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CASE REPORT

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"Cheerios in the lung" as first metastases from endometrial endometrioid adenocarcinoma with adequate response to immunotherapy

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Abstract

Background Metastases from endometrial carcinoma to the lungs are uncommon and cavitating metastases are even rarer. In some cases, lung cavitating metastases may resemble diffuse "Cheerios in the lung."

Case presentation A 58-year-old woman, smoker, with a history of hysteroannessiectomy and pelvic lymphadenectomy for a low stage endometrial endometrioid adenocarcinoma, came under our attention for dry cough without fever that persisted for over three months, and computed tomography (CT) revealed diffuse cavitating lung metastases resembling "Cheerios in the lung".

After standard chemotherapy proved ineffective, Lenvatinib plus Pembrolizumab (immunotherapy) was administrated, leading to the disappearance of all lung nodules, leaving behind a diffuse emphysematous-like pattern.

Conclusions This case is a rare example of metastatic endometrioid adenocarcinoma, manifested with chronic dry cough, with "Cheerios in the lung" appearence. The metastases responded well to immunotherapy, resulting in the regression of nodules into areas of diffuse emphysematous-like changes.

Keywords Lung metastases, Endometrial endometrioid adenocarcinoma, Immunotherapy

Background

Endometrial carcinoma is the most commonly occurring gynecologic cancer in high-income countries. While most patients have the disease confined to the uterus with a favorable prognosis, 13% of all endometrial cancers experience recurrence, with 68%–100% occurring within three years. The typical metastatic sites include local pelvic recurrence, pelvic and para-aortic nodules, peritoneum, and lungs [1]. Lungs metastases from endometrium carcinoma are usually manifest as multiple small nodules [2, 3]. Additionally, cavitation of lung metastases is a rare occurrence [3–5], more commonly found in cervical cancer [2].

Case presentation

A 58-year-old woman, smoker, with a history of hysteroannessiectomy and pelvic lymphadenectomy (2 years earlier) for an endometrial endometrioid adenocarcinoma (FIGO stage Ia) come under our attention for dry cough without fever for over three months. She denied dyspnea, chest pain, or palpitations. She was in follow-up with tumoral biomarkers (CEA, CA 125, CA 19.9),

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that were in normal ranges. A chest X-ray shows a diffuse pattern of pulmonary nodules (Fig. 1). A CT scan showed diffuse multiple nodules with a random distribution, ranging from 2 to 10 millimeters, most with a central hyperlucency and thin-walled, resembling the aspect of "Cheerios in the lung" (Fig. 2). The lymph nodes in the mediastinum were normal in size. Non-infectious agents (including fungi or mycobacteria) or cancer cells were found in the bronchial lavage. Therefore, a surgical biopsy was performed with a wedge resection of the right upper lobe. The histologic analysis of the specimen revealed a proliferation of confluent, back-to-back glands, lacking intervening stroma cytologically similar to proliferative endometrium. The neoplastic cells tested positive for estrogen receptor (ER) in 100%; PAX8 and TTF-1 were positive and negative, respectively (Fig. 3). Immunohistochemistry confirmed microsatellite stability for mismatch repair (MLH1, MSH2, MSH6, and PMS2). Hence, the diagnosis of metastases from endometrial endometrioid adenocarcinoma was made.

Fig. 1 AP chest X-ray shows a diffuse pattern of pulmonary nodules

The first treatment she received involved cycles of Carboplatin and Paclitaxel. However, a follow-up CT scan revealed four new abdominal nodules near the left iliumpsoas muscle, indicating peritoneal carcinosis, as confirmed by the PET-CT. After a multidisciplinary meeting, the therapy changed to Docetaxel and then Doxorubicin.

Lastly, a follow-up CT scan revealed increased abdominal nodules dimension; the lung nodules were described as stable. The therapy was switched to Lenvatinib plus Pembrolizumab.

