radiotherapy. She was of lower socioeconomic strata and had not kept her wound covered. Urgent computed tomography scan of the head showed soft tissue mass with irregular and ulcerated surface, involving medial canthus of left orbit and left side of the nose, with destruction of anterior part of maxillary sinus and sphenoid bone, suggesting a soft tissue malignancy. This infestation was managed with manual removal of larvae by forceps, one by one, until no visible larvae were identified. About 60 larvae were found in the facial wound. The larvae were whitish in color and measured 12–15 mm in length. The site of infestation was irrigated with normal saline. Eventually, she was discharged on oral antibiotics. Two days later, approximately ten live larvae were extracted again from deeper tissues of facial wound. A few of them were preserved in ethanol, submitted to the Department of Entomology for identification of its species. The species was confirmed to be *Chrysomya bezziana*.

Myiasis is defined as the infestation of live vertebrate animals with dipterous larvae which, for a certain period, feed on the hosts' dead or living tissues, body fluids, or ingested food.[1] Myiasis is categorized as specific or obligatory and semi-specific or accidental depending on the life cycle of the flies concerned.[3] *C. bezziana*, also known as 'Old World Screwworm', is an obligate parasite and belongs to the order Diptera, family Calliphiphidae, and suborder Cyclorrhpha.[1] The adult fly of *C. bezziana* is a green or blue-green fly and widely distributed in tropical and subtropical countries of Africa and Asia, including Southeast Asia, India, Saudi Arabia, Indonesia, the Philippines, Papua, New Guinea, and Persian Gulf.[1,3]

The development of *C. bezziana* from egg to adult fly can be completed in 18 days under optimal conditions. The adult female fly lays eggs on live mammals and deposits around 150–200 eggs every two days at the site of the wound in body orifices.[1] The eggs hatch after 12–18 hours and the first-stage larvae, white in color and 1.5 mm in length, will emerge from the eggs and then burrow into wound or wet tissues. They feed not only on the hosts' dead tissues but also on the living tissues, and the wounds increase in sizes as they feed. In about four days, the larvae moult into the second and third stages, 4–18 mm in length. After 5–7 days, the third-stage larvae would leave the wound and fall to the ground to pupate, transformed into adult fly around seven days later.[1]

In humans, several risk factors for development of myiasis have been described, such as diabetes mellitus, infected dermatitis, psychiatric illnesses, elderly with dementia, leprosy, and mental subnormality, all of which predispose to poor hygiene and occurrence to chronic wounds.[1,4] Involvement of cancerous wounds, such as SCC, with myiasis is reported very rarely. There are four reports of cutaneous myiasis in skin tumors. The first case is of opportunistic infestation of an ulcerative, neglected SCC with *Diptera* larvae in a 63-year-old man. The second one is of traumatic myiasis in Bowen's carcinoma. The third is a report of myiasis in melanoblastoma in an 83-year-old woman, and the last one, following radiotherapy for SCC of the temple. [2] Rubio et al., reported three additional cancer-associated myiasis – one laryngeal carcinoma infested by *Chrysomya*, two others, cutaneous BCC infested by *Sarchophaga*.[5]

Our case is also an additional report of myiasis caused by *C. Bezziana* following radiotherapy for SCC on the left side of the face.

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Pulse therapy for pemphigus: The burden of proof

Sir,

Recent retrospective case series on dexamethasone...
Letters to the Editor

cyclophosphamide pulse (DCP) therapy for pemphigus concludes with “the modifications employed in this study could ensure the cure of all pemphigus patients”, “with DCP therapy...pemphigus can now be considered to be a completely curable disease”, and that “pulse therapy should be the first (and the only) choice for treatment in all pemphigus patients until some better regimen evolves”.[1] These conclusions are unacceptable for the following reasons.

Out of 143 patients selected, results are reported for 123. Patients’ characteristics (e.g., age mean (SD), duration of disease, previous treatment, body surface area affected, severity, general condition, number of patients with oral, skin, and both involvements, concomitant diseases, etc), which help in deciding whether similar results may be obtained in other patients, are not mentioned. Seventeen patients did not start/continue the treatment, while three died during treatment. Statement about the 17 patients doesn’t clarify reasons for drop-outs. Causes of deaths of three patients and whether autopsy was performed are not mentioned. These 20 patients are not included in analysis. This seriously overestimates the intervention effect, a situation akin to doing as-treated analysis instead of intent-to-treat analysis.[2]

Apparently, patients received treatment as outpatients (no mention of admission). Despite pulse therapy being experimental (i.e. not based on randomized controlled trials’ results as discussed below), patient consents were not taken.

All patients received same doses of medications irrespective of body weights. Patients with diabetes (number unknown) were given the pulses in 5% glucose (with insulin; normal saline would be better). Unmarried patients and those willing to have children were given 50 mg cyclophosphamide daily during phase I (about 3 months to >12 months), and phases II and III (9 months each) (i.e. about 21 months to >30 months; cumulative doses of approximately 31.5 g to >45 g). Cyclophosphamide produces cumulative dose-dependent gonadal failure.[3] Standard recommendation forbids use of cyclophosphamide as a first-line drug for men and women wishing to conceive post-treatment.[3] Cyclophosphamide is also teratogenic, but pregnancy tests were not done in female patients and contraception advice is not mentioned.

