangechun321@sina.com.