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Case report

Acitretin induced lung injury by differentiation syndrome

Sarah Khan [a], Achuta Kumar Guddati [b], Creticus Marak [c,*]

[a] Department of Medicine, Northeastern Health System, Tahlequah, OK, USA
[b] Division of Hematology/Oncology, Augusta University, Augusta, GA, United States
[c] Department of Rural Medicine - Pulmonary and Critical Care, Oklahoma State University College of Osteopathic Medicine, Tahlequah, OK, USA

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ABSTRACT

Differentiation syndrome is a life-threatening complication observed when retinoic acid is given to patients with acute promyelocytic leukemia. Retinoid compounds are also used in non-malignant conditions like psoriasis and it is rare to see differentiation syndrome in such settings. This reports details the clinical presentation and successful management of a patient with psoriasis who developed differentiation syndrome while on treatment with acitretin. The patient was managed with steroids and the differentiation syndrome abated with eventual complete resolution. This report exemplifies the need to consider differentiation syndrome in patients who have non-malignant conditions and are being managed with retoinds.

1. Introduction

Differentiation syndrome or retinoid acid syndrome (RAS) is a well-known complication that is commonly described in patients with acute promyelocytic leukemia (APL) who are treated with all-trans retinoic acid (ATRA). It can occur in up to 25% of APL patients treated with ATRA [1]. Patients with this syndrome usually present within 2–21 days of treatment initiation with fever, pulmonary infiltrates, hypoxemia, respiratory distress, generalized edema, pleural and pericardial effusions; hypotension, renal and hepatic dysfunctions [2]. Acitretin is retinoic acid derivative that is approved for treatment of severe psoriasis [3]. There have been many reports of acitretin causing differentiation like syndrome [4], but acitretin causing an isolated lung injury without systemic involvement is rare entity [5–7].

2. Case presentation

A 62-year-old lady, non-smoker, morbidly obese with history of obstructive sleep apnea, hypertension, diabetes mellitus type 2 and pustular psoriasis presented to our facility with acute dyspnea of 1 day's duration. She had an associated nonproductive cough but denied fever, chills, wheezing, chest pain, palpitations, syncope or leg edema. Physical examination revealed a morbidly obese woman, in moderate respiratory distress, with ability to speak in short sentences only. She was hypoxemic with an oxygen saturation of 70% on room air at rest. She had bilateral crepitations with no associated wheeze or leg edema. Dermatologic examination was remarkable for pustular psoriasis. WBC was normal at 9k, brain natriuretic peptide (BNP) was mildly elevated at 324, and procalcitonin was normal at 0.01. Arterial blood gas showed a pH of 7.29 with a PCO2 of 55. Her liver and renal functions were within normal limits. Chest x-ray showed bilateral alveolar infiltrates (Fig. 1 A). CT angiogram was negative for embolism but revealed bilateral ground glass opacities with no associated pleural or pericardial effusion (Fig. 1B). She was admitted to MICU with a diagnosis of acute hypoxemic respiratory failure due to presumed pneumonia. She was placed on noninvasive positive pressure ventilation and started on broad spectrum IV antibiotics. Despite treatment with antibiotics, she continued to remain symptomatic with persistent dyspnea and hypoxemia. Then she was also started on IV furosemide (due to mildly elevated BNP and bilateral ground glass opacification on CT chest). Despite adequate diuresis and a negative fluid balance of close to 7 L she remained dyspneic with persistent hypoxemia and requiring 6–8 L/minute of oxygen supplementation and intermittent non-invasive positive pressure ventilation (NIPPV) to maintain an adequate saturation. A transthoracic cardiac echocardiogram showed a normal ejection fraction (EF) of 65% with a mildly elevated pulmonary artery systolic pressure of 48 mmHg. Due to persistent hypoxemia, a Pulmonology consult was sought on her 6th day of hospital stay. CT of the chest was repeated and it showed worsening bilateral pulmonary infiltrates with small bilateral pleural effusions (Fig. 1 C). On further questioning she then reported to the pulmonary service that she was started on acitretin for pustular psoriasis 2 weeks prior to her onset of symptoms. She was then diagnosed with

* Corresponding author.Department of Medicine, Northeastern Health System, Tahlequah, OK, 74464, USA.
E-mail addresses: cmarak@nhs-ok.org, creticus@hotmail.com (C. Marak).

