CASE REPORT

Lungs on fire

Sandeep Batra,¹ A K Vaid,¹ Rahul Bhargava,¹ Sachin Gupta²¹Department of Medical Oncology, Medanta, The Medicity, Gurgaon, Haryana, India²Department of Medical Oncology, Max Hospital, Mohali, Punjab, India**Correspondence to**

Dr Sandeep Batra, sandeepriya2000@yahoo.com

SUMMARY

A 50-year-old man was diagnosed as classical Hodgkin's lymphoma stage III B. He had been a reformed smoker and has had a coronary artery disease as his comorbidity. He was started on adriamycin, bleomycin, vinblastine, dacarbazine (ABVD)-based chemotherapy. An interim disease evaluation was suggestive of metabolic complete response after four cycles of ABVD. After completion of his sixth cycle, he presented with low-grade fever, dry cough, generalised malaise and increasing dyspnoea on exertion. FDG (18 fluoro-deoxyglucose) positron emission tomography (PET)-CT revealed intensely FDG avid diffuse activity in mid and lower zone both lung fields. He was started on intravenous steroids along with broad spectrum antibiotic and antifungal cover. Clinical, radiological and laboratory assays did not reveal any infective pathology. He was diagnosed as bleomycin-induced pulmonary toxicity (BIP). Despite best supportive care, his pulmonary functions deteriorated and he developed cardiac arrhythmias. He finally succumbed to the irreversible chemotherapy toxicity of a curable malignancy.

BACKGROUND

Fluorodeoxyglucose (FDG) positron emission tomography-CT (PET-CT) is routinely done during the management of Hodgkins' lymphoma for the baseline staging, interim evaluation and the end of treatment response evaluation. Regular pulmonary function testing and/or diffusing capacity of lung for carbon monoxide (DLCO) testing helps in deciding about the continuation or discontinuation of bleomycin from the treatment protocol. Many times in medical science, while evaluating patients, we come across findings, which we did not anticipate and/or which were not intended to be the subject matter of investigation. Sometimes, they are so unique that you want them to be brought to the notice of the rest of the world.

In our images also, we are bringing to the world's notice, the potential life-threatening manifestation of bleomycin-induced pulmonary toxicity (BIP) on 18-FDG PET-CT, performed for disease evaluation.

In these images, FDG avid BIP is emphasised, which is an uncommon finding seen on PET-CT.

Thus, during disease assessment of Hodgkin's lymphoma while on chemotherapy including bleomycin, if one comes across similar findings, one would be wiser for timely bleomycin discontinuation and reducing the risk of developing life-threatening bleomycin-induced lung toxicity.

These images also highlight the fact that inflammations, whether acute or chronic can avidly accumulate FDG, thus confusing a benign inflammatory lesion with a malignancy.

CASE PRESENTATION

A 50-year-old man presented with generalised lymphadenopathy, fever, loss of weight and loss of appetite. He was a reformed smoker and had a history of coronary artery disease as his comorbidity.

On diagnostic and staging workup including cervical lymph node biopsy, he was diagnosed as classical Hodgkin's lymphoma, nodular sclerosis type, stage III B.

He was started on adriamycin, bleomycin, vinblastine, dacarbazine (ABVD)-based chemotherapy. He needed granulocyte-colony stimulating factor (G-CSF) support for the maintenance of the drug intensity of chemotherapy. An interim disease evaluation with a FDG PET-CT after four cycles of ABVD was suggestive of metabolic complete response. There was no evidence of BIP toxicity on CT component of PET-CT. After the completion of his sixth cycle, he presented with low-grade fever, dry cough, generalised malaise and increasing dyspnoea on exertion. His chest examination revealed fine inspiratory crepitations at both lung bases. A chest X-ray revealed a bilaterally symmetrical reticulonodular shadowing in both lower zones. With a presumptive diagnosis of bleomycin-induced lung toxicity, he was started on high-dose oral steroids at 1 mg/kg dose under oral antibiotic and antifungal cover. He was scheduled for a FDG PET-CT as the end of the treatment response evaluation, which was performed as planned. The PET-CT revealed intensely FDG avid diffuse activity in mid-zone and lower zone of both lung fields suggesting both, middle and lower lobe lung involvement (figures 1 and 2). In view of his increasing dyspnoea, he was admitted in high-dependency unit and started on high-dose intravenous steroids along with intravenous broad spectrum antibiotics and antifungal. Clinical, radiological and laboratory assays including serum procalcitonin, sputum Gram staining and bronchoalveolar lavage and sputum cultures did not reveal any infective pathology.

