

## Case Report

**A methylprednisolone induced hypertension and bilateral pleural effusions as acute adverse effects in a young woman “Yahya Al-Fifi’s Syndrome”****Yahya Salim Yahya AL-FIFI**

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**Abstract:** We describe a rare case of hypertension and bilateral pleural effusion simultaneously in twenty-two years old otherwise healthy young female in March 2017. The patient presented with an allergic reaction to an insect sting. Hence, she developed a generalized rash and shortness of breathing where she received a methylprednisolone 80 mg intravenously every 8 hourly for five days where she was discharged home. However, the patient readmitted within 24 hours with non-resolving shortness of breathing, dry cough, hypertension and bilateral pleural effusions more significant on the right side are confirmed clinically and radiologically. Five days after methylprednisolone was discontinued, patient became normotensive and chest x-rays was normal. These manifestations that include symptoms, signs and radiological images and their resolutions are given a name of a syndrome called “Yahya Al –Fifi’s syndrome.”

**Keywords:** Yahya Al-Fifi’s syndrome, hypertension, methylprednisolone , pleural effusions

**INTRODUCTION:**

Methylprednisolone is essential medication for clinical use in various diseases; as anti-inflammatory and immunosuppression medication. It was approved for clinical use in 1955. The World Health Organization listed methylprednisolone as an essential drug in 19th edition 2015 and considered as the safest and effective medication for management of several diseases including infectious diseases; tuberculosis meningitis, and pericarditis, rheumatology diseases; systemic lupus erythematosus (SLE), and Rheumatoid arthritis (RA), gastrointestinal diseases; Crohn’s diseases and ulcerative colitis [1,2]. It is one of the mainstay therapies for post kidney and liver transplant but not limited to these [5]. The methylprednisolone chronic complications of prolonged usage are well known including osteoporosis, avascular necrosis, cushioned features, hypertension, pericardial effusion and increase intracranial pressures with papilledema [3,4]. However, as in this case report a short course of methylprednisolone inducing hypertension and bilateral pleural effusions is Very uncommon. The methylprednisolone or other corticosteroid derivatives acute adverse effect appreciation could be a challenging clinical issue. On the contrary, if such acute manifestation is not appreciated at the presentation that may trigger a cascade of unnecessary investigations looking for the etiology, as well as patient suffering and dilemma of physicians in effort reaching the diagnosis ever.

**CASE PRESENTATION**

22 years old woman presented with shortness of breathing, cough, and wheezing after she has been stung by an unknown insect. The patient was treated with methylprednisolone 80 mg intravenous three times a day for five days. Patient experiences a persistent dry cough with occasional chest wheezing and shortness of breathing after completing the course of five days of methylprednisolone. However, fever, chest pain, headache, visual disturbances, were absent. She is well-known to have an allergic reaction to insect’s and bees’ stings where she responded to a short course of antihistamines and methylprednisolone and recovered completely, without requiring a ventilation support. Patient’s travel, drug, family, social histories were unremarkable. The rest of systemic reviews were non-contributable.

On examination, the patient is awake, alert, orient to place and person. She is an overweight female in her estimated age. Vital signs: temperature is 36.7° C, pulse rate is 80 per minute, respiratory rate 18 per minute, blood pressure is 166/90 mm Hg, Saturation is 96 % on room air. She is not pale or jaundiced and no lymphadenopathy. The jugular venous pressure is 4 centimeter above the sternal angle with normal hepato-jugular reflux. Chest examination showed decreased movement in the right side. The tactile vocal fremitus and vocal resonance are diminished bilaterally in both

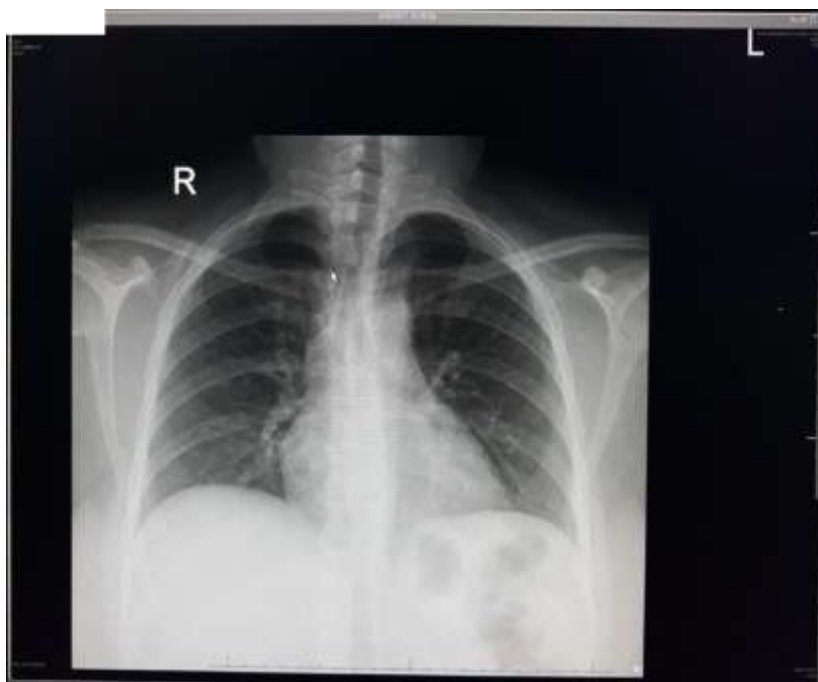
lower sides of the chest. Stony dullness with an absence of air entry in the lower chest bilateral was present in both bases of the lungs but more prominent on the right side. Cardiovascular examination was unremarkable. Abdomen examination revealed obese abdomen with no organomegaly, ascites or abdominal bruit. Neurological examination as are peripheral vascular and locomotors examinations are within normal limit.

