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Uncommon Presentation of Bloch-Sulzberger Syndrome in a Male Neonate: Case Report and Literature Review

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ABSTRACT

Background: The uncommon X-linked dominant inheritable disorder known as Bloch-Sulzberger Syndrome (BSS) or Incontinentia Pigmenti (IP) affects the skin, eyes, teeth, and nervous system. The syndrome is typically lethal in hemizygous male embryos, making survival to term extremely rare.

Case Presentation: A full-term male infant delivered to a primigravida woman who had no family history of such conditions, and no history of consanguinity presented with convulsions, vesicular lesions on the vertex, alopecia, varied pigmentation on the trunk and limbs, and ocular manifestations. Diagnostic criteria for BSS included major criteria of stages 1, 2, and 3 skin manifestations, minor criteria of ocular, hair, and neurological involvement, and additional criteria of increased eosinophils in blood and vesicular fluid. Differential diagnoses were ruled out based on clinical and histopathological features. Affordability influenced the consideration of molecular tests for IKBKG gene mutation and MRI brain. Genetic counseling was provided to the parents.

Conclusion: This case highlights the importance of comprehensive clinical evaluation, multidisciplinary management, and genetic counseling in BSS. The survival of this male infant for a few days after birth with BSS adds valuable insight into the syndrome's variability and presentation, emphasizing the need for accessible genetic testing and ongoing research to improve patient care.

Keywords: Bloch-Sulzberger Syndrome, Incontinentia Pigmenti, genetic disorder, vesicular lesions, alopecia, ocular manifestations, multidisciplinary care, genetic counseling

INTRODUCTION

BSS is an uncommon genodermatosis that manifests as a variety of anomalies including skin lesions. Because it usually leads to the death of male foetuses in utero, the instance of a full-term male fetus born with the disease is especially notable (1). The syndrome's manifestations can extend beyond the skin, including neurological features such as convulsions (2). Additionally, it is associated with Klinefelter syndrome, a hereditary condition where male infants possess an additional X chromosome, that might account for the male infant's survivability in this particular condition(3). The syndrome can be confused with other conditions, such as Schimmelpenning syndrome, which also presents with skin abnormalities and ocular manifestations (4).

BSS has a prevalence of approximately 0.7 per 1,000,000 individuals worldwide (5). There were 1,393 instances documented worldwide from 1993 to 2012, with an average of 28 instances per every year (6). There are notable sex disparities in the condition, with a 1: 37 male to female proportion. In 92–97% of instances, women make up the bulk of people with this condition (7). The functional mosaicism brought on by the deactivation of X chromosomes is thought to be responsible for female survival. On the other hand, because the disease is fatal in hemizygous male human embryos, male foetuses containing the lethal gene usually result in miscarriage (8).

Incontinentia Pigmenti (IP) present with a range of clinical manifestations. Alshenqiti (2017) reported a case of IP complicated by pulmonary arterial hypertension, highlighting the need for comprehensive care in these patients (9). Melek (2023) presented two cases of IP with dental abnormalities, emphasizing the importance of recognizing these features for accurate diagnosis and treatment(10). Arora (2014) discussed the importance of distinguishing IP from other dermatologic conditions, such as Bloom syndrome, which can have similar presentations but different management approaches(11). Lastly, Porto (2013) underscored the significance of early detection and management of Cowden Syndrome, another rare genodermatosis, to reduce the risk of cancer(12). These studies collectively emphasize the essential of an interdisciplinary approach in IP patient care, including thorough clinical evaluation and appropriate management of associated complications.

Skin, nerve, eye, and teeth anomalies are the hallmarks of this multisystem illness. The primary feature of IP is changes in the skin. As they progress across 4 stages—vesicular, hyperkeratotic, hyperpigmented, and hypopigmented—these symptoms may alter or even disappear (2). On the other hand, dental anomalies are thought to be the most common extracutaneous symptoms and are persistent (2). The clinical manifestation is often used to make the diagnosis, while occasionally a skin biopsy linked to a genetic analysis is used (13).

Here, we report a case of BSS brought to a peripheral hospital in Maharashtra India. The case was observed online in a video mode by the pediatrician, and anatomists to evaluate different physical, clinical, and genetic anomalies, additionally, an overview of the available literature was carried out using databases such as "Google Scholar" and "Pubmed".

