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Incidence of vesicobullous and erosive disorders of neonates

Goyal Tarang[1], *Varshney Anupam*[2]

1. Department of Dermatology Venereology and Leprology, Muzaffarnagar Medical College and Hospital, Muzaffarnagar, Uttar Pradesh, India.
2. Department of Pathology, Muzaffarnagar Medical College and Hospital, Muzaffarnagar, Uttar Pradesh, India.

Corresponding author:

Dr. Goyal Tarang

Muzaffarnagar Medical College

Opp.Begrajpur Industrial Area,

115 Km Stone, Delhi-Dehradun Road, Muzaffarnagar, Uttar Pradesh, India

E-mail: *tarang_derma@yahoo.co.in*

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Abstract

Background: The entity vesicobullous disorders in neonates encompasses a varied spectrum of disorders varying from self limiting to potentially life threatening infectious diseases.

Objective: To analyse the incidence of dermatoses in neonates, stress the importance of simple noninvasive diagnostic procedures with perspective to actual need of active intervention.

Patients and methods: Forty four neonates with vesicobullous lesions in departments of dermatology and pediatrics were evaluated with respect to diagnosis, required treatments and follow ups.

Results: Out of total 44 neonates, 29 were males and 15 females. Iinfectious dermatoses accounted for: 9% - staphylococcal pyoderma, 4,5% - Group A Streptococcal impetigo, 4,5% - neonatal tinea faciei, 2,3% - neonatal candidiasis, 2,3% - neonatal varicella/chickenpox and 2,3% - scabies. Transient skin lesions were: 41% - erythema toxicum neonatorum, 9% - milia crystallina, 6.8% - neonatal acne, 4,5% - sucking blisters, 2,3% - transient neonatal pustular melanosis, 2,3% - epidermolysis bullosa simplex, 2,3% - incontinentia pigmentii, 2,3% - eosinophilic pustular folliculitis, 2,3% - pemphigus vulgaris and 2,3% - neonatal herpes simplex.

Conclusions: Care has to be instituted to identify accurately infectious diseases and distinguish them from benign transient neonatal dermatoses. Some disorders first manifesting during the neonatal period may also represent harbingers of potential problems during adulthood. Finally, it is relevant to judge whether the treatment is required or not. (*J Dermatol Case Rep*. 2011; 5(4): 58-63)

Introduction

A number of dermatoses in neonates present as vesicles, pustules, bullae, erosions and ulcerations during their first 28 days of life.[1] They differ considerably in etiology, age of first appearance and pattern of lesion distribution, necessitating a systematic approach to their evaluation and timely treatment. Also, differentiation between transient and noninfectious and potentially life threatening disorders is essential for saving unnecessary anxiety amongst both treating physician, parents and also saving valuable lives by timely diagnosis and intervention. We studied 44 neonates with vesicobullous skin disorders with emphasis on differential diagnosis, simple diagnostic tests and follow up.

Patients and methods

This study was carried out in 44 neonates with vesicobullous presentations in our teaching institute during a period of two years from January 2008 to December 2009. All the neonates attending dermatology or paediatrics OPD and admitted in paediatrics neonatal ward unit with these lesions were examined and followed up for a period of twenty eight days of birth. These infants were examined both by a dermatologist and a paediatrician and diagnosis made on the basis of clinical data. Apart from this the mode of delivery, Apgar score, gestational age at birth, birth weight, sex, history of drug intake by mother during pregnancy, history of any maternal illness and consanguinity were also recorded.

Wherever required, additional diagnostic tests such as bacterial and fungal cultures, scrapings for KOH examination, peripheral blood smear, Tzanck smear, biopsy were done to confirm the diagnosis. Hospital Ethics committee written prior approval for conducting the study was obtained.

