Received: 9 February 2024 | Accepted: 27 February 2024

DOI: 10.1002/rcr2.1320

CASE REPORT

Respirology Case Reports OPEN ACCESS APSR WILEY

Relapsing eosinophilic pneumonia in a patient with recurrent breast cancer receiving abemaciclib plus endocrine therapy

Hiroaki Ogata[1] | Chinami Koga[2] | Toyoshi Yanagihara[1] | Yuki Moriuchi[1] | Aimi Enokizu-Ogawa[1] | Akiko Ishimatsu[1] | Junji Otsuka[1] | Kazuhito Taguchi[1] | Atsushi Moriwaki[1] | Eriko Tokunaga[2] | Makoto Yoshida[1]

[1]Department of Respiratory Medicine, NHO Fukuoka National Hospital, Fukuoka, Japan

[2]Department of Breast Oncology, NHO Kyushu Cancer Center, Fukuoka, Japan

Correspondence
Hiroaki Ogata, Department of Respiratory Medicine, NHO Fukuoka National Hospital, 4-39-1 Yakatabaru, Minami-ku, Fukuoka 811-1394, Japan.
Email: md105020@gmail.com

Associate Editor: Arata Azuma

Abstract

This report presents the case of a 42-year-old Japanese woman with recurrent hormone receptor–positive breast cancer who developed eosinophilic pneumonia (EP) during treatment with abemaciclib combined with endocrine therapy. Seven years after a radical surgery and definite diagnosis of Stage I breast cancer, her cancer recurred with metastases to multiple organs. Initially treated with abemaciclib plus letrozole and goserelin for 3 months, she developed EP, which improved after the discontinuation of anti-cancer treatment and the administration of prednisolone. However, EP occurred again upon the reintroduction of endocrine therapy (i.e., letrozole and goserelin). It improved gradually with the suspension of endocrine therapy and the re-administration of prednisolone. This case underscores the need for further research into the prevention and management of EP in patients receiving abemaciclib with endocrine therapy for advanced breast cancer.

KEYWORDS
abemaciclib, breast cancer, eosinophilic pneumonia, goserelin, letrozole

INTRODUCTION

Breast cancer has been a global threat to human health. Endocrine therapy plays a key role in the management of hormone receptor–positive advanced or recurrent breast cancer, and it was recently updated to be used in combination with abemaciclib, the orally available cyclin-dependent kinase 4/6 inhibitor. Although clinical studies have shown good efficacy of abemaciclib with endocrine therapy, sometimes it can be seriously toxic[1]; clarification of its safety profile is highly needed.

Interstitial lung disease (ILD) is one of the most potentially serious adverse events of anti-cancer therapy. Abemaciclib has been reported to induce ILD as frequently as about 3% of the time,[1] whereas endocrine therapy is known to be less likely to cause ILD (<1%).[2] Eosinophilic pneumonia (EP) is a common subtype of ILD characterized by migratory consolidative opacities located in the upper lung zones with eosinophilia in peripheral blood and/or bronchoalveolar lavage fluid.[3] EP can be associated with abemaciclib treatment,[4] although it is considered to be relatively rare among cases of abemaciclib-induced ILD,[1] whereas there has been no reported case of EP developing during endocrine therapy. Here we present a case of EP, developed during abemaciclib plus endocrine therapy for recurrent breast cancer, that relapsed after the resumption of letrozole and goserelin.

CASE REPORT

A 42-year-old Japanese woman with a smoking history of 12 pack-years and without any medical or allergy history including asthma had been diagnosed with breast cancer and underwent a right mastectomy and axillary lymph node dissection (ductal carcinoma, pT1aN0M0, Stage I). Immunohistochemistry assay showed oestrogen-receptor (ER) positivity (95%) and progesterone-receptor (PgR) positivity (95%). Seven years after surgery, the patient was diagnosed