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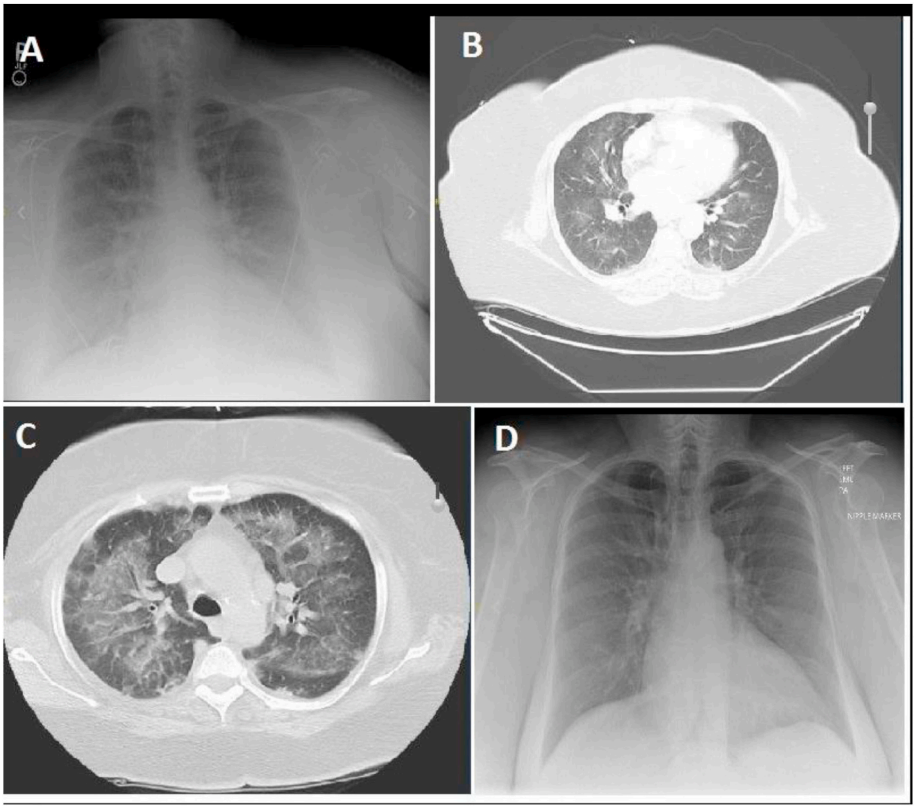

Fig. 1. Serial radiographic Imaging.

drug induced lung injury (DILI) due to acitretin and started on high-dose IV methyl prednisone. She received 125 mg every 6 hourly for the initial 2 days, followed by 60 mg every 12 hours for 2 days, 60 mg once a day for 2 days, and then per oral prednisone 50 mg once daily for 2 days. She was eventually discharged on oral prednisone 20 mg once daily that was tapered over 5 weeks. She responded well to systemic steroids with symptomatic improvement within 24 hours and resolution of hypoxemia within 6 days of steroid treatment. At the time of discharge her saturation was 94% on room air at rest with no desaturation after exertion. Repeat chest x ray 3 weeks after discharge (Fig. 1 D) showed resolution of the pulmonary infiltrates.

3. Discussion

Acitretin is approved for treatment of severe pustular psoriasis. Unlike amiodarone or other drugs that are well known for causing pulmonary toxicities; not many health care professionals are aware of acitretin induced lung injury. So far there are only few reported cases of acitretin induced acute respiratory distress syndrome and capillary leak syndrome [8,9]. Drug induced lung injury (DILI) even though common is frequently missed and an under reported cause of both acute and chronic lung disease [10]. Detailed medication history is therefore an important aspect in the initial workup of every patient that presents with a new or recurrent pulmonary problems. As in this case the diagnosis of DILI is often not considered thus resulting in treatment delay, unnecessary diagnostic tests and prolongation of hospital stay. Unlike the differentiation syndrome due to ATRA, there are no established recommendations for treatment of isolated lung injury caused by acitretin. Based on the limited information that is available in medical literature; high dose systemic steroids are often recommended for treating this disease entity.

Declaration of competing interest

The authors declare that they have no conflicts of interest.
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All authors have read the manuscript and agree to the content.

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