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Unusual Life-threatening Adverse Drug Effects with Chloroquine in a Young Girl

Sir,

Of all patients admitted to the general wards of general hospitals, adverse drug effects account for an estimated 2–5%. We document two unusual life threatening adverse drug effects occurring in a patient who had ingested chloroquine as an empirical anti-malarial therapy for fever.

A 16-year-old girl presented with cyanosis and altered consciousness after consuming 3 tablets of chloroquine (450 mg of chloroquine base) as an empirical therapy for malaria. There was no history of any hazardous chemical exposure to industrial nitro-compounds or solvents. Examination disclosed a pale, jaundiced, disoriented and breathless patient. Apart from tachycardia, the blood pressure and the systemic examination was normal. On investigations the haemoglobin level was 11.3 g/dL and the peripheral blood smear showed microcytic red blood cells and no malarial parasites. Arterial blood gases were; oxygen saturation 95%, pH of 7.32, bicarbonate 18 milliEq/L and partial pressures of oxygen and carbon dioxide 98 and 36 mmHg respectively. Blood sugar at admission was 27 mg/dL, serum bilirubin 7.7 mg/dL with conjugated fraction 1.4 mg/dL, no haemoglobin in plasma, methaemoglobin levels 70.4% and normal RBC glucose-6-phosphate dehydrogenase. The Coomb’s test for autoimmune haemolytic anaemia was negative.

Treatment for chloroquine-induced methaemoglobinaemia and hypoglycaemia was started and intravenous methylene blue was administered as a bolus and 25% dextrose for hypoglycaemia. Over the next few days, the intravascular haemolysis subsided and the levels of circulating methaemoglobin continued to decline requiring a total of 16 mg/Kg intravenous methylene blue.

Acquired causes of methaemoglobinaemia are the result of an oxidant stress by certain drugs and chemicals, which overwhelm the reductive capacity of red blood cells. Many drugs can lead to such an oxidative stress, like nitroprusside, dapsone, primaquine, quinolones, sulphonamides and others. Chloroquine has been reported to cause acquired methaemoglobinaemia, in a case report of six American soldiers in Vietnam who developed methaemoglobinaemia after usual doses of chloroquine. Investigations in these six cases disclosed a heterozygous state of NADPH methaemoglobin reductase as the causative factor for methaemoglobinaemia. In our patient this deficiency could not be investigated due to unavailability of this investigation. The treatment of methaemoglobinaemia consists of repeated administration of methylene blue intravenously till methaemoglobin declines to less than 20%.

Our patient also had hypoglycaemia as a second adverse effect following chloroquine intake. Hypoglycaemia as an adverse effect has been seen most frequently with quinine. Although there have been case reports of chloroquine-induced hypoglycaemia, yet hypoglycaemia has occurred only when the drug was consumed in toxic doses with a suicidal intent.

Other studies have demonstrated that hypoglycaemia occurs as a manifestation of severe malaria and not due to chloroquine therapy per se. In our patient, there was no fever during the in-hospital stay and examination of the peripheral blood smear did not show malarial parasites. Moreover, to the best of our knowledge, the simultaneous occurrence of hypoglycaemia and methaemoglobinaemia as occurred in this patient with chloroquine ingestion has never been reported before.

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References
Endotracheal Intubation Related Massive Subcutaneous Emphysema and Tension Pneumomediastinum Resulting in Cardiac Arrest

Sir,

Tracheal injuries account for 15% of all airway injuries and in majority of the cases involve routine tracheal intubation and appropriate anaesthesia care.1 The authors would like to describe a patient who developed subcutaneous emphysema and tension pneumomediastinum related to multiple intubation attempts resulting in cardiac arrest.

A 42-year-old man underwent left hemimandiblectomy and radical neck dissection. Difficult intubation was anticipated as the mouth opening was 2 fingers, Mallampati grade II airway and tumour was bulging inside the oral cavity. After confirming adequacy of bag mask ventilation, muscle relaxant was given. Laryngoscopy revealed a Cormack and Lehane grade 3 glottic view and orotracheal intubation was achieved at the second attempt after using a stylet and applying external laryngeal pressure and a gentle pull on the angle of the mouth. The surgery later necessitated a change to nasal tube which required two more attempts. No air leak or loss of ventilation was observed during the IPPV. The subsequent course of anaesthesia and surgery was uneventful.

The patient was shifted to ICU for elective ventilation in view of the surgical oedema. He developed bouts of coughing on the tube when a T piece weaning trial was given with a partially deflated cuff next morning. Within 10 minutes, the oxygen saturation decreased to 80% and a swelling with palpable crepitus appeared over the face, neck, chest and upper extremities. The patient became cyanosed and developed cardiac arrest, which was treated, and a normal sinus rhythm was restored.

An x-ray chest revealed the presence of air in the subcuta-