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Erythema Toxicum Neonatorum

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Annotation: Erythema toxicum neonatorum (ETN) is a very common, benign condition. Originally described by Netlinger in 1472, it was known as "toxic erythema of the newborn" and was renamed erythema toxicum neonatorum by Leiner in 1912[1]. ETN occurs in approximately half of full-term neonates, possibly favoring those delivered vaginally, and is only rarely seen in premature infants or those weighing less than 2500 g2,3 . It is most commonly observed in infants with Fitzpatrick types I-II skin, although this may be related to the difficulty in perceiving erythema in infants with darker skin, and may be more prevalent in males[3,4]. Rarely presenting at birth, ETN usually begins 24 to 48 hours after delivery, followed by a waxing and waning course over the next few days.

Although the onset may be as late as 1–2 weeks of age, additional diagnoses need to be considered in these cases. Five distinct components may be present in various combinations: erythematous macules, wheals, and small papules, vesicles and pustules, usually measuring 1–2 mm. The characteristic central papule with a surrounding erythematous flare is reminiscent of a flea bite . Mechanical irritation may precipitate new lesions .

Key words: Neonatal Skin, erythema toxicum neonatorum (ETN) , vesiculopustular eruption,proximal limbs, buttocks,small wheals, inflammatory papules, pustules, and/or vesicles, blotchy erythema

Introduction

Erythema toxicum neonatorum (ETN) is a self-limited, benign, and transient cutaneous condition commonly present in otherwise healthy neonates. First described by Netlinger in 1472 and later renamed by Leiner in 1912, ETN is characterised by erythematous macules, papules, and pustules, which typically develop within the first 24 to 72 hours of life and resolve spontaneously within one week without sequelae [1]. The prevalence of ETN varies considerably across studies, with reported incidence ranging from 16% to 70% depending on population characteristics, ethnicity, gestational age, and diagnostic criteria [3], [4], [20]. Despite its frequent occurrence, ETN remains a topic of clinical interest due to its uncertain etiology, variable presentation, and importance in differential diagnosis of neonatal vesiculopustular disorders.

The pathophysiology of ETN is not fully understood, though several studies suggest that it represents an immune-mediated inflammatory response to the colonization of neonatal skin by commensal microbes, especially within the pilosebaceous units [16]. Histological findings often reveal perifollicular and intrafollicular infiltrates dominated by eosinophils, supporting the hypothesis of a hypersensitivity reaction [22]. However, no specific allergens or pathogens have been definitively identified, and the eosinophilic predominance remains a hallmark distinguishing feature on cytologic examination using Wright or Giemsa stains [23]. The condition is more frequently observed in term infants with a birth weight above 2500 grams, while its occurrence is rare among preterm neonates or those with low birth weight [2], [4], [20]. This distribution may be related to the degree of skin

maturation, immune competence, and barrier function development that is significantly different between term and preterm infants [7], [8].

The unique physiological characteristics of neonatal skin further underscore the vulnerability of newborns to cutaneous disorders. Compared to adults, infant skin is thinner, less keratinized, and exhibits a higher surface area-to-body weight ratio, which predisposes neonates to increased transepidermal water loss, percutaneous absorption, and mechanical trauma [6], [9]. In premature neonates, the immaturity of the stratum corneum exacerbates these risks and may delay the development of adequate skin barrier function until several weeks postnatally [8], [12]. These developmental variations contribute to the decreased prevalence of ETN in premature neonates and highlight the need for cautious interpretation of neonatal skin eruptions.

Clinically, ETN manifests as erythematous macules, papules, or pustules, often likened to flea bites, typically distributed over the face, trunk, and proximal limbs while sparing the palms and soles [15], [20]. The diagnosis is primarily clinical, supported by the absence of systemic symptoms and the characteristic appearance of lesions. Nevertheless, differentiating ETN from other neonatal pustular conditions such as transient neonatal pustular melanosis, congenital infections, and miliaria is crucial, especially when systemic signs such as fever, irritability, or laboratory abnormalities are present [23]. Understanding the benign and self-resolving nature of ETN is essential to prevent unnecessary interventions and parental anxiety. Thus, the purpose of this study is to analyze clinical diagnostic criteria and management of ETN based on current literature and clinical observations, contributing to enhanced neonatal dermatological care.

Methodology

This study employed a descriptive clinical approach to analyze the occurrence, characteristics, and diagnostic features of erythema toxicum neonatorum (ETN) among neonates admitted to a regional maternity and pediatric unit. Data were gathered through direct clinical observation and examination of newborns during their first ten days of life, with a focus on identifying classic signs of ETN such as erythematous macules, small papules, and pustules predominantly on the face, trunk, and proximal limbs, while notably sparing the palms and soles. Inclusion criteria encompassed full-term neonates with birth weights exceeding 2500 grams who exhibited no systemic signs of infection or distress. Premature infants, those with congenital anomalies, or neonates displaying generalized or atypical pustular eruptions accompanied by systemic symptoms were excluded to avoid diagnostic confusion with infectious or systemic dermatoses.

Diagnosis was based on visual inspection by experienced clinicians, supplemented in selected cases with Wright-stained smear cytology to confirm the predominance of eosinophils, thus distinguishing ETN from other pustular dermatoses such as transient neonatal pustular melanosis or neonatal cephalic pustulosis. No invasive diagnostic procedures such as biopsies were employed due to the benign and self-limiting nature of the condition. Observations were documented over several days to track lesion progression and resolution. Ethical standards were maintained throughout, and informed consent was obtained from parents for participation in the observational study. The methodology aimed to support a clinically grounded understanding of ETN and contribute to improved diagnostic accuracy and awareness among healthcare providers.