Results

The study group consisted of 44 neonates aged 1-28 days old, of which 29 were males and 15 were females. 29 neonates (10 males and 19 females) were having low birth weight (< 2500 g birth weight as per WHO Criteria). Of the infectious bacterial dermatoses, 4 neonates (9% of total cases) were of Staphylococcal pyoderma presenting as bullous impetigo. Two neonates (4.5%) were of Streptococcal impetigo. There were neither any desquammation nor any systemic signs present in them. One case aged 16 days (2.3 %) was diagnosed to be of neonatal candidiasis. There was involvement of diaper area, umbilicus and other intertriginous areas showing erythema with small papules and pustules with distinctive satellite lesions present at the periphery. Diagnosis was confirmed by KOH examination and culture which showed budding yeast cells with pseudohyphae. 2 cases (4.5%) of neonatal Tinea infection were suspected and confirmed by KOH examination and culture on Sabroaud's agar media.

One case (2.3 % of total cases) of neonatal varicella zoster was seen in a 23-day-old infant with involvement of skin and mucus membranes. Family history of chicken pox was positive in other siblings. Fever and constitutional signs were present. Tzanck smear showed multinucleate giant cells. The neonate was put on I/V Acyclovir (60mg/kg/day) in divided doses and responded well.

One neonate (2.3 %) had scabies with extensive involvement of head and neck, face, palms and soles with vesicular crusted lesions. The child showed irritability with poor feeding. Mother on examination had scabies lesions.

One case (2.3%) of neonatal herpes simplex with meningeal involvement was seen. Unfortunately the child could not be saved.

Amongst the transient skin lesions, erythema toxicum neonatorum (ETN) was most frequently observed with 18 patients (41% of total cases) presenting with these lesions. Eruption began within first 24 hours as blotchy erythematous macules, surrounding 1-3 mm papule or pustule. The rash first started on face and spread rapidly in a centrifugal manner to involve other body areas. Maximum number of cases reported (9 cases) were on second day of life, followed by 7 cases on first day. Least number of cases were seen on fourth day (2 cases). Maximum number of cases (10 cases) were seen in >2500 g birth weight, followed by 5 cases in 2000-2500 g birth weight group. 3 cases were in < 1000 g birth weight group. In 15 cases the rash persisted for 1-2 weeks time while in 3 cases it persisted for more than 3 weeks.

1 case (2.3%) of Transient neonatal pustular melanosis was observed. The neonate was term baby and male in gender.

4 cases (9% of total cases) of Miliaria crystallina were recorded. They were seen in summer humid months. Most

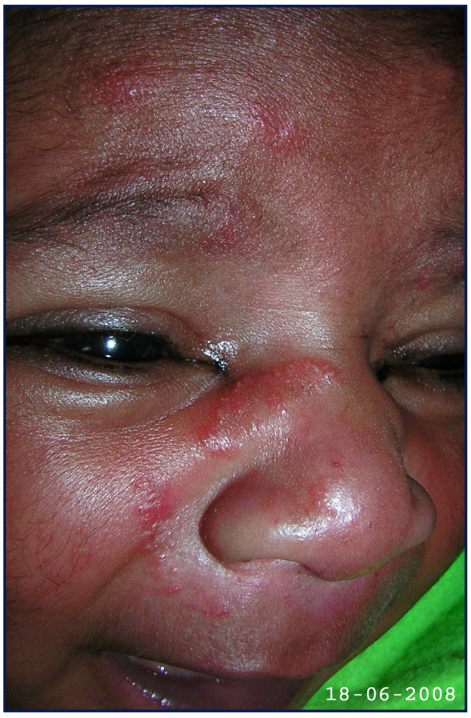

Figure 1
Tinea faciei in a neonate showing annular lesion with peripheral extension and vesicular lesions at margins.

