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A case report of ciprofloxacin induced fixed drug eruption with QT prolongation in a hypothyroid patient

Adnan Imam, Prashant ED
Department of General Medicine, Rajiv Gandhi University of Health Sciences, Khajabandanawaz Teaching and General Hospital, Gulbarga, Karnataka, India

Abstract
Fixed drug eruption (FDE) are the common adverse drug reaction. QT prolongation is also caused by various group of drugs including antiarrhythmic and fluroquinolones which can lead to potentially life threathning situations. Here we report a case of hypothyroid patient who developed FDE and QT prolongation both after the administration of ciprofloxacin.

Keywords: QT prolonfation, fixed drug reaction, ciprofloxacin, hypothyroidism

Introduction
Fixed drug eruption is a distinctive variant of drug induced dermatoses characterized by erythematous patches with or without blistering that develop within hours after the administration of the causative drug and heals with the postinflammatory residual hyperpigmentation. Fluoroquinoles are widely used antibiotics which can cause cutaneous drug reactions in about 1-2% of individuals [1]. However bullous FDE with QT prolongation is very rarely reported. Herein we report a rare case of FDE with QT prolongation induced by ciprofloxacin administration in a hypothyroid patient.

Case Report
A 19 years old male presented to us with 4 days history of multiple collapsed blisters on both arms, hands, both legs, chest and neck which were purple in colour (Figure 1, 2, 3). Erosions were also present in oral cavity and on the glans. Glans also showed some pus discharge from the erosive area with crusty lesions associated (Figure 4). The patient also complained of face swelling, swelling and dark discolouration of lips and the lower lip was more swollen than the upper lips.
He stated that 4 days back he was having fever, cold and sore throat for which he took ciprofloxacin 500mg which was obtained from a local private medical shop over the counter. After 1 hour of ingestion he began itching in whole body followed by burning sensations and subsequent development of fluid filled blisters which were purple in colour. Vitals for the patient were within normal limits except bradycardia (pulse rate was 48 b/min). The ECG (Figure 5) of the patient showed long QT interval (0.56 ms) with a QTc of (0.47 ms) as calculated by the Bazzet Formula [2]. There was no medical history of any drug reactions or any allergic reactions in the past. Patient gave a history of consuming levo thyroxine theray for few weeks which he left on his own without any medical advice. Patient was further evaluated for TSH levels which was >60 micro IU/ml. All the other routine lab tests were within normal limits including serum electrolytes, serum calcium, serum magnesium. Patch test and oral provocation testing with ciprofloxacin could not be done as patient did not gave consent for the procedure. Patient was treated conservatively by removal of the causative agent, was given antihistaminics, topical emollients and levothyroxine therapy as well for hypothyroidism. Bradycardia as well as QT interval came back to normal limits in a week after discontinuation of the causative agent as well as after administration of the levothyroxine therapy. Skin lesions started showing improvement gradually within a week leaving behind hyperpigmentation gradually over 2 months. The patient was strictly advised not to take any fluoroquinolones in the future.

Discussion
Brocq defined the term in French as eruption erythemato-pigmentee fixe meaning “fixed drug eruption” [3]. Morbilliform rash and photosensitivity have been reported with fluoroquinolones but FDE is quite uncommon.[4]The most characteristic finding of the FDE is the recurrence of similar lesions on the similar sites that heal with residual hyperpigmentation which may stay for months to years.[5] FDE is a delayed type hypersensitivity reaction which is mediated by the CD8+ T-cells. These activated T-cells kills the surrounding keratinocytes and release cytokines. Delayed type and IgE-mediated hypersensitivity reactions can also be caused by quinolones [6]. A genetic susceptibility to developing a fixed drug eruption is also associated with HLAB-22 [7, 8]. Normally the QTc is 0.33sec to 0.44sec, the QT interval is measured from the beginning of the QRS complex to the end of the T wave. Number of factors can prolong the QT interval such as antiarrhythimic drugs (amiodarone, sotalol, quinidine, procainamide, dronedarone, ibutilide, dofetilide, disopyramide) as well as large numbers of other non cardiac drugs (fluroquinolones, phenothiazines, pentamadine) [4]. The symptoms and sign of hypothyroidism include tiredness, weakness, hair loss, feeling cold, constipation, poor memory, weight gain, dyspnea, hoarse voice, menorrhagia, puffy face, hands and feet; bradycardia, peripheral edema, carpal tunnel syndrome [9]. On basis of signs and symptoms the diagnosis is then confirmed by the laboratory blood reports of TSH, T3, T4. Values above 10 µIU/ml is tagged as overt hypothyroidism.

