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Doxorubicin as an unusual cause of organizing pneumonia

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Summary. Organizing pneumonia is a syndrome that is characterized by respiratory illness that can be severe and life threatening. There are several well-well known causes of organizing pneumonia, including infections, environmental exposures and drugs. More specifically, there are several chemotherapeutic agents that are associated with organizing pneumonia. In addition, a very common cause is exposure to radiation in the context of radiation therapy in the treatment of breast cancer. However, in the presented case, a female with breast cancer was treated with doxorubicin in the absence of radiation therapy and developed organizing pneumonia. The cause was thought to be secondary to doxorubicin. Previously, there has only been one reported case of organizing pneumonia secondary to doxorubicin. This poses the question that perhaps drug induced organizing pneumonia, specifically secondary to chemotherapeutic agents, is more common than previously reported and the association with radiation therapy may be overestimated.

Key words: cryptogenic organizing pneumonia; drug-related side effects and adverse reactions; doxorubicin

Organizing pneumonia (OP), is a clinicopathologic syndrome characterized clinically by respiratory illness. A variety of etiologies have been reported, including several chemotherapeutic drugs. In addition, a well known cause of OP is radiation therapy, especially seen in those with a history of breast cancer. However, it is less common in those who receive only chemotherapy without radiation therapy. Here we describe a case of a patient with breast cancer, treated with doxorubicin and cyclophosphamide who developed OP, in the absence of radiation therapy. A 52 year old female, with a diagnosis of Stage IIIC infiltrating ductal carcinoma of the left breast, who had recently completed her fourth cycle of dose dense doxocrubicin and cyclophosphamide one month prior, presented with shortness of breath and fever. An chest x-ray showed mild congestion of the lungs, initially mistaken for pulmonary edema. A computed tomography (CT) thorax showed generalized, non-specific, patchy opacities (Figure 1). She was started on broad spectrum antibiotics for presumed pneumonia, but remained hypoxic and required management in the intensive care unit for respiratory failure. Her entire infectious disease workup was negative, including for bacterial, viral and fungal causes. A transbronchial biopsy was consistent with organizing pneumonia. Once started on the corticosteroids (1 milligram/kilogram), tapered over four weeks, her respiratory status and hypoxia improved. A repeat CT thorax eight weeks later showed resolution of the opacities.

Organizing pneumonia was first described by Epler et al. in 1985 and is characterized by respiratory illness and at times, failure. It is histologically defined by the presence of buds of endoalveolar connective tissue resulting from injury to the alveolar epithelium, with deposition of fibrin in the alveolar spaces (1). Radiation therapy is also a widely recognized cause of pulmonary toxicity, specifically organizing pneumonia and is most commonly seen in breast cancer patients. Of the studies that have focused on radiotherapy induced OP, up to 60% of the reported patients were also undergoing chemotherapy. The reported regimens included doxorubicin and cyclophosphamide, similar to the regimen seen in our patient (2). In severe, ster-

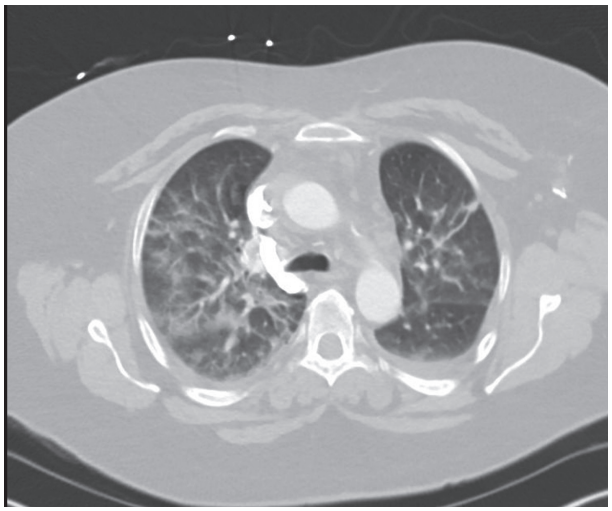

Figure 1.

oid resistant cases, cyclophosphamide, despite being reported as an agent of pulmonary toxicity, has been reported as an alternative therapy (3, 4). Because OP may also be treated with cyclophosphamide, it is possible that doxorubicin may also be a precipitant of OP. To our knowledge, there has only been one reported case of OP secondary to doxorubicin (5). Given that many patients undergo sequential or concurrent radiation and chemotherapy, it is possible that the documented cases of organizing pneumonia that are generally thought to be related to radiation therapy may actually be related to specific chemotherapeutic agents and may have been underreported. Specifically, chemotherapeutic agents precipitating organizing pneumonia, such as doxorubicin, used in our patient, may be more prevalent, though underreported and thought to be due to radiation therapy. Though of course it is difficult to definitively establish this relationship, this case highlights the importance of a careful assessment of pulmonary symptoms during and after chemotherapy treatment.

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