After six months of immunotherapy, a total body CT scan showed a complete regression of lung nodules, replaced by a diffuse emphysematous-like pattern (Fig. 4). A decrease in the size of abdominal nodules was also observed.

Conclusion

Lung metastases from endometrial carcinoma in a large cohort of patients were described in 2-3 % of cases [6] and usually manifested as small bilateral solid nodules [2, 3], often with an intra-abdominal involvement [2]. Less commonly, metastases may be single or involve the pleura [2, 3]. Endobronchial involvement or lymphangitic spread is uncommon, and cavitation is infrequent [3–5].

The "Cheerio sign" describes a radiographic observation of multiple bilateral pulmonary nodules with central hyperlucency, resembling breakfast Cheerio cereals distributed along the small airways. Pathologically, it is defined by the proliferation of malignant or non-malignant cells around the bronchioles. Malignant conditions that can exhibit this sign include primary lung adenocarcinoma, metastatic adenocarcinoma, sarcoma, squamous cell carcinoma, and lymphoma. Non-malignant conditions include pulmonary Langerhans cell histiocytosis, lymphangioleiomyomatosis, fungal and mycobacterial infections, rheumatoid arthritis, and antineutrophil cytoplasmic antibody–associated vasculitis (granulomatosis

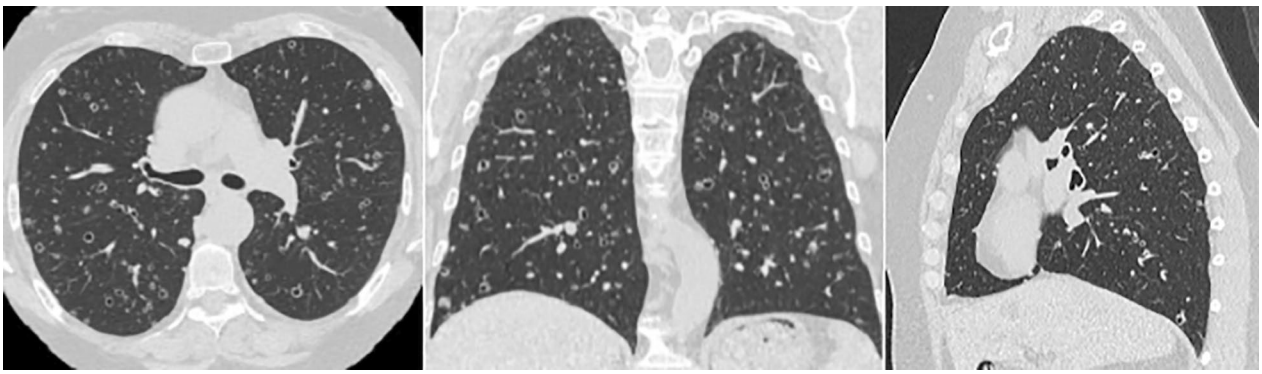

Fig. 2 First chest CT showing multiple small nodules with a random distribution; most are cavitated