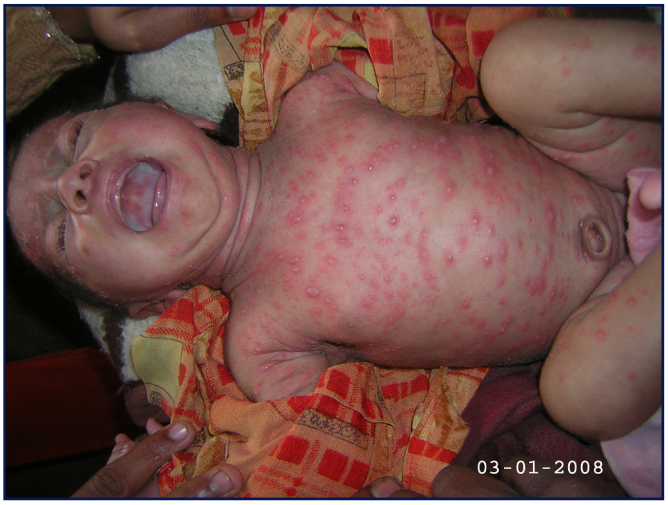

Figure 2. *Varicella zoster / chicken pox rash with vesicular rash on an erythematous base. Note the mucosal lesions on palate.*

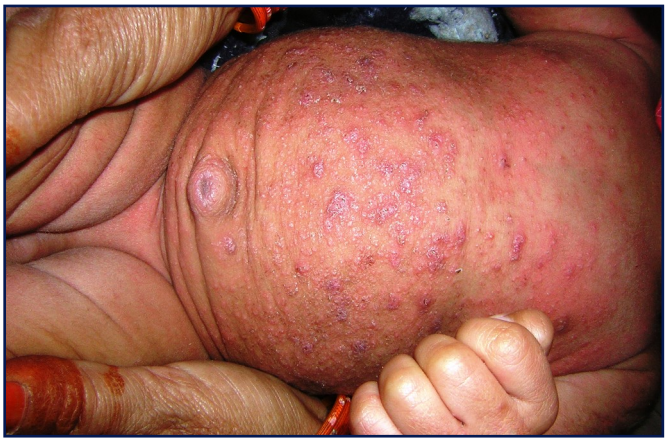

Figure 3. *Scabies rash showing extensive involvement. Typical lesions present on hand.*

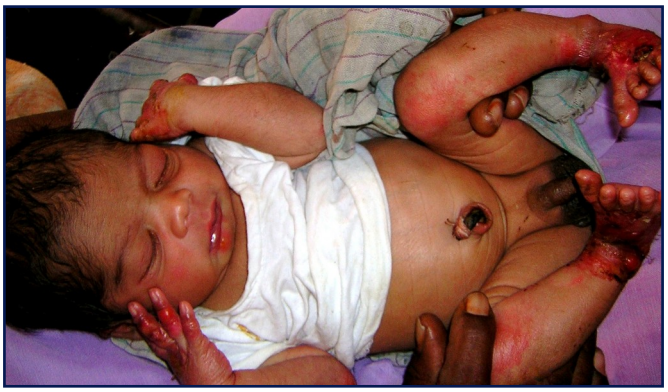

Figure 4. *Epidermolysis bullosa simplex showing erosive vesicobullous lesions at sites of friction.*