The Investigation showed the white blood count is  $13.00 \times 10^9$  per liter (L) with predominantly 85% neutrophil, hemoglobin 10.4 gm/dl and platelets 339

with the hypochromic microcytic picture. The renal, liver, and lipid profiles, calcium, albumin, protein, phosphate, magnesium, PT, PTT, BT, D-dimer, thyroid hormones, protein (S), and protein (C) are normal. Chest-x-ray showed a bilateral pleural effusion more prominent in the right hemi-thorax (Image I). The repeated chest x-rays in five days post discontinuation of methylprednisolone revealed complete resolution of bilateral plural effusion (Image II). The electrocardiography (EKG) and Echocardiography are normal. Abdominal ultrasound with renal duplex showed fatty liver and the rest of abdominal examination is normal.



**Fig-1: Chest x-rays posterior anterior image after short course of five days of methylprednisolone treatment. (Bilateral pleural effusion chest x-rays image)**



**Fig-2: Chest x-rays posterior anterior image after five days of methylprednisolone treatment discontinuation. (Normal chest x-rays image)**

#### **DISCUSSION:**

Pleural effusion manifestation is due to several causes including infectious diseases; tuberculosis, rheumatological diseases; systemic lupus erythematosus (SLE), malignancy; lymphoma, pulmonary embolism, cardiac, hepatic and renal failures and others. However, pleural effusion incidence is equally distributed between two sexes. It was found that in females has more than two-third due to malignant diseases [1,2,3,4]. Methylprednisolone is used as a primary medication or in combination with other antimicrobial or immunosuppression agents for management of several diseases including rheumatology, malignant and infectious diseases [1]. Our patient is a healthy young female found to have bilateral pleural effusions and hypertension simultaneously, where the causes for both findings individually or in combinations must have an intensive work up to delineate a secondary etiology.

So, the history of the patient presentation reveals a dry cough, shortness of breathing occurred after completing a five days course of methylprednisolone 80 mg intravenously every eight hours that was treating an allergic reaction due to insect sting where the allergic reaction clinical improvement is observed. In the initial evaluation of this case, we observed two findings; hypertension and a bilateral pleural effusion in a previously healthy young woman. So, we started a work up toward ruling out causes of a secondary hypertension and pleural effusion in a young person.

So, the emergency department assessment of the patient disclosed that her vital signs revealed a high blood pressure of 166/90 mmHg pulse rate of 82 per minute, with respiratory rate of 18 beat per minute, temperature of 36.7 C and Saturation of 96% Room air.

So, patient was admitted for further evaluation where the blood pressure was measured in both right and left upper arm with three different and proper size cuff of sphygmomanometer automated and manual which disclosed a blood pressure of 164/92 161/93 & 177/92 mmHg in the right arm and 165/95, 159/97 & 197/92 mmHg in the left arm, pulse 80, 75 & 76 with respiratory rate 18, 20 & 16 beat per minute respectively, temperature 36.5 C and Saturation 99% in room air at sea level over the five days of inpatient admission.

The cardiovascular examination reveals good volume and synchronous pulses in both upper and lower limbs, no carotid bruit, normal first and second heart sounds and no added sounds or murmurs. The chest showed a decreased expansion on the right side compare to the left side, vocal fremitus and resonance were absent in both sides more prominent in the right side and absent air entry in both lung bases and stony dullness bilaterally were found but prominently on the right side indicating the finding of bilateral pleural effusions. The rest of examinations were unremarkable.

The laboratories investigations revealed

complete blood count that showed a high white count with predominantly neutrophilic picture reflecting demargination due to methylprednisolone. The arterial blood gas and D-dimer were normal which ruled out pulmonary embolism as possible cause of pleural effusion. The chest x-rays disclosed a bilateral pleural effusion more significant in the right lung base (image 1). Furthermore; the ultrasound of the abdomen with renal duplex showed that the patient has normal renal arteries, which rules out renal arteries stenosis, obstructive uropathy and other major renal pathology. The urine analysis and microscopy were normal.

