Rare disease

Pemphigus vulgaris in a pregnant woman and her neonate

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Summary

A 23-year-old pregnant woman in her second trimester of pregnancy presented with blisters on the face, abdomen and the leg. Based on the clinical presentation and skin biopsy (histopathology and direct immunofluorescence) the diagnosis of pemphigus vulgaris was established. The child born to this patient also had similar skin lesions. The lesions in the mother and the child improved after treatment. The authors report a rare case of pemphigus vulgaris in a pregnant lady and neonatal pemphigus in her child, both of whom were treated successfully.

BACKGROUND

Pemphigus in pregnancy is rare with impact on pregnancy and its outcome. Literature review on pemphigus in pregnancy is limited to 47 cases in the form of case reports and small case series. The neonatal pemphigus is a very rare complication and there are only 29 reported cases of simultaneous occurrence in pregnant women with pemphigus on literature review.^{1–3}

CASE PRESENTATION AND TREATMENT

A 23-year-old Burmese national, with no known chronic illness or medication use, presented during her 22nd week of pregnancy with multiple oral ulcers in buccal mucosa and ulcers over the left big toe for one month. She received oral acyclovir, cloxacillin and was advised to come after a week for follow-up that she defaulted. At 33 weeks of gestation, she came to the emergency department due to painful oral lesions and inability to take any solid food. On examination, there were multiple ruptured blisters (figures 1–6), no hepatosplenomegaly, singleton fetus with cephalic presentation and rest of the examination was normal. Differential diagnoses as mentioned below were considered. In view of recurrent

Figure 2 Lesions around lips, as first presentation; lesions resemble herpes simplex.

Figure 1 Lesions on the abdomen of the pregnant woman, lesions resemble those of herpes zoster.

Figure 3 Lesions on the back; some blisters are ruptured, pigmented, healing.

oral ulcers and new skin blisters appearing all over the body, unresponsive to acyclovir (oral and parenteral) along with multiple courses of intravenous antibiotics, skin biopsy (histopathology and immunofluorescence) and antinuclear antibody (ANA) tests were done considering the possibility of auto-immune blistering disease or systemic lupus erythematosus (SLE). The biopsy results were confirmative of pemphigus vulgaris (PV). ANA was also positive, but not suggestive of SLE. She was started on oral prednisolone 40 mg daily following these results. Oral ulcers improved, lesions on the lips started healing

Figure 4 Lesions on the dorsum of the hand, blisters in the healing stage.

Figure 5 Lesions on the foot, ruptured blisters, pigmented and healing.

and lesions over hands and fingers began to dry up. The mother underwent emergency caesarean delivery due to fetal distress and it was noted that the neonate had multiple bullous skin lesions over the front and back of the trunk, buttocks and groin (figures 7–9). Skin biopsy was done and sent for histopathology and immunofluorescence, which confirmed PV in the neonate. In the mother, there were also appearance of new bullous lesions on the left forearm while she was on prednisolone. Hence she was started on oral methotrexate 12.5 mg/week gradually increased to 20 mg/week with folic acid. She was advised not to breastfeed. However, weeks after starting methotrexate, new tense bullae were noted at the right axilla, forearm, abdomen and thigh and treated with occlusive dressing. She was given two courses of intravenous immunoglobulin (Ig) 2 g/kg/day for 5 days at the interval of 1 month in view of partial response to prednisolone and methotrexate. The patient responded very well to intravenous Ig and showed marked improvement with no new active lesions (figure 10). Her lesions over the body dried up. The baby was diagnosed with neonatal PV and cutaneous candidiasis. The skin lesions improved after treatment with steroids, intravenous antibiotics and

Figure 6 Lesions on the abdomen, ruptured, denuded skin (changed in appearance compared to figure 1, after oral and intravenous acyclovir).

Figure 7 Blisters on the arm of the newborn girl.

Figure 8 Lesions in the genital region of the newborn girl with candidiasis.

Figure 9 Blisters on the foot of the newborn girl.

antifungal treatment (figure 11). We observed a few complications during treatment as depicted in the table 1, and treated them successfully.

INVESTIGATIONS

Apart from the earlier mentioned confirmatory tests for PV that were positive, all other tests were normal. Tzanck smear for herpes, herpes simplex virus (HSV) antibodies, PCR for HSV 1 and 2 were negative. Routine urine examination was normal and negative for porphobilinogens. Lab investigations for hepatitis B virus (HBV), hepatitis C virus (HCV) and HIV infection were negative. At different

Figure 10 Lesions on the abdomen completely healed leaving behind pigmentation after oral prednisolone, methotrexate and intravenous immunoglobulin.

Figure 11 Lesions in the genital area of the newborn girl after treatment for candidiasis and on prednisolone.

intervals skin swab cultures, blood, urine, vaginal, cervical cultures were done, which mainly showed gram negative bacteria, candida and chlamydia infections.