CASE PRESENTATION:

A full-term male infant, delivered to a primigravida woman who had no family history of such conditions and no history of consanguinity, was referred to the pediatrician due to convulsions. The newborn exhibited many erythematous vesicular lesions based on the vertex, alopecia, varied pigmentation on different parts of the trunk and limbs, and ocular manifestations (Figure 1&2). The diagnostic criteria in this case included major criteria such as stages 1, 2, and 3 skin manifestations in the newborn, minor criteria involving ocular, hair, and neurological manifestations, and other criteria such as increased eosinophils in the blood and vesicular fluid. The peculiarity of this case was that the male fetus had no familial history of such conditions, and the condition was lethal in hemizygous male embryos, with the baby succumbing to seizures.

Further investigations included molecular tests for IKBKG gene mutation and MRI Brain, both subject to affordability. The diagnosis of Bloch-Sulzberger Syndrome (BSS) was primarily clinical and depends on the distinctive cutaneous outcomes observed in the infant. Differential diagnoses, including viral infection of herpes simplex, linear and whorled nevoid hyper melanosis, and linear epidermal nevus, were ruled out based on clinical and histopathological features. Symptomatic treatment of skin lesions during the blistering stage included gentle wound care and topical antibiotics. Ophthalmologic evaluations and dental examinations were performed to detect and manage associated abnormalities. The patient's parents received genetic counseling regarding the inheritance pattern of BSS.

Figures:

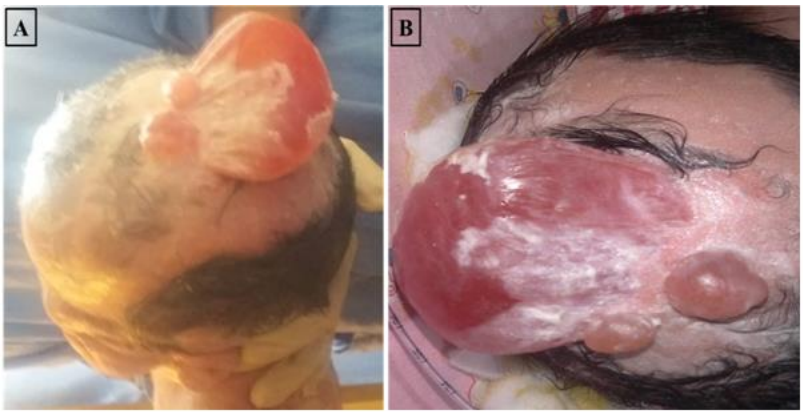

Figure 1: Photographs A] and B] exhibiting Multiple vesicular lesions with the erythematous base on the head with alopecia

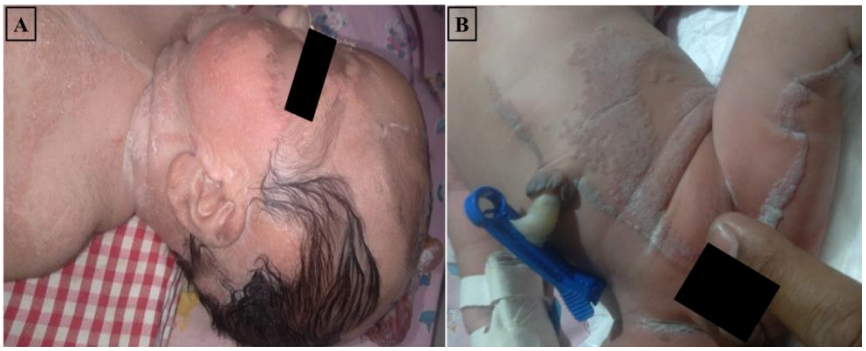

Figure 2: Photographs A] exhibiting newborn presented with multiple vesicular lesions on an erythematous base, alopecia, and varied pigmentation, Photographs B] showing Verrucous/ hyperkeratotic stage Varied pigmentation – brown or greyish blue hyperpigmentation.

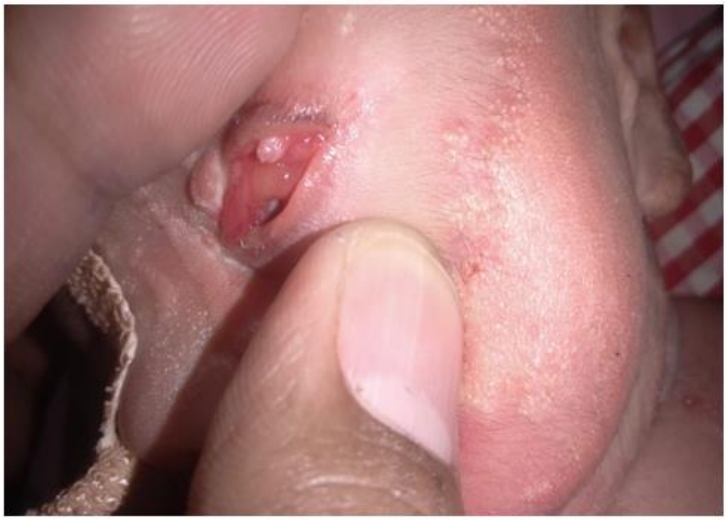
Figure 3. Left eye showing upper lid dysgenesis. Coloboma, ocular dermoid, and microphthalmos.