He was finally diagnosed as BIP rapidly progressing to pulmonary fibrosis. In view of rapidly deteriorating pulmonary functions and the inability to maintain optimum oxygen saturation on non-invasive positive pressure ventilation, he was electively intubated and mechanically ventilated. He was nursed predominantly in prone position to allow better middle and lower lobe lung expansions. Despite best supportive care, his pulmonary functions deteriorated and he developed cardiac arrhythmias. After 10 days of hospitalisation in the intensive care unit of a tertiary care centre, he finally succumbed to the irreversible chemotherapy toxicity of a curable malignancy.

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Figure 1 A coronal section on a positron emission tomography-CT showing symmetrical diffuse fluorodeoxyglucose uptake in both mid and lower zones of both lung fields, looking as they have been put on fire.

INVESTIGATIONS

FDG PET-CT, pulmonary function tests, bronchoalveolar lavage, serum procalcitonin.

DIFFERENTIAL DIAGNOSIS

- ▶ Infective pneumonitis
- ▶ BIP
- ▶ Cardiomyopathy

TREATMENT

ABVD-based chemotherapy for six cycles.

OUTCOME AND FOLLOW-UP

After 10 days of hospitalisation in the intensive care unit of a tertiary care centre, he finally succumbed to the irreversible chemotherapy toxicity of a curable malignancy.

DISCUSSION

Bleomycin, an antitumor antibiotic, is an essential component of chemotherapy of curable malignancies like germ cell

tumours, lymphomas both Hodgkin's and non-Hodgkin's. Bleomycin is recognised to cause an interstitial pneumonitis that can lead to fibrosis.¹ The diagnosis of bleomycin induced pulmonary toxicity is often one of exclusion by sputum analysis, serology or antigen detection for micro-organisms.² Patients with BIP are often treated for infection unsuccessfully before the diagnosis is confirmed. Although the incidence of pulmonary toxicity is often quoted as 6–10%, it may occur in up to 46% of patients receiving bleomycin with a mortality of 3–5% in those affected.³ Age, cumulative drug dose, renal function, stage of disease at presentation, radiation therapy, concomitant oxygen use, other chemotherapeutic agents and G-CSF use may all influence the risk of developing BIP.⁴ Concomitant treatment with G-CSF has been identified as a possible risk factor for the development of BIP in animal studies. However, data in humans are conflicting as to whether G-CSF increases the risk of BIP.^{5 6}

Interestingly, in our case, the patient had all the risk factors (advanced age, advanced stage other chemotherapeutic agents and concomitant G-CSF use) of developing BIP. However, there was no clinical, radiological or pulmonary function testing evidence of early BIP. In all probabilities, it was the cumulative bleomycin dosing, previous smoking history and CAD which were co-morbid; this led to the rapid development of BIP and mortality.

This case again highlights the tough task of balancing the tightrope walk in the management of advanced curable malignancies in elderly by choosing the chemotherapy drugs carefully so as to have similar efficacy with lesser toxicity.

Learning points

- ▶ Bleomycin is an important component of chemotherapy regimens of curable malignancies.
- ▶ Bleomycin-induced pulmonary (BIP) toxicity is associated with cumulative dosing of bleomycin.
- ▶ Lungs+bleomycin+Hodgkins' lymphoma +advanced age + advanced stage±G-CSF=BIP.
- ▶ Regular pulmonary function tests and diffusing capacity of lung for carbon monoxide (DLCO) monitoring should be carried out in patients on bleomycin-based chemotherapy.

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Competing interests None.

Patient consent Obtained.

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Figure 2 A transverse section on a positron emission tomography-CT showing diffuse fluorodeoxyglucose uptake in both lower lobes lung.

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