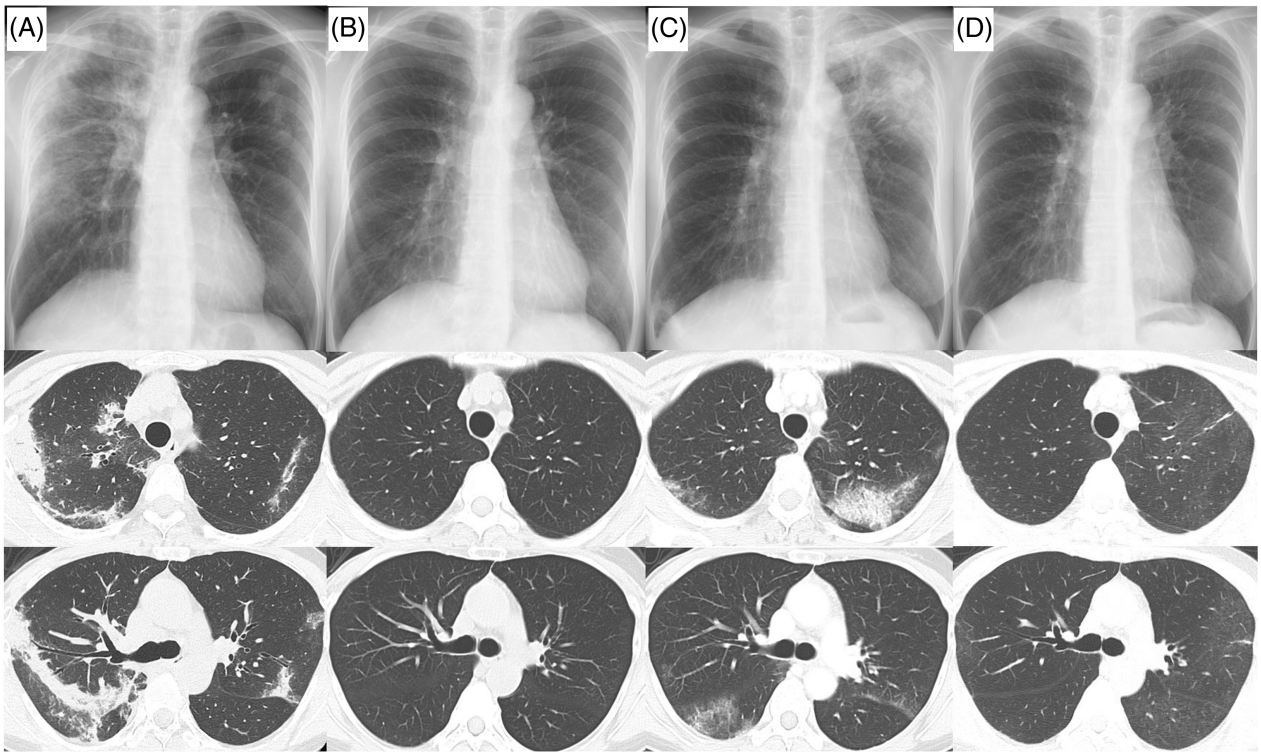

FIGURE 1 Computed tomography images of the chest (A) when developing eosinophilic pneumonia (EP) during abemaciclib combined with letrozole and goserelin treatment, (B) when EP improved, (C) during EP relapse after the discontinuation of prednisolone (PSL) and resumption of letrozole and goserelin, and (D) 2 weeks after the re-administration of PSL.

as having recurrent breast cancer with metastases to the lung, liver, bone, and lymph nodes; abemaciclib combined with letrozole and goserelin was initiated. Three months later, however, the patient developed a dry cough, dyspnea, and pyrexia. The peripheral blood test showed eosinophilia (3286/μL), and computed tomography scans of the chest revealed bilateral patchy consolidation with upper lobe dominance (Figure 1A); a working diagnosis of abemaciclib-induced EP was established. Abemaciclib together with endocrine therapy was withdrawn, and prednisolone (PSL) 50 mg per day was started; pneumonitis quickly improved (Figure 1B). PSL was tapered and discontinued over 3 months, and letrozole and goserelin were restarted. Two months after withdrawal of PSL, however, blood eosinophilia (2692/μL) and nonsegmental opacities of the lung recurred (Figure 1C). Therefore, the patient was referred to our hospital for further examination. The level of serum total immunoglobulin E was also elevated (488 IU/mL), and a pale yellow transparent bronchoalveolar lavage fluid with a markedly increased level of eosinophil fraction (94.3%) was collected through bronchoscopy. Serum anti-parasitic antibodies and myeloperoxidase-antineutrophil cytoplasmic antibodies were negative. Since letrozole and/or goserelin-induced EP was suspected, both medications were stopped, and PSL was administered again at a daily dose of 30 mg. The EP improved gradually (Figure 1D), and we are tapering PSL along with the suspension of any endocrine therapy or chemotherapy.

