

Pleural Effusion Associated to Isotretinoin Treatment

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Article Info

Received: February 28, 2021

Accepted: March 08, 2021

Published: March 11, 2021

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Citation: Batoczki B, Galvis AE, Pecson I, Featherstone Z, Nakamura C. "Pleural Effusion Associated to Isotretinoin Treatment". *Clinical Case Reports and Clinical Study*, 2(5); DOI: 10.61148/2766-8614/JCCRCS/032

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Abstract

A 17-year-old previously healthy female presented to the pulmonology clinic for chest pain and tightness found to have a pleural effusion while on isotretinoin acne treatment. Alongside well documented teratogenic side effects isotretinoin has been linked to adverse manifestations related to other systems. A rare eosinophilic pleural effusion (EPE) may occur while on treatment with isotretinoin.

Key Words: Pleural effusion; isotretinoin

Introduction

Numerous drugs used in everyday medical practice can affect the pleura; these effects can go from confined reactions to severe life-threatening systemic disorders. The most frequently observed drug-related pleural manifestations are pleural effusions [1].

To this day systemic isotretinoin is the most effective treatment for severe acne or acne unresponsive to other treatment modalities. It may also used to treat other disorders related to keratinization. However, the wide spectrum of side effects related to isotretinoin calls for a judicious risk-benefit evaluation before treatment onset [2, 3].

We present a case of a 17-year-old female under treatment with isotretinoin who developed chest pain and tightness with later identification of pleural effusion on chest Magnetic resonance imaging (MRI).

Case report

A 17-year-old previously healthy female presented to the pulmonology clinic for chest pain and tightness. A prior work-up included an incidental finding of pleural effusion on MRI.

Medical history was remarkable for acne, allergic rhinitis, an episode of acute sinusitis, and atypical pneumonia for which she received antibiotics 2 months before the visit and chronic mid-back pain with added chest tightness for approximately 4 months. She denied any cough, fever, or unintentional weight loss. Due to back pain a thoracic and lumbar spine MRI was ordered showing a trace pleural effusion, and was referred to Pulmonology.

Medications were relevant for isotretinoin 40 mg twice a day (BID) for acne treatment and inhaled corticosteroids for the treatment of allergic rhinitis. On physical exam, weight was 69.4 kg (83 percentile), height 165 cm (63 percentile), BMI 25.46, temperature 97.6 F (36.4 C), and SpO2 98% on room air.

Isotretinoin was stopped with plans for reassessment due to the probability of isotretinoin being the causative factor for the pleural effusion.

On follow-up the patient referred the chest tightness had resolved; isotretinoin was discontinued and a chest CT without contrast to confirm resolution was ordered.

Discussion

The outer surface of the lungs and inner surface of the thoracic cavity is covered by the visceral and parietal pleura respectively which is an elastic membrane with a lubricant surface that forms the pleural cavity. Within the pleural cavity, a small



amount of pleural fluid (less than 1 ml) creates a fine layer between the visceral and parietal pleura with an approximate content of 1-2 grams of protein per 100 ml of pleural fluid and 1400-4500 cells per each μ l of fluid, mostly macrophages and scant lymphocytes and red blood cells [4, 5].

Pleural fluid production and absorption are mainly performed by the surface of the parietal pleura, relying on the balance of hydrostatic and oncotic pressure differences between systemic and pulmonary circulations and the pleural space, with lymphatic vessels on the parietal pleura being responsible for the majority of pleural fluid resorption. When the balance between pleural fluid production and resorption is disrupted, pleural effusions present [5].

Isotretinoin (13-cis-retinoic acid) is a non-aromatic retinoid approved for the treatment of severe and recalcitrant inflammatory acne [6]. The teratogenic effects of isotretinoin have been well documented, additionally, isotretinoin has been reported to cause pulmonary manifestations including eosinophilic pleural effusions (EPE), interstitial parenchymal lung disease, bronchospasm and asthma exacerbations [2, 6, 7-9]. EPE is defined as a pleural effusion with an eosinophil count \geq 10%; it is commonly associated with conditions where blood or air occupy the pleural space, infections, inflammatory disorders, malignancy, and pulmonary embolism; with a small portion of cases attributed to drug-induced EPE.

Although the etiology for EPE has not been elucidated some suggested mechanisms include hypersensitivity or allergic reaction, direct toxic effect, increased oxygen free-radical production, suppression of antioxidant defense mechanism, and chemical-induced inflammation [10].

Isotretinoin related EPE has been described to occur 1-7 months after treatment onset with symptoms ranging from insidious dyspnea to the acute presence of cough and fever. Isotretinoin associated EPE symptom resolution can be expected from 1-3 months after discontinuation of the drug [1].

Conclusion

Isotretinoin is to this day the most effective treatment for severe acne. The presence of EPE has been associated with isotretinoin treatment. In this case, the resolution of symptoms after discontinuation of isotretinoin strongly suggests causality of the pleural effusion due to isotretinoin. It remains important to keep in mind a medication side effect when evaluating a patient's symptoms and physical findings.

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