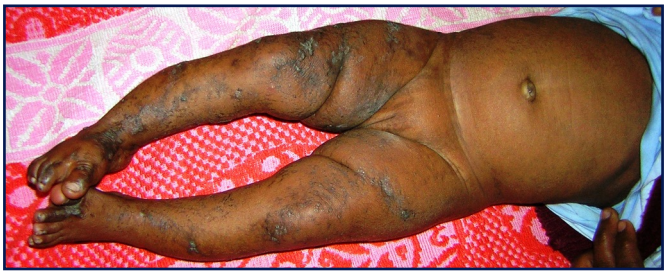

Figure 5. *Incontinentia pigmentii in a female neonate.*

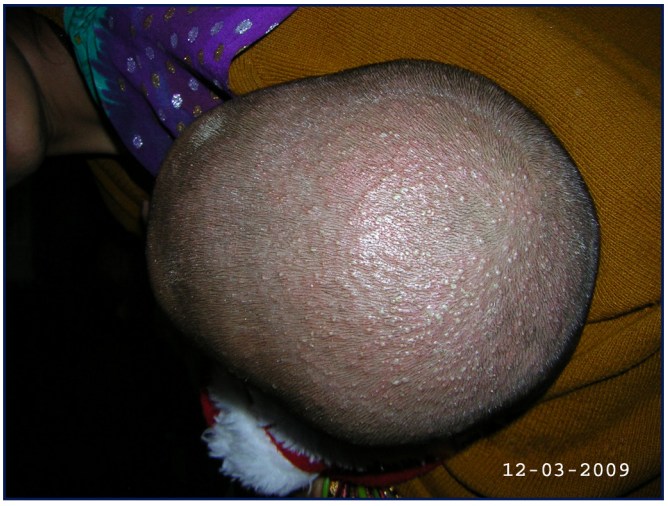

Figure 6. *Eosinophilic pustular folliculitis of scalp region showing pustular lesions.*

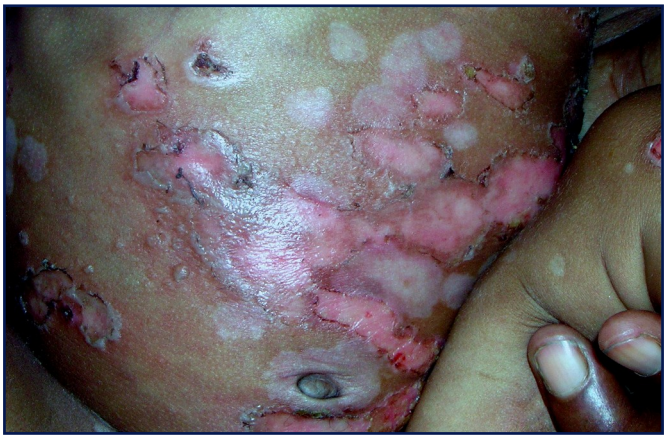

Figure 7. *Pemphigus vulgaris showing flaccid bullae and erosions.*

common sites involved were forehead, followed by nose, flexures, chest and groin. All of them had vesicular lesions with fine desquamation and no associated systemic signs or symptoms.

3 cases (6.8%), one male and two females of Neonatal cephalic pustulosis (Neonatal acne) were seen in our study. All three were in 3rd week of life. Papules and pustules on an erythematous base were distributed on cheeks, forehead regions. Trunk and back were spared.

Sucking blisters were present in 2 cases (4.5%). Both had involvement of fingers. Lesions were present since birth. Solitary flaccid bullae were noted. Some very rare and interesting dermatoses were also observed in our study.

One case (2.3%) of Epidermolysis bullosa simplex was seen with skin involvement seen as serosanguinous non-scarring vesicles and bullae on peripheral extremities, elbows, knee joints and buttocks. Hair, nails and mucus membranes were normal. VDRL was non reactive. Parents did not consent for biopsy in this case.

One case (2.3%) was observed as Incontinentia Pigmentii in a female neonate of 25 days of age. Verrucous, linear hyperkeratotic plaques were present on both lower extremities and back along the lines of Blaschko. Lesions were confirmed on histopathology. No cutaneous or extracutaneous abnormality was detected. Patient was advised regular follow up for monitoring of CNS manifestations as seizures, dental or eye involvement.

One case (2.3%) of Eosinophilic pustular folliculitis was seen in a male neonate of 15 days age presenting with sterile pustules on scalp and face and occurring in crops. A smear of pustule contents demonstrated primarily eosinophils without bacterial or yeast forms. Peripheral blood eosinophilia was present.