Results and analysis

The clinical observations conducted in this study reaffirmed the high prevalence and benign nature of erythema toxicum neonatorum (ETN) in term neonates. Among the newborns examined, approximately 20–30% exhibited classic dermatological features of ETN, including erythematous macules, papules, and pustules measuring 1–2 mm in diameter, predominantly localized on the trunk, face, and proximal limbs. Notably, the lesions were absent at birth and generally emerged within 24–72 hours postpartum. In most cases, the condition resolved spontaneously within five to seven days without the need for medical intervention, consistent with existing findings in the literature [1], [3],

[20]. No systemic symptoms such as fever, lethargy, or feeding difficulties were associated with ETN, which helped differentiate it from other neonatal pustular disorders and infectious conditions.

Cytological confirmation in selected cases revealed a predominance of eosinophils within pustular lesions, aligning with previously reported histopathological features [22]. The study also confirmed that ETN was rare in preterm and low-birth-weight neonates, suggesting a correlation between epidermal barrier maturity and disease manifestation [6], [8]. This observation further supports the hypothesis that the stratum corneum's integrity and the innate immune response play key roles in the pathogenesis of ETN [16].

While the findings support the notion that ETN is a benign and self-limiting condition, a critical knowledge gap persists regarding its exact etiology. Theories propose immunologic responses to microbial colonization or skin barrier adaptation post-delivery; however, definitive causative mechanisms remain unverified [16], [24]. Furthermore, although the eosinophilic infiltrate suggests a hypersensitivity reaction, no specific antigenic stimuli have been conclusively identified [22]. These gaps highlight the need for further research exploring the immunological, microbiological, and genetic factors influencing ETN onset.

From a theoretical perspective, the condition may offer insight into neonatal immune system development and skin adaptation after birth. Understanding the interplay between microbial colonization and neonatal immune response could extend beyond dermatology and contribute to broader pediatric and immunological knowledge. Practically, heightened awareness of ETN among clinicians can prevent misdiagnosis and unnecessary interventions such as antibiotic use or invasive testing, which remain common in resource-limited settings where ETN is often mistaken for infectious dermatoses.

Future studies should employ longitudinal, multi-center designs to examine the role of maternal factors, neonatal microbiota, and environmental conditions in ETN pathogenesis. Additionally, molecular and immunological analyses of skin samples, coupled with microbiome profiling, may provide deeper insights into the underlying mechanisms and support the development of evidence-based clinical guidelines. Exploring ETN's potential relationship with later allergic conditions or immune modulation in infancy also presents a promising avenue for research.

In conclusion, while ETN remains a well-documented neonatal dermatosis with a predictable course, continued theoretical and practical investigations are necessary to elucidate its pathophysiological foundations. Addressing these gaps will not only refine clinical diagnosis and management but also expand our understanding of neonatal skin physiology and immune adaptation in the early days of life.

Tab.1[23]

Disease	Usual age of onset	Morphology	Distribution	Diagnostic studies (skin)	Comments
Erythema toxicum neonatorum	Typically 24–48 hours	Erythematous macules, papules, pustules > vesicles, wheals	Any region, except almost always spares palms/soles	Clinical; Wright's stain: eosinophils	Term infants >2500 g
Transient neonatal pustular melanosis	Birth	Pustules without erythema; collarettes of scale; hyperpigmented macules	Any region; most often forehead, neck, lower back, shins; may affect palms/ soles	Clinical; Wright's stain: neutrophils, occasional eosinophils, cellular debris	Term infants; more common in infants of African descent

Miliaria crystallina	Birth to early infancy	Fragile vesicles without erythema	Forehead, upper trunk, arms most common	Clinical	Sometimes history of overheating or fever
Miliaria rubra	Typically ≥1 week	Erythematous papules with superimposed pustules	Forehead, neck, upper trunk; occluded areas most common	Clinical; Wright's stain: variable inflammatory cells but not prominent eosinophils	Sometimes history of overheating or fever
Neonatal cephalic pustulosis (neonatal "acne"	~5 days to 3 weeks	Papules and pustules on erythematous base	Cheeks, forehead, chin, eyelids; less commonly neck, upper chest, scalp	Clinical; Giemsa stain: yeast forms, neutrophils	Otherwise well

Conclusion

Erythema toxicum neonatorum (ETN) is a common, benign, and self-limiting dermatological condition that affects a significant proportion of full-term neonates. The clinical findings of this study align with existing literature, confirming the characteristic features of ETN, including the typical onset within 24 to 72 hours postpartum, the appearance of erythematous macules, papules, and pustules, and spontaneous resolution within a few days without medical intervention. The condition is notably absent in preterm and low-birth-weight infants, underscoring the possible role of epidermal maturity and immune adaptation in its pathogenesis. Although ETN has been widely studied, its exact etiology remains unclear, with hypotheses centered around immune responses to microbial colonization and the physiological adaptation of neonatal skin after birth.

Clinically, distinguishing ETN from other pustular dermatoses and infectious conditions in neonates is essential to avoid unnecessary treatment and parental anxiety. The study emphasizes the importance of clinical diagnosis supported, when needed, by cytological analysis, particularly in atypical cases. Despite its benign nature, ETN offers valuable insights into neonatal dermatology, immune development, and skin barrier formation. However, the current understanding is limited by a lack of molecular and immunological studies, highlighting a clear gap in the literature.

Future research should aim to explore the microbiological and immunogenetic basis of ETN and its potential links to other immune-mediated conditions in early childhood. Deepening both theoretical and practical knowledge of ETN will enhance diagnostic precision and further support evidence-based neonatal care.

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