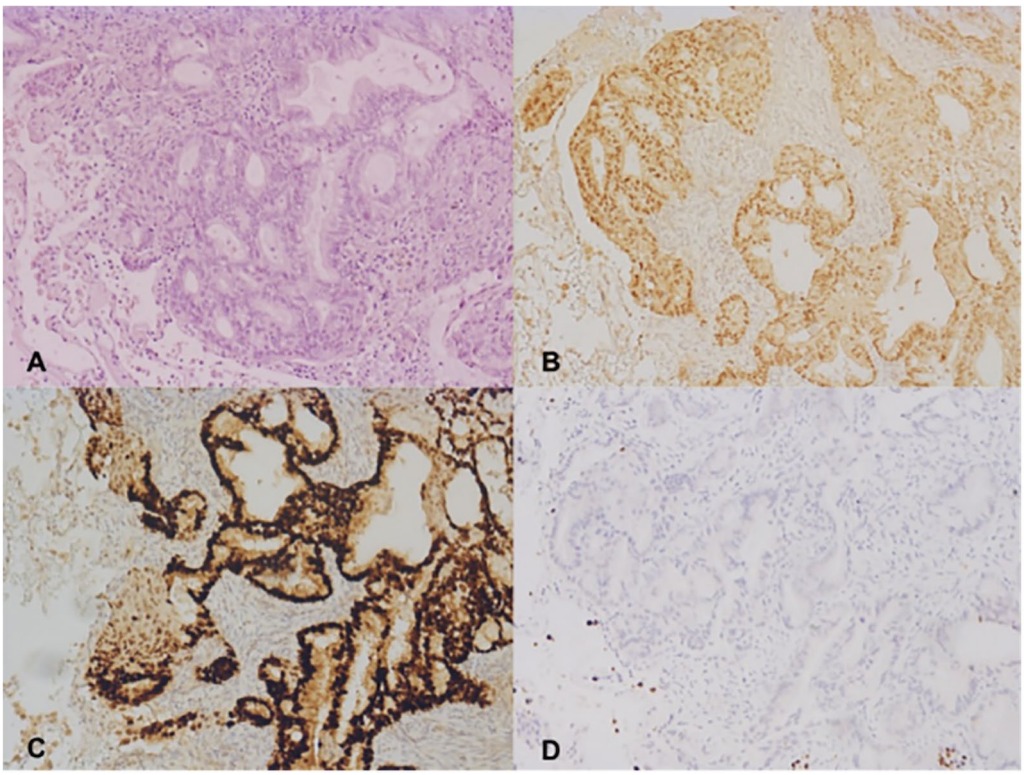

Fig. 3 Histologic findings: back-to-back glands resembling proliferative type endometrium (Hematoxylin-Eosin, magnification 10x) (**A**). Immunostain for PAX 8 (**B**), ER (**C**) and TTF1 (**D**)

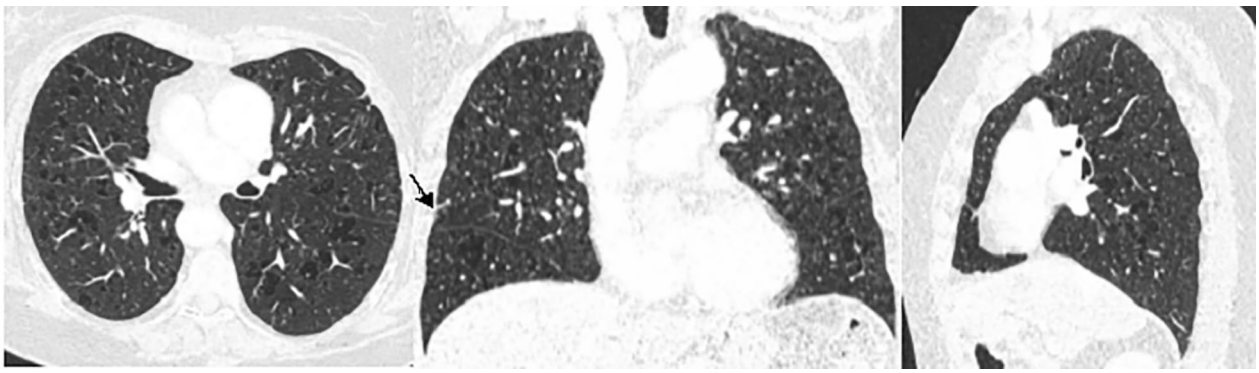

Fig. 4 Chest CT after six months of treatment with Lenvatinib plus Pembrolizumab

with polyangiitis). Very rarely, these nodules can also be due to meningothelial-like nodules [7].

Our patient, with a low-risk type I mucinous endometrial adenocarcinoma, had previously tested negative for humoral biomarkers and came to our attention due to a chronic dry cough. Chest imaging revealed diffuse cystic nodules (Fig. 2), which were randomly distributed; a random distribution is typical of hematogenous infection (i.e., fungi or tuberculosis) or metastatic spread [8]. Our patient's histological specimen revealed metastatic lesions from endometrioid, mucinous adenocarcinoma.