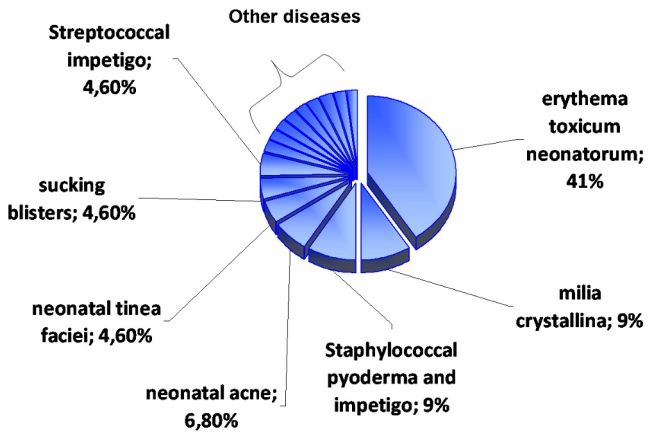

Figure 8. *Most common vesicobullous diseases in neonates.*

We report one case (2.3%) of Pemphigus vulgaris presenting as flaccid bullous lesions on whole body and was confirmed by biopsy and histopathology and subsequently immunoflorescence. Frequence of vesiculobullous diseases in our neonate patients is presented in Figure 8. Clinical details are summerized in Table 1.

Table 1. Diagnosis and management of neonates in this study.

S No.	Diagnosis	Diagnostic studies done during the study	Treatment given
1	Erythema toxicum neonatorum	Tzanck smear: Eosinophils	None, Reassurance
2	Miliaria crystallina	Wright's stain, Gram's stain, Giemsa stain: Negative	Reduction of room temperature with air circulation, cooling soothing agents
3	Staphylococcal pyoderma and impetigo	Gram's stain: Gram positive cocci in clusters Culture	Antibacterial washes containing chlorhexidine, triclosan Antimicrobial ointments as Fusidic acid, Mupirocin Systemic antibiotics as beta - lactams, macrolides
4	Neonatal acne	Giemsa stain: Neutrophils, occasional yeast forms	Erythromycin, Benzoyl Peroxide,Topical Imidazoles
5	Sucking blisters	Clinical	None required
6	Group A Streptococcal impetigo	Gram's stain: Gram positive cocci in chains. Culture	Antibacterial washes containing chlorhexidine, triclosan Antimicrobial ointments as Fusidic acid, Mupirocin Systemic antibiotics as beta lactams, macrolides
7	Neonatal Tinea faciei	KOH: hyphae and arthroconidia visible Culture on fungal media	Topical antifungals as Azoles, Terbinafine, allylamines
8	Transient neonatal pustular melanosis	Tzanck smear: Polymorphs, occasional eosinophils.	None, Reassurance
9	Epidermolysis bullosa simplex	Biopsy of fresh blisters EM, IF, Gene analysis	Avoid friction Mild broad spectrum topical antibiotics Non adhesive dressing
10	Incontinental pigmentii	Biopsy of lesion	None available Baseline ophthalmic, neurological and dental evaluation
11	Eosinophilic pustular folliculitis	Wright's stain: Eosinophils Biopsy of lesion	Potent topical corticosteroids Oral antihistaminics
12	Pemphigus vulgaris	Biopsy of perilesional skin Tzanck smear: large acantholytic cells with basophilic cytoplasm	Most cases resolve spontaneously in 3 weeks Parenteral steroids Immunosuppressants
13	Neonatal candidiasis	KOH: budding yeast cells and pseudohyphae Culture on fungal media	Topical Clotrimazole, Nystatin, Econazole, Miconazole 1% Hydrocortisone cream for 1-2 days if inflammation is prominent
14	Neonatal varicella/chickenpox	Tzanck smear: multinucleate giant cells DFA, Viral culture, serology, PCR	I/V Acyclovir
15	Neonatal scabies	Mineral oil preparation: mite, scyballa or eggs visible	Permethrin 5% for 4 hours head to toe is treatment of choice
16	Neonatal Herpes simplex	DFA, Viral culture, Serology, PCR	Acyclovir 20 mg/kg IV 8 hourly for 14 days

