Case Report: Harlequin Ichthyosis

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Abstract

Harlequin Ichthyosis (HI) is a rare autosomal recessive congenital ichthysosis, due to mutations in the ABCA12 gene, leading to defects in lamellar granules of stratum granulosum. A clinical diagnosis was estabilish based on typical features of Harlequin Ichthyosis (HI), armorlike plates of scale and deep fissures. Harlequin Ichthyosis (HI) has a high mortality rate. **Case:** We reported a baby girl aged one day with yellowish scales and cracked skin since birth. Examination revealed eclabium, ectropion, and agenesis of the fingers and toes. The management of Harlequin Ichthyosis (HI) requires a supportive care, including the treatment in the incubator with NGT inserted, gentamicin eye ointment, sterile eye drops, gentamicin ointment, NaCl 0,9% dressing and emollient (olive oil). The patient died on the 8th day of treatment. **Discussion:** Supportive care was given to the patient. But the management was not optimal due to the difficulties in maintaining peripheral venous system access for the provision of systemic therapy, and laboratory examination. And moreover, the unavailability of systemic retinoid worsened the condition. The patient died on the 8th day of treatment due to respiratory failure and leading to sepsis. **Conclusion:** A clinical diagnosis was estabilish based on typical features of Harlequin Ichthyosis (HI) in this case. The failure in maintaining peripheral venous system access and the unavailability of systemic retinoid worsened the prognosis of this patient.

Keywords: Harlequin Ichthyosis, Autosomal Recessive, Gene Mutations, skin disorder, genetic

Introduction

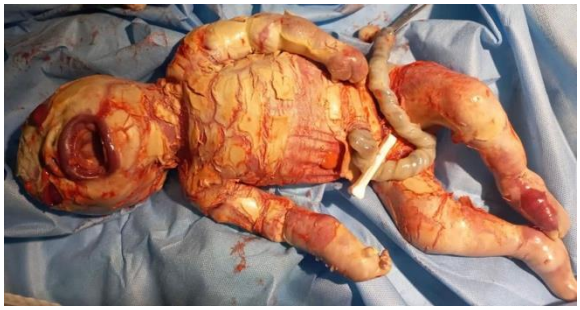
Harlequin Ichthyosis (HI) is a very rare form of autosomal recessive congenital ichthyosis, with a prevalence of 1 case per 300,000 people. The disease is caused by the inheritance of a recessive autosomal mutation in the adenosine triphosphate (ATP)-binding cassette sub-family A member 12 (ABCA12) gene, which results in the absence of normal lamellar bodies in the stratum granulosum of the epidermis.

Diagnosis is established through a distinct clinical presentation. Patients are often born prematurely and exhibit classical signs, including armor-like thick plates of skin with deep fissures that appear at birth and peel off, exposing severe erythroderma. Other clinical features of HI become more apparent over time, such as absent nasal structure, malformed ears, alopecia, sweat gland dysfunction, bilateral eclabium, and ectropion. Genetic testing can assist in diagnosis. Currently, ABCA12 gene mutation detection can be done less invasively through fetal DNA testing via amniocentesis or chorionic villus sampling, and messenger RNA (mRNA) analysis from hair samples.

Newborns with Harlequin Ichthyosis have a very high mortality rate. Management focuses on supportive care, including fluid, electrolyte, and nutritional therapy, and the use of topical emollients to hydrate the skin. Systemic retinoids have also been shown to improve survival rates. However, in Indonesia, systemic retinoids such as acitretin are rarely available and relatively expensive. The effectiveness of systemic retinoids remains difficult to evaluate due to the rarity of the disease and the critical role of neonatal intensive care.

To date, epidemiological data and research on Harlequin Ichthyosis in Indonesia are still limited, particularly in remote areas with limited healthcare equipment and medications. This case report aims to raise awareness and encourage further studies on the epidemiology and treatment of HI, especially in resource-limited settings, in order to improve survival rates.

Case Study



A 1-day-old female infant was referred to the Dermatology, Venereology, and Aesthetic Department from the Pediatric Department at RSUD Sultan Imanuddin Pangkalan Bun with complaints of yellowish, scaly, crusted skin and open wounds over almost her entire body since birth. Physical examination revealed eclabium, ectropion, and agenesis of fingers and toes. The infant was delivered via cesarean section on November 20, 2023, at 12:36 PM with an APGAR score of 5/7. Birth weight was 2640 g, body length 46 cm, head circumference 35 cm, and chest circumference 32 cm. The mother was 30 years old, in her second pregnancy at 37 weeks gestation, complicated by premature rupture of membranes and breech presentation. The father worked in the private sector, and the mother was a housewife. There was no family history of skin disorders or genetic diseases, and no consanguinity between the parents was reported.

On general examination, the infant appeared dyspneic, with a respiratory rate of 58 breaths per minute, heart rate 115 bpm, body temperature 35°C, and oxygen saturation of 100% with 0.5 L/min nasal cannula oxygen. Supportive care included incubator treatment, nasogastric tube feeding of 30 mL formula every 3 hours, gentamicin eye ointment twice daily, sterile eye drops three times daily, gentamicin ointment applied to the skin twice daily, compresses with 0.9% NaCl and sterile gauze twice daily, and moist gauze covering the eyes.