Lastly, following this patient, we had the chance to describe the evolution and resolution of lung nodules after therapy. Carboplatin and Paclitaxel are typically the first-line treatments for metastatic disease, but in this case, they proved to be ineffective; looking retrospectively at the whole-body follow-up CTs (2 years intervals), we noticed that the lung nodules actually had a progression over time, especially at lung bases. This confirms

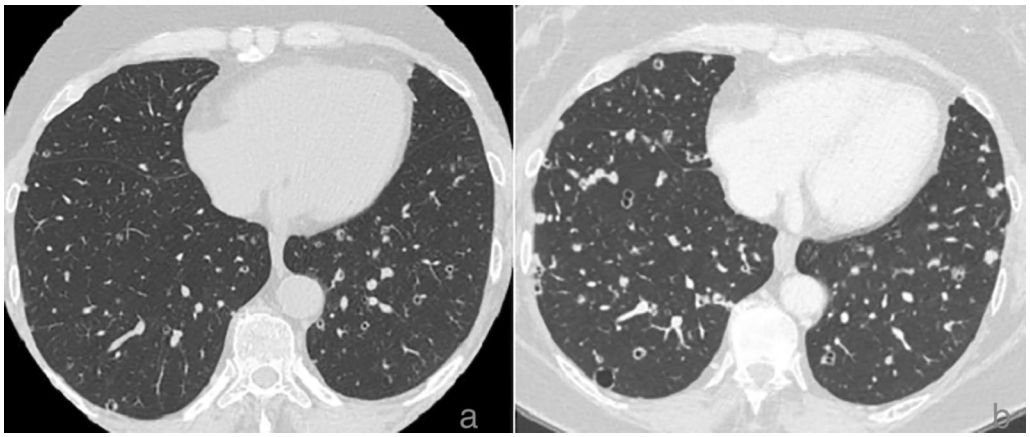

Fig. 5 First CT (**a**) and last CT (**b**), scanned before treatment with Lenvatinib plus Pembrolizumab, in comparison: a progression of lung nodules may be observed

that lung metastases must be carefully compared with previous examinations (Fig. 5), especially with indolent tumors like this. On the other hand, immunotherapy is a potential option for those with advanced endometrial cancer. Specifically, Lenvatinib plus Pembrolizumab, as second-line therapy, has shown promising [9]. In this case, the lung nodules led to a complete regression of pulmonary nodules, and we showed a reduction of abdominal nodules. Responder cavitating metastases from adenocarcinoma were described as areas of bullae, resembling emphysema [4].

Similarly, our patient's nodules disappeared, leaving emphysematous-like changes (Fig. 4). Interestingly, the patient had no smoking-related alterations on CT during metastases diagnosis. Thus, radiologists must carefully consider emphysematous lung changes as related to smoking habits in patients treated for metastatic endometrial adenocarcinoma, since they can be related to responsive metastases.

In conclusion, our case report has shown a rare metastatic endometrioid adenocarcinoma, manifested with chronic dry cough, that appeared as "Cheerios in the lung" on CT. Luckily, metastases were responsive to immunotherapy, and the nodules regressed to diffuse areas of emphysematous-like changes.

Abbreviation

CT Computed tomography

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Not Applicable.

Author contributions

All authors have contributed significantly to the content of the article. All authors analyzed and interpreted the patient data and help in writing the manuscript. All authors read and approved the final manuscript. There is no ethical problem or conflict of interest.

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Availability of data and materials

The data that support the findings of this study are available from the authors,upon reasonable request.

Declarations

Ethics approval and consent to participate

The research project was approved by the local institutional ethics committees: University of BLINDED, BLINDED, protocol number 468/2023.

Consent for publication

The patient has consented to the sharing of anonymised data.

Competing interests

The authors declare that they have no competing interests.

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