DISCUSSION

Skin, ophthalmic, and neurological manifestations are features of BSS, an extremely uncommon X-linked dominant inheriting the condition. With several additional alterations, it falls within the category of genodermatosis disorders. It is brought on by a mutation in the NEMO gene, which is found on the X chromosomes q28 region (14). It is typically lethal in hemizygous male embryos, making the instance of a male newborn without a familial history of the disorder particularly unusual (15). BSS is generally diagnosed clinically according to the patient's distinctive dermatological characteristics (15). Early diagnosis is crucial to prevent deadly complications (16). The condition is brought on by a mutation in the IKBKG gene, and it might be challenging to distinguish its skin symptoms from those of other illnesses(17). The importance of a multidisciplinary approach, including genetic counseling, is emphasized in the management of BSS (18).

The primary feature of IP is skin changes. The available research claims that these appearances undergo four phases and might eventually alter or even disappear: The initial stage, known as vesicular or vesicular-bullous, can endure for weeks or months and might start at the time of birth or throughout the initial two months. The emergence of linear verrucous hyperkeratotic plaques is the second. Subsequently, the hyperpigmentation phase presents with gradually disappearing brown-black lines. The hypopigmentation phase is the final one (2,19). Extracutaneous signs of BSS are seen in up to 80% of patients (19).

There may be effects on the central nervous system, teeth, eyes, and bones. Permanent oral anomalies are thought to be the most common extracutaneous indications. The second most commonly impacted region is the ocular(2,20,21). Therefore, oro-facial outcomes are adequate to identify other afflicted individuals and detect the existence of the IP gene(13,20). The percentage of examined BSS patients with teeth and oral malformations was significant, ranging from 80% to 90%, according to certain documented literature of IP case series with teeth abnormalities in the existing literature(22). We present the findings of a short review of the literature that was done using the databases "Pubmed" and "Google Scholar."

The most important dental abnormalities associated with IP disease were earlier tooth loss, malformed teeth, and a developmental failure to develop six or more teeth (23). In the present case, we did not identify such anomalies. Studies have shown that although the manifestations of dermatology are moderate, the presence of symptoms other than alterations in the skin, especially oral abnormalities, is important, and vice versa (13), it is consistent with the clinical presentation of dermatological problems in patients. We must remember that IKBKG mutations, which result in catastrophic cellular disorders in the skin and various other affected tissues, primarily of ectodermal origin, correspond with mutation of genes recognized to trigger oral and tooth deformities(19). Although dental and oral abnormalities hardly cause a threat to life, they can nonetheless have an influence on a patient's quality of life. For IP individuals, some of these defects may result in eating issues, whereas others can lead to major psychological issues(19).

Since dermal changes appear almost soon after birth, dermatologists are in a unique position to detect patients with Bloch Sulzberger disease in the early stages of the condition. This condition frequently manifests as dental and oral abnormalities, including agenesis and conic teeth. Dentistry plays an essential part in both the detection of IP and, more specifically, improving the quality of life for people with this condition, which is the second most common finding in IP, especially in cases without dermal anomalies. It is possible to determine if interdisciplinary therapy is necessary to advance patients' physical, social, and emotional well-being through a precise and accurate diagnosis.

This case report addresses a significant lacuna in the literature by documenting a rare case of BSS in a male infant surviving to term, providing valuable insights into the clinical presentation, management challenges, and genetic implications of this complex disorder. It emphasizes the need for continued research to improve diagnostic strategies, therapeutic interventions, and genetic counseling approaches for patients and families affected by BSS.

CONCLUSION

This case report contributes valuable knowledge to the understanding of BSS, particularly in the rare context of a male infant. The detailed clinical presentation, thorough differential diagnosis, challenges in genetic testing and affordability, and the multidisciplinary management approach provide a comprehensive overview of managing complex genetic conditions. The insights gained from this case underscore the importance of coordinated care, accessible healthcare resources, and ongoing research to improve outcomes for patients with rare genetic disorders like BSS.

Informed consent: Written Informed consent was obtained from the parent of the infant for the use of findings for educational and research purposes. Confidentiality was maintained throughout the process.

Data access: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of interest: There are no conflicts of interest.

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