On the fourth day of hospitalization, attempts to place an intravenous line and obtain blood samples for laboratory tests were unsuccessful. On the sixth day, olive oil was added as an emollient,

applied twice daily. On the seventh day, the infant's scaly skin began to peel, accompanied by fever and worsening respiratory distress. On the eighth day of treatment, the patient was declared deceased.

Results and Discussion

Harlequin Ichthyosis (HI) is a form of Autosomal Recessive Congenital Ichthyosis (ARCI) with the most severe and rare manifestation. HI results from a recessive autosomal mutation in the ABCA12 gene located on chromosome 2q35. Mutations in ABCA12 lead to deactivation of the lipid transport system in the stratum corneum, resulting in the absence of normal lamellar granules and extracellular lamellar lipids between the stratum corneum and stratum granulosum. This leads to massive hyperkeratosis, impaired desquamation, and loss of skin barrier function.

A detailed family history is essential, as it may reveal genetic risk factors, prior occurrences of similar diseases, consanguinity, and other keratinization disorders. The risk of an affected offspring from two autosomal recessive carriers is 25%. In autosomal recessive inheritance, the disorder manifests when both parents, who appear healthy, carry the mutated allele. There may be no similar disorders in previous generations, and consanguinity increases the likelihood of occurrence.

In this case, there was no consanguinity or family history of similar disorders. The patient's parents are likely heterozygous carriers of the HI gene mutation.

Diagnosis is primarily clinical, with newborns typically born prematurely and encased in thick, yellow-brown plaques tightly adherent to the body, limiting movement. Shortly after birth, the taut skin cracks into deep red fissures, forming a diamond-shaped or Harlequin-like pattern. The face appears distorted with bilateral ectropion and eclabium. The nose and ears are rudimentary and fused to the skin. Hands and feet may be edematous and encased in a mucoid membrane, and necrosis of the digits can occur. Microcephaly may also be observed.

In this case, the infant presented with thick, yellowish, scaly skin and wounds covering almost the entire body. By the second day, the skin had darkened and thickened further with deeper fissures. On the seventh day, the skin began to peel. Clinical signs included eclabium, ectropion, and agenesis of fingers and toes, with generalized hyperkeratosis and fissures. These findings are pathognomonic for HI.

Additional diagnostic tests can include prenatal fetal skin biopsy and electron microscopy at 19–23 weeks of gestation, or genetic testing for ABCA12 mutations through fetal DNA analysis. Postnatal histopathology may reveal orthokeratotic or parakeratotic features in the stratum corneum and ultrastructural findings of absent lamellar bodies and extracellular lipids. In this case, diagnosis was based solely on clinical examination, with no histopathology performed. The parents did not undergo any prenatal screening beyond routine antenatal care.

HI has a high neonatal mortality rate. Until the 1980s, all affected newborns died within days or weeks. Despite advancements in neonatal care, HI remains life-threatening and requires a multidisciplinary approach. Complications from hyperkeratosis include sepsis (75% of cases),

respiratory failure (25%), or both. Severe skin barrier disruption makes neonates susceptible to excessive trans-epidermal water loss (TEWL) and electrolyte imbalances with dehydration.

Supportive care includes neonatal intensive care with temperature and humidity control, fluid and electrolyte balance, infection prevention and treatment, adequate nutrition, and management of physical deformities. In this case, the patient was treated in an incubator with 60–80% humidity and 32–34°C temperature. However, hydration, electrolyte, and sepsis control were suboptimal due to unsuccessful IV access and inability to perform laboratory tests. Nutritional support was provided via NGT with formula feeding every 3 hours.

Topical emollients and systemic retinoids, especially acitretin (initial dose 1 mg/kg/day), should be initiated early to improve outcomes. Acitretin is preferred due to its shorter half-life and fewer side effects. In one study, 83% of HI cases survived with systemic retinoid therapy. However, such drugs are rarely available in Indonesia and are expensive. Topical retinoids like 0.1% tazarotene may help manage hyperkeratosis, contractures, and ectropion.

In this case, treatment focused on topical medications as first-line therapy to hydrate the skin and prevent infection. Water-in-oil emollients, such as olive oil, were used to reduce TEWL. Olive oil contains high levels of oleic acid, maintaining moisture, flexibility, and smoothness of the skin. Emollients are recommended at least twice daily, particularly after bathing. Emollients containing urea are not recommended for inflamed, eroded, or folded skin areas. Additional care included 0.9% NaCl compresses with sterile gauze twice daily for 30 minutes to hydrate and soften scales and remove topical residue.

Topical gentamicin ointment was applied twice daily to prevent secondary infections. The eyes were treated with gentamicin eye ointment and sterile eye drops, followed by covering with moist gauze to prevent ocular damage due to the absence of protective eyelids.

In this case, the infant died after 8 days of treatment, likely due to respiratory failure and sepsis as complications of Harlequin Ichthyosis.

Conclusion

This report describes a case of Harlequin Ichthyosis in a 1-day-old female infant. Diagnosis was made based on history and characteristic physical findings, including thick yellowish scales, red fissures, bilateral ectropion, eclabium, and agenesis of fingers and toes. Management consisted of incubator care, nasogastric feeding with 30 mL of formula every 3 hours, gentamicin eye ointment, sterile eye drops, gentamicin skin ointment, 0.9% NaCl compresses, and olive oil as an emollient. The prognosis in such cases is poor. The patient passed away on the eighth day of treatment.

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