



# Acute Pulmonary Embolism Induced by Pomalidomide Plus Low-Dose Dexamethasone

Kusano Y\*, Terui Y, Nishimura N, Takahashi A, Inoue N, Ueda K, Mishima Y, Yokoyama M and Hatake K

Department of Hematology and Oncology, Japanese Foundation for Cancer Research, Japan

## Abstract

Usage of non-ionic contrast agents in patients with multiple myeloma, who have normal creatinine level, is not high risk to develop contrast-induced nephropathy. Novel agents has improved prognosis of patients with myeloma but immunomodulatory drug-containing therapy such as lenalidomide and pomalidomide has a risk of venous thromboembolism (VTE) and pulmonary embolism (PE). Contrast-enhanced CT (CECT) is gold standard to detect PE and should be considered particularly when severe secondary complications including PE are suspected to detect and treat patients in haste if creatinine clearance level is normal. Here, we present a case presented massive pulmonary embolism on the first cycle of pomalidomide plus low-dose dexamethasone (PoMdex), which has an incident rate of 2% in all grades VTE/PE and of 1% in grade 3/4 VTE/PE. The patient has not impaired renal function since we performed CECT.

**Keywords:** Multiple myeloma; Pulmonary embolism; Venous thromboembolism; Pomalidomide

## Introduction

A regimen consisting of pomalidomide plus low-dose dexamethasone (PoMdex) has efficacy in patients with refractory or relapsed multiple myeloma, which was resistant to bortezomib and lenalidomide. This regimen has low risk (1%) of venous thromboembolism (VTE) by prophylaxis according to MM-003 trial [1]. Here, we present a case presented pulmonary embolism on the first cycle of PoMdex. The patient had already received 49 cycles of a lenalidomide-based regimen, which also has a risk of VTE but patient had no notable adverse events. In patients who receive PoMdex, incident rate of VTE or pulmonary embolism (PE) of all grades was 2% and of grade 3/4 was 1% [1]. In addition, contrast-enhanced CT (CECT) is gold standard to detect PE and should be considered particularly when severe secondary complications including PE are suspected if creatinine clearance level is normal even though patients have myeloma. A usage of non-ionic contrast agents in patients with multiple myeloma who have normal creatinine levels is not high risk to develop contrast-induced nephropathy [2,3]. In fact, renal function has never impaired in this case since CECT was performed.

## Case Presentation

A 65-year-old woman, who was diagnosed as symptomatic multiple myeloma, had iterated relapses of myeloma and suffered a fourth relapse in 2015. Since she was diagnosed with myeloma, she had given regimens as following; vincristine, doxorubicin, and dexamethasone; bortezomib plus dexamethasone; lenalidomide plus dexamethasone; and two times of high-dose melphalan followed by autologous stem cell transplantation. With the last regimen, lenalidomide plus dexamethasone, complete remission was not achieved but the efficacy had continued for four years (49 cycles). In 2015, M protein eventually increased again and then, she switched from the regimen to pomalidomide plus dexamethasone (PoM+dex). She had continued aspirin for thromboprophylaxis. On the day 23 of first course of PoMdex, she admitted hospital to treat febrile neutropenia and pneumonia. She had short-lasting dyspnea after administration either cefepime or piperacillin-tazobactam. After modification to levofloxacin, dyspnea has never returned. However, at follow-up of three days, plasma of fibrin fragment started increasing (D-dimer increased to 8 from 0.81). Echogram demonstrated extensive VTE on her right foot's vein from popliteal to middle of femoral vein. Therefore, CECT was performed after confirmation of normal creatinine clearance. CECT showed massive PE at right main pulmonary artery and one of left branches of pulmonary arteries (Figure). Immediately, she received anticoagulant therapy immediately then, disappearance of thromboses

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### \*Correspondence:

Yoshiharu Kusano, Department of Hematology and Oncology, Cancer Institute Hospital of Japanese Foundation for Cancer Research, 3-8-31, Ariake, Koto-ward, Tokyo, 135-8550, Japan, Phone: +81-3-3520-0111; Fax: +81-3-3520-0141; E-mail: yoshiharu.kusano@jfcrc.or.jp

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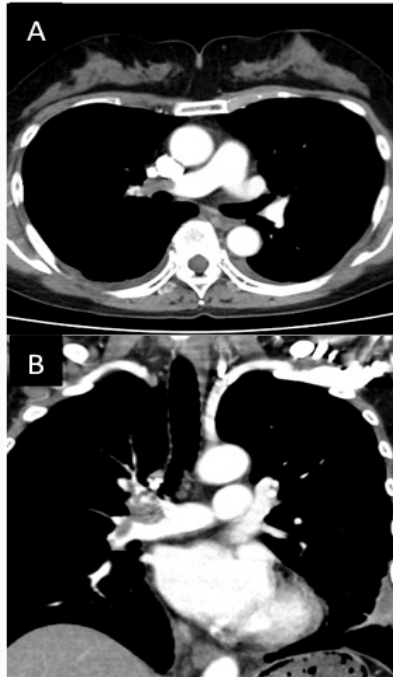
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**Figure:** Pulmonary embolism, detected by using enhanced-contrast CT scans. Thromboses were founded at right main pulmonary artery and one of left branches of pulmonary arteries. (A: Transverse Plane; B: Coronal Plane)

was confirmed two weeks later by CECT. Her renal function has remained normal level from then on.

## Discussion

According to MM-003 trial [1], the most common non-hematological adverse events of PoMdex are following; pneumonia (13%), bone pain (7%), and fatigue (5%). The same safety profiles were mentioned as similar with previous trials. In terms of events

of VTE and PE were rare under thromboprophylaxis. All grade events of thrombosis formation were seen six (2 %) and grade 3/4 events were three (1%) [1]. The median time to onset of any grade VTE/PE by PoM+dex was four months and range of time to onset was one month to six months [1]. In our case, what the real onset of pulmonary embolism was unremarkable. Neither increased level of fibrin fragment or signs suggested VTE were problems in this case despite VTE extended to the femoral vein was another one. Although CECT is gold standard for detect pulmonary embolism, using ionic contrast agents contraindicated in patients with myeloma because of high risk of contrast-induced nephropathy. However, in patients who have normal renal function, CECT was not high risk for them even though they have myeloma [2,3]. MM-003 trial also suggested that VTE events might occur from first cycles such as our case. We need to follow plasma of fibrin fragment. In conclusion, this case demonstrated that VTE/PE is rare but may progress rapidly during courses of PoM+dex. Therefore, routine follow-up of fibrin fragments level on the courses of PoM+dex without suspicious manifestations and signs of VTE are essential. Contrast agents should be used in patients with myeloma particularly when severe secondary complications including PE are suspected and are needed to detect and treat in haste.

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