

Immunodermatology and Blistering Disorders

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Excessive immunoglobulin molecules catabolized pathogenic autoantibodies: A case study of a patient with steroid-resistant pemphigus foliaceus during intravenous high-dose immunoglobulin therapy

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Pemphigus foliaceus is an autoimmune blistering disease, which is associated with IgG autoantibodies against desmogleins (Dsg) 1. We describe a 69-year-old man with steroid-resistant and severe pemphigus foliaceus and results of a weekly follow-up study of the anti-Dsg1 antibody (Ab) values by enzyme-linked immunosorbent assay (ELISA) during intravenous high-dose immunoglobulin (IVIg) therapy. He developed erosion and erythema, and was given diagnosis of pemphigus foliaceus by characteristic results of histochemical and immunological analysis of skin specimen and sera (Dsg1 ELISA index:1420). A combination therapy of systemic corticosteroid (50 mg/day) and mizoribine (150 mg/day) following three courses of methylprednisolone pulse therapy had been ineffective. During these therapies, ELISA value of anti-Dsg1 Ab was increased from 900 to 2662. After these therapies, although five courses of plasmapheresis had been performed, the ELISA values increased up to 3763. As bacterial infection had occurred, we could not increase the grade of immunosuppressive therapy. Three courses of IVIg therapy (400 mg/kg/day, 5 days) were performed in combination with systemic corticosteroid (50 mg/day) and ciclosporin (200 mg/day). The ELISA values had been decreased to 42%, 60% and 74% after three courses of IVIg therapies respectively, when serum IgG levels decreased approximately from 3,500 to 1,500 mg/dL, and increased in turn when IgG levels reached down to 1,400 mg/dL, a normal range. We inferred that because the quantity of auto-Ab was decreased during the phase of degradation of high levels of IgG, auto-Ab might be subjected to catabolism induced by extremely excessive immunoglobulin molecules. This interpretation may be supported also by the fact that the ELISA values of anti-Dsg1 Ab increased again when serum IgG level decreased to normal range, because anti-Dsg1 Ab synthesis had not yet been well controlled with systemic corticosteroid and ciclosporin. Additional IVIg therapy with increased doses of systemic corticosteroid (80 mg/day) and azathioprine (100 mg/day) was performed. After that, the ELISA values continued to decrease and without rebound phenomenon, suggesting anti-Dsg1 Ab synthesis had then been well controlled with increased doses of systemic corticosteroid and ciclosporin. These observations suggest that the increase in total serum IgG in IVIg therapy resulted in a marked increase in catabolism of all immunoglobulin molecules including auto-Abs.

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Erlotinib-induced toxic epidermal necrolysis localized to previous sites of radiation and herpes zoster infection: A two-hit hypothesis

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Background: Epidermal growth factor receptor (EGFR) inhibitors are used in the treatment of refractory colorectal adenocarcinoma, unresectable squamous cell carcinoma of the head and neck, metastatic pancreatic cancer, and unresponsive non-small-cell lung cancers. Several dermatologic sequelae have been recognized, with the most frequent being a papulopustular eruption. Since the severity of this form of eruption is known to correlate directly with favorable tumor response, cutaneous reactions rarely are dose-limiting.

Observation: We report a Cantonese patient with stage IV lung adenocarcinoma who developed full thickness epidermal necrosis localized to areas of previous skin trauma (previous radiation and herpes zoster infection) following administration of erlotinib, an EGFR-inhibitor. We diagnosed the patient with erlotinib-induced toxic epidermal necrolysis.

Conclusions: This case represents a severe, dose-limiting complication of erlotinib that must be recognized as a potential complication of therapy. We offer a two-hit hypothesis, by which previous external beam radiation or zoster-associated inflammation resulted in epidermal vulnerability (hit #1), and that subsequent exposure at these sites to an EGFR inhibitor led to near-complete epidermal apoptosis (hit #2). The patient's ethnicity also may have played a role in the pathogenesis, as this population has been shown to have decreased constitutive levels of EGFR in normal, non-cancerous tissue.

