Interesting Case – Bleomycin-induced pneumonitis

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This 72 year-old woman presented with dry cough which did not resolve with empiric azithromycin therapy. CT demonstrated extensive right hilar and mediastinal lymphadenopathy. Her histochemical diagnosis was classical Hodgkin lymphoma. Initial staging PET/CT revealed multiple hypermetabolic skeletal lesions (Stage IVA). She was treated with 6 cycles of ABVD (Adriamycin, Bleomycin, Vinblastine, Dacarbazine). Pretreatment diffusing capacity of lungs for carbon monoxide (DLCO) was normal and post-treatment evaluation revealed DLCO reduced to 48%. She experienced progressive worsening cough with shortness of breath and fatigue during the treatment. Symptoms improved upon completion of chemotherapy without any active intervention.

Figure 1: Pre-chemotherapy PET/CT

F-18 FDG PET/CT from skull base to mid-thigh demonstrated markedly hypermetabolic lymph nodes in the neck, chest, abdomen, and pelvis. SUVmax of the hypermetabolic lymph nodes ranged from 5.7 to 17.4. Average liver SUV measured 1.78. All SUV were based on lean body mass. No consolidation was visualized on this baseline PET/CT.
Figure 2: Post-chemotherapy PET/CT

Focal subpleural consolidations with moderate metabolic activities are noted in both lungs, new since the prior PET/CT. Mediastinal lymphadenopathy with metabolic activity (SUVmax 1.5, average liver SUV measures 1.6) not exceeding mediastinal blood pool was noted on CT. Findings were unusual for active Hodgkin lymphoma. Bleomycin-induced lung toxicity was the most likely diagnosis based on history and PET/CT results.
**Figure 3: Axial post-chemotherapy PET/CT**

Axial CT and PET/CT images demonstrated the bilateral hypermetabolic subpleural consolidations with SUVmax 2.4.

**Discussion:**

Bleomycin is a commonly used chemotherapeutic agent for certain germ-cell tumors, cervical cancer, lymphomas, Kaposi’s sarcoma, and squamous cell carcinomas of the head and neck. It is also used as a sclerosing agent to treat pleural effusions. It is an antibiotic class of antineoplastic drugs that targets the G2 cell cycle phase and a cytostatic agent that blocks DNA synthesis by binding to the DNA helix and causing single- and double-strand breaks [1]. Other proposed mechanisms of action include lipid peroxidation and oxidative degradation of RNA.

Bleomycin is given parenterally because of poor GI absorption. It gets distributed in multiple tissues and organs like skin, kidney, lungs, lymphatics, and the peritoneum and is metabolized by bleomycin hydrolase which is present in most tissues except lungs and skin, the primary sites of toxicity. Primary excretion is through the kidneys, correlating with creatinine clearance. Dosage adjustment is important in patients with creatinine clearance of less than 50 mL/min.

Close monitoring is recommended for bleomycin-induced pneumonitis (BIP), or ultimately, pulmonary fibrosis, especially in patients with history pulmonary disease or an established diagnosis of pulmonary fibrosis. BIP is reported in 0% to 46% patients who have undergone bleomycin therapy. BIP and ensuing fibrosis is more frequent in patients who receive more than 400 units of bleomycin cumulative dose (maximum cumulative lifetime dose). Additionally, treatment with bleomycin may lead to “radiation recall”- reactivation of prior radiation-induced lung disease. Other risk factors include age > 70 years, preexisting lung disease, and/or concomitant additional chemotherapeutic agent(s) use. Frequent imaging studies (especially in the setting of symptoms) and sequential measurements of pulmonary diffusion capacity for carbon monoxide are recommended for patients undergoing bleomycin therapy. Some other less common variants of bleomycin-induced lung disease include hypersensitivity reactions, nodular pulmonary lesions mimicking tumor metastasis (sometimes requiring tissue sampling to differentiate) [2], pneumothorax, and pneumomediastinum.

**References:**

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