DIFFERENTIAL DIAGNOSIS

- ▶ Herpes simplex infection
- ▶ Herpes zoster
- ▶ Steven Johnson's syndrome
- ▶ Systemic lupus erythematosus
- ▶ Toxic epidermal necrolysis
- ▶ Staphylococcal scalded skin syndrome
- ▶ Impetigo
- ▶ Herpes gestationalis (Pemphigoid gestationalis)
- ▶ Ig A deposition diseases
- ▶ Bullous pemphigoid
- ▶ Porphyria

DISCUSSION

The word pemphigus comes from the Greek word pemphix that means to blister or bubble. It describes a group of disorders that have varied presentation involving skin and mucous membranes; PV produces blisters in skin and

Table 1 Complications observed during treatment

Pedal oedema due to hypoalbuminaemia
Hypokalaemia
Hospital acquired skin infections
Preterm labour with fetal distress requiring emergency caesarean section
Prolonged hospital stay
Neonatal pemphigus (less severe)
Neonatal sepsis

Table 2 Medications for pemphigus vulgaris

Cyclophosphamide 2 mg/kg/day
Azathioprine 2.5 mg/kg/day
Methotrexate 20 mg/week
Mycophenolate mofetil 3g/day
Prednisolone 1.5 mg/day

mucous membranes, while pemphigus foliaceus involves skin only, paraneoplastic pemphigus produces blisters in patients with underlying malignancy and endemic pemphigus is seen in Brazilian population.⁴ PV is an autoimmune, blistering, inflammatory disease of epidermal layer of the skin. The disease occurs in genetically susceptible individuals due to environmental triggers that activate T and B cells producing autoimmunity, memory B cells producing antibodies to desmogleins.^{5–6} There are four types of desmogleins (DSG) which bind the cells in the tissues; DSG-1 and DSG-3 are found in stratified squamous epithelia like the skin, DSG-3 found in the mucosa, DSG-2, found in simple epithelia and heart and DSG-4 found in hair follicles.⁷

The disease commonly affected humans during 4–6th decades of life.^{8–9} Clinically, patients present with thin blisters on the skin and mucous membranes, prolonged severe course with a mortality of 5–10%.^{7–10} The diagnosis is made by the typical clinical presentation (appearance and healing of lesions on skin and mucous membranes), excluding other differential diagnosis, skin biopsy and immunofluorescence, which show characteristic intraepidermal separation (acantholysis) and IgG deposition intraepidermally. Antibodies detected in pemphigus are of IgG type – IgG1 and IgG4^{7–8–11} – the damage to the skin mainly mediated by IgG4 subclass antibodies.¹¹ The antibodies formed in the mother cross the placenta to produce the disease in the newborn. In one study it was observed that these antibodies in the neonate disappear after many weeks and hence it is less severe in the neonate, as observed in our case.¹² Our patient presented during her second and third trimesters of pregnancy with blisters involving mucous membranes (oral, eye, pharynx and probably oesophageal mucosa) and skin of various parts of body from lips to limbs, trunk, genital area; lesions appeared and healed at different points in time. The new lesions showed positive Nikolsky's sign. Patients usually seek medical attention because of dysphagia or odynophagia caused by oral mucosal lesions or because of blisters in the skin, as noted in our patient. More than 90% patients present at 40 years of age but it has been reported between 15 and 87 years of age.⁴ Oral steroids till the lesions heal are sufficient in 40% cases, while in the remaining 60% cases other immunosuppressants are required.⁴ The treatment outcomes are measured by PV disease area index as well as pemphigus severity

score.¹³ Therapy failure is considered if new lesions appear or old lesions do not heal with the medications as shown in table 2 for 12 weeks.¹³

The disease requires long-term treatment with a mean of 6 months, up to 36 months.⁴ The patient is considered to be in remission off therapy, in the absence of new lesions or established lesions for at least 2 months without treatment and remission on therapy, in absence of lesions with minimal therapy; which is defined as requirement of 10 mg/day of prednisolone or 50% of the dose of immunosuppressants as required in therapy failure.¹³ Rituximab, a monoclonal antibody against CD-20, is used in refractory cases of PV. It acts by depleting the B cells producing antibodies against desmogleins. Serological tests for HIV, HBV and HCV should be done before administering rituximab. The dose is 375 mg/m² administered at weekly intervals for 4 weeks is the standard dose of rituximab.¹⁰ Other modes of therapy in severe cases are administration of intravenous Ig, plasmapheresis, plasma exchange and immunosuppressives.³ Intravenous Ig decreases pemphigus antibodies probably by blocking synthesis of pathologic antibodies or enhancing the catabolism of pemphigus antibodies.¹⁴ Our patient received intravenous Ig apart from prednisolone and methotrexate. Common complications observed in these patients are skin infections, sepsis, hypokalaemia, hypoalbuminaemia and Cushing's syndrome due to steroid usage. Our patient was treated for 5 months and is still under follow-up. She developed skin infections and sepsis many times, and treated with antibiotics. She also developed hypokalaemia and hypoalbuminaemia that were treated successfully. Her facial plethora related to steroid usage improved after reducing the dosage of steroids. The girl child born to the patient had a milder form of the disease and treated successfully with steroid alone.

Learning points

- ▶ The disease in pregnant women is difficult to treat, while pemphigus in the neonate is milder.
- ▶ The correct choice of medications is important.
- ▶ Intravenous Ig and rituximab are of proven benefit in refractory cases.

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Competing interests None.

Patient consent Obtained.

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