DISCUSSION

Drug-induced EP is the majority of secondary EP. Bartal et al. reported that most cases of EP demand not only the cessation of implicated medication but also the administration of systemic steroid treatment.[3] On the other hand, systemic steroid use over 2–3 months has been reported to result in a high cure rate and low recurrence rate of EP.[3] There has been one case report of abemaciclib-associated EP[4]; meanwhile, endocrine therapy including letrozole and goserelin has not been reported to have a risk of inducing EP. Taking these findings into account, we first speculated that the present case was abemaciclib-induced EP; however, the recurrent nature of the patient's condition did not align with the initial diagnosis, and endocrine therapy was subsequently considered as a potential causative agent for EP. To the best of our knowledge, this is the first case of abemaciclib plus endocrine therapy–associated EP, relapsed upon restarting endocrine therapy after 3 months of PSL treatment.

Although the precise pathogenesis of drug-induced EP is not elucidated, several possible mechanisms have been suggested: exaggerated immune response mediated by eosinophil-specific chemoattractant (e.g., eotaxin), direct cytotoxic injury of alveolar capillary endothelial cells by oxygen radicals, and activation of the angiotensin enzyme system.[3] Apart from cytotoxic chemotherapy drugs, endocrine therapy has never been reported to cause EP[3]; a novel

pathophysiological mechanism might have contributed in the present case.

One limitation should be noted: we cannot deny the possibility of idiopathic EP. In this case, however, the patient suffered from EP 3 months after the initiation of concomitant use of abemaciclib and endocrine therapy. Moreover, the EP relapsed after the re-administration of endocrine therapy despite the fact that EP was well treated with adequate use of PSL. Considering the clinical course, we speculate that the present case is an endocrine therapy (letrozole and/or goserelin)–induced EP, and it will be hard for the patient to try endocrine therapy again, even if it is highly effective against recurrent breast cancer.

In conclusion, EP can occur in patients with advanced or recurrent breast cancer who are receiving endocrine therapy combined with abemaciclib. Although it is rare, EP associated with abemaciclib plus endocrine therapy can be refractory or relapse easily. Further studies evaluating the pathophysiology, prevention, and management of endocrine therapy and/or abemaciclib-induced EP are highly warranted.

AUTHOR CONTRIBUTIONS

H.O. contributed to the conception of the work, the acquisition and interpretation of data for the work, and drafting of the manuscript. Y.M., A.E.O., A.I., J.O., K.T., A.M., and E.T. contributed to the interpretation of data for the work and revision of the manuscript. C.K., T.Y., and M.Y. contributed to the conception of the work, interpretation of the data, and revision of the manuscript. All authors critically reviewed the manuscript and approved the final version.

CONFLICT OF INTEREST STATEMENT

Eriko Tokunaga received lecture fee from Eli Lilly. Other authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

All relevant data are within the manuscript.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

ORCID

Hiroaki Ogata https://orcid.org/0000-0002-6932-747X

REFERENCES

1. Rugo HS, Huober J, García-Sáenz JA, Masuda N, Sohn JH, Andre VAM, et al. Management of abemaciclib-associated adverse events in patients with hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: safety analysis of MONARCH 2 and MONARCH 3. Oncologist. 2021;26:e53–65.
2. Wu B, Shen P, Yin X, Yu L, Wu F, Chen C, et al. Analysis of adverse event of interstitial lung disease in men with prostate cancer receiving hormone therapy using the Food and Drug Administration adverse event reporting system. Br Pharmacol Soc. 2023;89:440–8.
3. Bartal C, Sagy I, Barski L. Drug-induced eosinophilic pneumonia: a review of 196 cases. Medicine (Baltimore). 2018;97:e9688.
4. Mitarai Y, Tsubata Y, Hyakudomi M, Isobe T. Drug-induced eosinophilic pneumonia as an adverse event of abemaciclib. Cureus. 2022;14:e21741.

How to cite this article: Ogata H, Koga C, Yanagihara T, Moriuchi Y, Enokizu-Ogawa A, Ishimatsu A, et al. Relapsing eosinophilic pneumonia in a patient with recurrent breast cancer receiving abemaciclib plus endocrine therapy. Respirology Case Reports. 2024;12(3):e01320. https://doi.org/10.1002/rcr2.1320