Discussion

Of all the infectious dermatoses, we found impetigo to be the commonest (13.5% of total cases). Both staphylococcus and streptococcus were found on Gram's stain and culture. Two variants, bullous and non-bullous have been seen. Bullous impetigo is at the mild end of a spectrum of blistering skin diseases caused by a staphylococcal exfoliative toxin that, at the other extreme, is represented by widespread painful blistering and superficial denudation (Staphylococcal Scalded Skin Syndrome). Non-bullous impetigo presents as honey coloured crust and mild systemic symptoms. Baruah *et al*[1] in their study have reported an incidence of 3% of bullous impetigo in Pondicherry. Nanda *et al*[2] found the incidence of impetigo to be 23% in New Delhi. Uncomplicated impetigo needs only topical antibiotics and cleaning the affected area.

The clinical manifestations candidiasis in the neonate varies ranging from localized infections of the skin and mucous membranes to life-threatening systemic infection with multisystem organ failure. Neonatal candidiasis is usually observed after the seventh day of life with involvement of intergluteal, cervical folds as scaling bright red plaques with satellite pustular lesions at the periphery. Host risk factors, such as prematurity and the use of invasive procedures, are important determinants that influence the severity and type of neonatal Candida infection. Baruah CM *et al*[1] found the incidence of cutaneous candidiasis to be 2.6% in their study. We found 2 cases of tinea in our study.

Varicella (Chicken pox), affects 2% of babies born to mothers who develop chickenpox at 13 to 20 weeks gestation and presents with skin scars, limb defects, growth retardation, chorioretinitis and neurological abnormalities.[3] Fetuses exposed to this infection are also at risk of spontaneous abortion, premature labour and the development of herpes zoster in infancy.[4] Infection presenting in first 28 days of life is called as neonatal chicken pox and is maximally due to infection acquired by mother during last 7 days of delivery and 7 days post delivery. Also, it can be acquired by other siblings getting infected in the house. Such neonates may develop pneumonia as a complication. Forrest J *et al*[5] have reported incidence of 1:17,000 cases of neonatal varicella in a study done in Australia in 2000.

Scabies, a disease caused by Sarcoptes scabiei, presents as distinctive pruritic papulo-vesicular lesions in neonates. Neonates present with generalised rash of palms, soles, scalp and face. Since incubation period ranges from 2-6 weeks, family history of contact can usually be elicited. Treatment of choice may be permethrin 5% applied for 6 hours.[6] Nanda *et al*[2] reported 6% incidence of scabies in their study. Baruah *et al*[1] did not find a case of neonatal scabies in their study of 500 neonates. In our study, one patient had neonatal scabies.

Erythema toxicum neonatorum, first described by Bartholomaeus melinger in 1472 is a benign self limiting dermatosis of neonates. It is very common in term neonates and less commonly seen in preterm infants and those with birth weight less than 2500 g. Usually one third of all full term neonates present with this disorder.[7] Recently, Liu C *et al*[8] have reported several predisposing factors for ETN where male sex, term birth, first pregnancy, summer and autumn months, powder milk feed and vaginal mode of delivery were associated with increased incidence of ETN. Cases of recurrent ETN and less number of lesions have been reported.[9] No treatment is necessary apart from reassurance as lesions resolve within few hours to days.

Transient neonatal pustular melanosis, again a transient skin condition is characterised by appearance of pustular or vesicular lesions with peripheral erythema, subsequently rupturing to form hyperpigmented macules. The exact cause is not known. Lesions are present on whole body including palms and soles. Giemsa or Wright stain shows neutrophils.

Miliaria results from obstruction of eccrine ducts and subsequent rupture of ducts into skin. Various forms depend on level of obstruction of duct. More commonly seen in hot and humid climates, lesions are either vesicles or erythematous papules present on face, chest, back or trunk. M. crystallina results from rupture at stratum corneum level, whereas M. rubra is result of rupture at intra-epidermal level. M. profunda is uncommon in neonatal age group. Energin *et al*[10] found 50% cases to be of M. crystallina in their study in Turkey. Neonatal cephalic pustulosis or acne appears as a result of stimulation of neonatal sebaceous glands by maternal and infant androgens.