In this case Naranjo's algorithm [10] was used to determine a probable reaction due to ciprofloxacin. The following criteria was considered: There were previous conclusive reports on this reaction (+1); the adverse event appeared after ciprofloxacin was administered (+2); adverse reaction improved when the drug was discontinued (+1); the adverse drug reaction appear when the drug was readministered (0); any alternative cause that could have caused the FDE (+2); the reaction reappeared when a placebo was given (0); the reaction was more severe when the dose was increased, or less severe when the dose was decreased (0); the patient have a similar reaction to same drug in any previous exposure (0); the adverse event was confirmed by an objective evidence (+1). As the total score is of 7 this FDE with QT prolongation was categorized as "probable" reaction to ciprofloxacin consumption.

With respect to the WHO-Uppsala Monitoring Centre causality assessment system the adverse drug reaction was found as "probable or likely" reaction due to ciprofloxacin [11]. Since the patient had overt hypothyroidism he would have already had bradycardia but QT prolongation is rarely seen in any hypothyroid patient without any associated factor. Here the patient developed FDE with a QT prolongation after the administration of ciprofloxacin which could have been fatal if the drug would not have been discontinued. QT prolongation due to ciprofloxacin consumption itself is also seen in very rare cases, which could have been developed in this case due to already present overt hypothyroidism causing bradycardia. The patient in this case may not have been developed QT prolongation if bradycardia was absent is still a question to be asked.

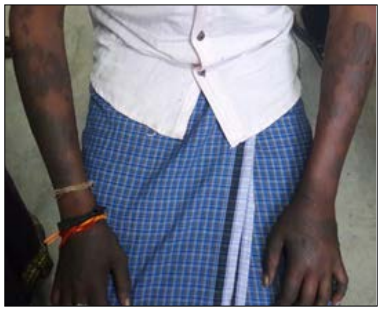

Fig 1: collapsed blisters on both arms

Fig 2: Collapsed purple colour demarcated blisters on chest and neck

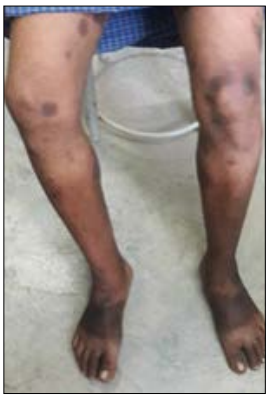

Fig 3: Collapsed purple blisters on both legs and foot

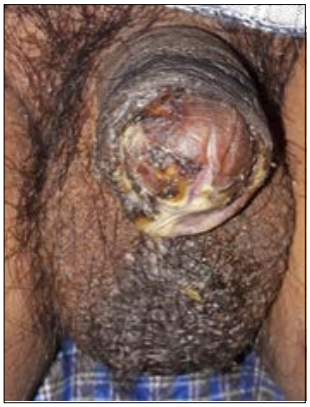

Fig 4: Pus discharge and crusty lesions on genitals

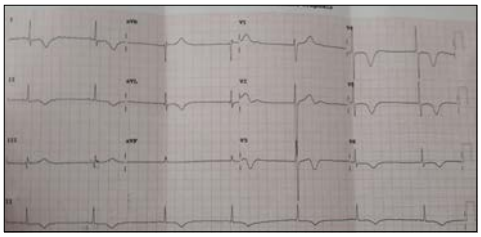

Fig 5: ECG of the patient

Conclusion

FDE with QT prolongation due to fluoroquinolones in hypothyroidism should always be included in the differential diagnosis whenever FDE is suspected. The causative drug should be stopped immediately to prevent further related complications. Fluoroquinolones are broad spectrum activity against gram positive and gram negative micro organisms so they are regularly used in day to day practice. Health care professionals should always be aware of the FDE and QT prolongation side effect (which is still rare) of fluoroquinolones.

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