A follow up in five days of admission, a chest x-ray was repeated to evaluate the status of the bilateral pleural effusion prior thoracentesis. However, the repeated chest x-rays revealed that the bilateral pleural effusion has been completely resolved without intervention and chest x-rays was normal (Image II). Furthermore, in the evaluation of the patient the blood pressure was found to be 119/77 and 116/74 mmHg in the right arm and 117/75 and 121/73 mmHg in the left arm applying an appropriate adult size cuff of sphygmomanometer a manually and automated, respectively. The temperature, respiratory rate and pulses were normal.

We observed that hypertension and bilateral pleural effusion both occurred after a short course of five days of methylprednisolone treatment for an allergic reaction due to unknown insect sting. However, hypertension normalized and the bilateral pleural effusion resolved completely in the fifth day of the discontinuation of methylprednisolone as repeated chest x-rays demonstrated in (Image II).

In spite of the appreciation the chronic adverse effects of methylprednisolone or corticosteroid in general, however, the clinical examination and radiological reevaluation of the patient disclosed the existence of the findings of a bilateral pleural effusion with hypertension simultaneously as an acute adverse effect due to the short course of methylprednisolone treatment that was given for five days duration. Similarly, these findings disappearance altogether in five days after discontinuation of the methylprednisolone was observed and hence confirming that these manifestation resolution of all these findings; hypertension and bilateral pleural effusions are due to methylprednisolone in the face of the absence of an existence of other etiologies.

To our best knowledge this is the first case report observed in a patient to develop significant high blood pressures, and clinical and radiological findings of bilateral pleural effusions after a five days course of methylprednisolone treatment as a rare acute adverse

effect of a short course methylprednisolone treatment which both normalized in five days after discontinuation of methylprednisolone treatment. It is the first time described in literature so, I would call this syndrome "Yahya Al -Fifi's Syndrome". However, increase the awareness of such a new syndrome will have direct beneficial influence on patient and health care system in many ways. It will minimize the unnecessary tremendous work up, cost in one hand and avoid patient suffering including psychological issues that may affect patient and patient's families on the other hand.

The challenging issue in this syndrome that it might occur during the treatment of methylprednisolone or other corticosteroid agent where, it may be passed unobserved for several reasons, for instances if the primary disease is known to cause a pleural effusion as in systemic lupus erythematosus, rheumatoid diseases and tuberculosis. However, this may be considered as part from the diseases that was not well controlled yet where this will be a quite challenging for the physicians in order to differentiate at the glance appearance of this syndrome.

This syndrome may appear at initial stage of the treatment of diseases with corticosteroid derivatives; as in this case that was treated with the methylprednisolone; or it may appear at any stage of the course of treatment for many diseases requiring steroid agent as a short, short frequent, pulse therapy and pulse therapy frequent or maintenance (high or low doses) courses which may make the physicians considering reevaluate the diagnosis and treatment which is a quite challenging approach. However, observation for the blood pressure with bilateral pleural effusions in a patient who started on corticosteroids treatment for example methylprednisolone is recommended at any stage being a rare adverse effect.

The other reasons this syndrome might be masked is in case, if the patient known to have hypertension prior to the treatment with corticosteroid. In such scenario the patient may experience an increase in blood pressure that will be managed by antihypertensive medications and passed unnoticed. In spite it is challenging issue to blame the methylprednisolone in such background, however, this case report will support close observation to detect an increase blood pressure in a previously well control hypertensive patient on anti-hypertensive medications with or without the presence of bilateral pleural effusions. The observation for such scenario required a low threshold of suspicion if an increase in blood pressure is seen without other cause with or without manifestation of pleural effusion.

At the end this Yahya Al-Fifi's syndrome is a rare syndrome and needs a multicenter study to evaluate

such syndrome manifestations and to increase the awareness and appreciation of the acute adverse effect of methylprednisolone or corticosteroid that may be passed or observed in many cases at the initial phase of treatment. However, it might be observed at any type of diseases that managed by corticosteroid, i.e methylprednisolone acutely or in long term management.

#### **CONCLUSION:**

Methylprednisolone is a highly effective treatment in various diseases management including infectious diseases, rheumatology, dermatology, and malignant diseases. However, these diseases may present with or without pleural effusion or hypertension.

We describe in this case report ; a young woman who was previously healthy , developed a bilateral pleural effusions and hypertension after she was treated with a short course of five days of methylprednisolone for an allergic reaction due to insect sting which was completely resolved. This demonstrated a normalization of blood pressure and resolution of the bilateral pleural effusions (image 1 and 2) after five days of discontinuation of methylprednisolone without intervention.

I would call these findings a syndrome and name it Yahya Al-Fif's syndrome. It is a rare, unusual clinical and radiological finding as an acute adverse effect of short course of methylprednisolone that was demonstrated in our patient which was observed to have a complete resolution of the bilateral effusion radiologically and normalization of hypertension after discontinuation methylprednisolone.

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