Recently, Malessezia has been implicated as an etiology of acne.[11] Additionally, use of oils act as aggravating factor for these disorders. Although erythromycin 2% or benzoyl peroxide 2.5% are safe alternatives, lesions are benign and heal without scarring. Sucking blisters are present due to in utero sucking of accessible areas by fetus.[12] Usually lesions are solitary in nature. Culture of the lesion is negative for bacteria, fungi or virus. Epidermolysis bullosa has till date been classified into 3 major groups, with 16 different forms being described. Most commonly seen is Simplex type where extra cutaneous involvement, nail dystrophy, musculoskeletal abnormalities, anemia, growth retardation and neurological abnormalities are absent. Energin *et al*[10] reported 3 cases out of total 22 neonates presenting as Epidermolysis bullosa simplex. Nobby *et al*[13] found 1 case out of total 500 neonates to be Epidermolysis bullosa simplex. We report one case out of 44 neonates in this study.

Incontinentia pigmentii (Bloch Sulzberger Syndrome) is a rare X-linked dominant ectodermal disease and presents in neonate as four stages of vesicular, verrucous, hyperpigmented and atrophic presentations. Additionally, hair, nail and teeth abnormalities may be present. Various isolated cases have been reported in literature due to its rarity, no analytical study with retrospect to incidence has been reported. Biopsy is usually confirmatory. We found the case to be in verrucous stage.

Duarte *et al*[14] have reported 9 cases of eosinophilic pustular folliculitis in neonates. It is a rare disorder of neonates, presenting as recurrent crops of pruritic pustular lesions on scalp and brow region of face. Usually it resolves spontaneously.

Neonatal Pemphigus Vulgaris is a rare disease, Seen soon after birth and characterized by cutaneous, mucosal or mucocutaneous erosions, it is diagnosed by histological and immunofluorescence studies. It results from transplacental

passage of IgG maternal autoantibodies, mainly class 4, against desmoglein 3 (Dsg3), a transmembrane glycoprotein of the cadherin family. Neonatal Pemphigus Vulgaris has not been reported to progress to adulthood, and if the lesions do appear on the neonate they tend to improve spontaneously within 3 weeks.[15] Furthermore, there is a lack of association between the clinical manifestations of the disease in mother and newborn.

Uhara *et al*[16] reported a male neonate with Down syndrome who had transient myeloproliferative disorder associated with skin lesions. On postnatal day 1, erythema with small papules, vesicles and pustules appeared on entire body. A smear preparation from pustules on postnatal day 2 showed 10% blast cells. A biopsy on postnatal day 5 revealed subcorneal pustules containing neutrophils and eosinophils. On postnatal day 10, the eruptions resolved spontaneously and the population of blast cells in peripheral blood decreased to 1%. The authors recommend that cytological examination should be performed as early as possible.

Van Emmen *et al*[17] evaluated four neonates with vesicopustular skin eruptions and diagnosed with feeding blisters, bullous impetigo, erythema toxicum neonatorum and transient neonatal pustular melanosis respectively. The neonate with bullous impetigo was treated with antibiotics; the remaining neonates were not treated. It is important to identify these neonatal skin eruptions based on a thorough history of the mother and child and clinical presentation.

Conclusions

Although much work has been done in the paediatric dermatolgic age group, vesicobullous dermatoses in neonates has been a much untouched area with perspective to diagnosis and treatment outcomes. Often timely intervention is needed and reversely, unnecessary intervention may lead to loss of physician's time and effort, with only what is truly required being reassurance. With more than 30 differential diagnosis of the spectrum of vesicobullous disorders, it becomes essential both for the dermatologist and paediatrician to be aware of them and manage the neonate effectively.

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