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Pemphigus vulgaris and pregnancy

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Background: Pemphigus vulgaris (PV) coinciding with pregnancy is extremely rare. **Objectives** We sought to study the available literature to determine how PV and pregnancy is managed and the corresponding neonatal and maternal outcomes.

Methods: A retrospective search of Medline was conducted and identified the 49 cases to date, to our knowledge, of pemphigus during pregnancy.

Results: There are 49 pregnancies associated with PV in 38 reports in the literature. 25 of the 39 symptomatic mothers exhibited oral lesions while 28 had cutaneous lesions. 6 were asymptomatic during their pregnancies. Corticosteroids were the mainstay of treatment in 37 of 49 patients with doses ranging from 5 – 300 mg / day. Concomitant therapies included plasmapheresis in 1 patient, plasma exchange in 1 patient, dapsone in 1 patient, azathioprine in 5 patients, and antibiotics to treat PV related infections. Of the 49 neonates, 20 (40%) had PV lesions when born, 24 (50%) were asymptomatic, and 5 (10%) were stillborn. All neonatal PV lesions resolved within 1 – 4 weeks either spontaneously or with mild treatment with topical medications. Of the 5 intrauterine deaths, one was due to obstetrical complications unrelated to PV, two were of unknown cause, and two were likely due to complications associated with steroid and immunosuppressive agents.

Limitations: Since it is a rare disease in young women, it is rare to see this disease in pregnancy as a result the number of cases in the literature is relatively small.

Conclusions: After data analysis, we present guidelines for the management of pemphigus vulgaris in the pregnant patient and neonate.

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Pseudoporphyria associated with chronic renal failure: Experience with oral N-acetylcysteine treatment in three cases

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Pseudoporphyria is a rare, acquired bullous disorder with clinical and histopathological features similar to those of porphyria cutanea tarda despite normal porphyrin metabolism. It is associated with chronic renal failure, excessive sun exposure and numerous medications such as naproxen, furosemid and hydrochlorothiazide. So far, there is no specific treatment for pseudoporphyria, although sun protection and discontinuation of the offending drugs may provide some benefit.

Oral N-acetylcysteine has recently been reported to be an effective treatment option for five cases in the English literature. We describe our experience with N-acetylcysteine treatment in three patients of pseudoporphyria associated with chronic renal failure.

Case 1: A 38-year-old woman with chronic renal failure undergoing hemodialysis had a 2-month history of multiple tense blisters, erosions with crusting and atrophic scars on her face and dorsum of the hands. She also had chronic hepatitis C infection.

Case 2: A 56-year-old woman presented with a 2-week history of multiple tense blisters, eroded and crusted areas on her face and dorsal hands. She had been undergoing hemodialysis for chronic renal failure for the last seven years

Case 3: A 72-year-old woman presented with a 18-month history of multiple hemorrhagic blisters on her abdomen and dorsal hands. She had been on hemodialysis for chronic renal failure for one year. Histopathological examinations revealed subepidermal bullae in all patients. Direct immunofluorescence studies were negative. Urine porphyrin analysis were within normal limits. Blood porphyrin analysis was performed on samples from cases 1 and 2, and the results were normal. All three patients were diagnosed with pseudoporphyria and oral N-acetylcysteine (1200 mg/daily) treatment was begun in addition to strict sun protection. After one-month of treatment, new bullae development had stopped in cases 1 and 3 and no further lesions occurred during a 6-month follow-up. However, new bullae continued to develop in case 2 despite dose increment (1800 mg/daily).

Oral N-acetylcysteine, which has been effective in two of our cases, may offer a safe therapeutic option for some patients of pseudoporphyria associated with chronic renal failure. However, further controlled studies are required to better define its efficacy.

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