Only general statements are written about adverse events. Their frequency, severity, times of occurrence, actions taken, and further management are not mentioned. Although dual energy X-ray absorptiometry was not done, it is mentioned that osteoporosis does not occur with pulse therapy. Adverse events are attributed to daily oral betamethasone given in phase I, the doses of which were miniscule to probably produce significant effects. Pulse therapy can result in all usual glucocorticoid complications, as well as cardiac arrhythmias and sudden death.[4] A study from India has also reported several other adverse events due to DCP therapy.[5]

Patients were investigated pretreatment and after phases II and III of nine months each. Average duration of phase I is not written, but it lasted from about 3 months (in 62 of 123 i.e. 50% patients and not in ‘most of the cases’ as written) to >12 months. Thus, the investigations to examine toxicity of cyclophosphamide and high glucocorticoid doses for taking corrective actions were performed not according to standard guidelines,[3,6] but after enormous intervals. Brand names of medicines used are not mentioned (a standard practice in international journals), yet relapses in some patients are attributed to spurious medicines. It is written that pulses be given exactly at 28-day intervals and phases II and III be of nine months each, yet no reasons (e.g., comparison with other studies) regarding strict desirability of these durations are provided.

Fatal arrhythmias, myocardial ischemia and cardiac arrest, severe bradycardia, atrial fibrillation, ventricular arrhythmias, potentially life-threatening hyperkalemia, and increase in blood pressure and blood glucose may occur during, and in the days after, high dose ‘pulse’ glucocorticoid treatment.[7-9] Some cardiac effects are usually delayed and appear several hours after last infusion and last for several days,[8] necessitating close clinical, blood pressure and electrocardiographic monitoring.[7] As patients were treated on outpatient basis and it is not mentioned for how long after pulse administration they were observed or whether and for how long electrocardiographic monitoring was done, possibility of serious adverse events after their leaving clinic exists. Examining causes of death in the three patients was important. Furthermore, all patients who had skin lesions were given antibiotics, although frequency of bacterial skin infection is unknown. Patients received ciprofloxacin or cefadroxil (number of patients receiving either unknown). Cephalosporins can induce or aggravate pemphigus.[10] These patients
therapy was an RCT [13] in which 11 patients received 
efficacy of DCP therapy. Closest to evaluating this 
and homeopathic medicines.

Dr. Pasricha’s influence in India with regard to 
treatment of pemphigus is noticeable. Despite our 
admiration of him, examining the evidence backing 
above-mentioned claims is important. Astronomer 
and rationalist Carl Sagan once said that extraordinary 
claims require extraordinary evidence.\cite{11} Science is 
self-questioning; experiments test our hypotheses. 
For knowing treatment effect, these experiments are 
randomized controlled trials (RCTs). In the hierarchy 
of evidence, expert opinion is at the lowest level 
and next is case series, lagging considerably behind 
conclusive evidence.\cite{12} RCTs (and meta-analysis) are 
the gold standards for determining treatment efficacy. 
Probably due to precisely these reasons (i.e. lack of 
evidence of efficacy) authors rightly forbade ayurvedic 
and homeopathic medicines.

Searching evidence, we found no RCT that tested 
efficacy of DCP therapy. Closest to evaluating this 
therapy was an RCT\cite{13} in which 11 patients received 
intravenous 100 mg dexamethasone on three 
consecutive days with cyclophosphamide (500 mg) on 
day one (D/C group). Pulses were initially repeated every 
2–4 weeks and then at increasing intervals. In between 
pulses, oral cyclophosphamide (50 mg) was given 
daily for six months. The control group (11 patients) 
received oral daily methylprednisolone (2 mg/kg) and 
azathioprine (2–2.5 mg/kg), subsequently tapered 
(M/A group). Two years after treatment initiation, 
5/11 patients in D/C group were in remission and 6/11 
patients had progression. In M/A group, 9/11 patients 
were in remission and one had progression. There 
were more relapses with M/A therapy after remission; 
also side effects were more common. These differences 
were insignificant. Authors concluded that because of 
high number of progressions with D/C therapy, they 
could not confirm the encouraging results of earlier 
reports.

Until RCTs clearly show superior efficacy of DCP 
therapy in pemphigus, patients’ best interests 
will be served by treatment comprising daily oral 
prednisolone and a glucocorticoid-sparing drug. 
Efficacy of prednisolone is enhanced with a cytotoxic 
drug.\cite{14} In this RCT, the most efficacious cytotoxic 
drug for glucocorticoid-sparing was azathioprine 
versus cyclophosphamide pulse (1000 mg monthly) 
and mycophenolate mofetil. Without evidence, it is 
premature and unscientific to favor pulse therapy for 
pemphigus. Let science be a candle in the dark.

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