Acta Dermatovenerol Croat 2020;28(2):70-74 CLINICAL ARTICLE

# Iatrogenic Anetoderma of Prematurity: A Series of 5 Clinical Cases and Literature Review

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Received: January 24, 2019
Accepted: May 15, 2020

**ABSTRACT** Iatrogenic anetoderma of prematurity (IAOP) represents a benign iatrogenic dermatosis characterized by focal, well-demarcated areas of atrophic skin in preterm infants. We present the cases of 5 infants diagnosed with IAOP during a 3-year period in a tertiary-care university hospital. Skin atrophy patches were absent at birth in all presented infants, and there was no family history of anetoderma. All of the infants were born with very low gestation and birth weight, with a clinical course that was complicated with several serious prematurity-related complications with consequent long periods of unstable vital functions and the need for continuous monitoring. Skin defects consistent with IAOP were located on the previous ECG electrode sites. IAOP changes in all the infants were in the form of oval patches of skin atrophy in the middle chest region, with an additional few small, round patches bellow the nipple on both sides in one girl. Diagnosis of IAOP was based on characteristic clinical findings. IAOP is rare, benign, but permanent skin injury in the most immature of infants, with a potential for considerable aesthetic and psychological burden. Due to the constant increase in survival of very and extremely preterm infants, more often without major developmental consequences, milder complications like IAOP will become more and more important.

**KEY WORDS:** anetoderma, premature infants, fetal monitoring

## INTRODUCTION

Iatrogenic anetoderma of prematurity (IAOP) represents a benign iatrogenic dermatosis characterized by focal, well-demarcated areas of atrophic skin in preterm infants. Skin atrophy occurs due to local loss of dermal elastic fibers. IAOP primarily affects the most immature infants (1). Having in mind the ever-increasing rate of birth and survival of very and extremely preterm infants, we can expect a growing number of children with skin changes that correspond to IAOP. Although the condition is considered benign, it is permanent, with aesthetic and sometimes disfiguring effects. IAOP is rarely reported in the literature.

## CASE REPORTS

We present the cases of 5 infants diagnosed with IAOP during a 3-year period (January 2015 – December 2017) in a single tertiary-care university

hospital. Data about their prenatal history, birth, primary hospitalization, and follow-up were retrospectively collected from their medical records. In all presented infants, skin atrophy patches were absent at birth, and there was no family history of anetoderma. Skin biopsy was not performed in any of the cases, and diagnosis of IAOP was based on characteristic clinical findings.

All of the infants were born at a very low gestational age; four of them were less than 26 gestational weeks (GW) old, and one was 30 GW old but with a congenital heart defect (pentalogy Fallot) which was surgically treated at an early age (4 months). All of them also had very low birth weight (BW) (four extremely preterm infants <800g at birth), but within eutrophic range for their gestational age. One infant was male and four were female, all from single pregnancies. The clinical course was complicated in all cases with the need for resuscitation at birth, endotracheal intubation, and ventilation, with subsequent development of bronchopulmonal dysplasia in four extremely preterm infants. Each of the presented infants also developed several other prematurity-related complications: late-onset sepsis in all five infants, hemodynamically important patent duct in 3 infants, severe retinopathy of prematurity in 3 infants, and severe intracranial hemorrhage in 2 infants (in a boy treated with ventriculo-peritoneal shunt). Additionally, all had very long primary hospitalizations. The most important perinatal and neonatal characteristics of the infants are shown in Table 1.

These perinatal-neonatal data illustrate the complicated clinical course in the presented infants, with long periods of unstable vital functions and a need for continuous monitoring. All the infants were monitored with use of ECG electrodes for a lengthy period of time. In all the cases, skin defects consistent with IAOP were located on previous electrode sites. In four infants, IAOP emerged as a single oval patch of skin atrophy in the middle chest region. In patient number 2, an extremely preterm girl, IAOP changes were much more extensive, with irregular heart-shape atrophic skin in the middle of the décolleté and a few smaller round patches bellow the nipple on both sides (Figure 1). In all our cases, IAOP emerged at the age of 3-5 postnatal months, with preceding skin changes. In patient 3, round hyperpigmentation on a previous electrode site was noticed initially, after which a telangiectatic area emerged, that gradually transformed into an atrophic lesion (Figure 2). In patient 5 there was an oval area of redness prior to fully-developed IAOP. In the remaining three patients, regions of redness with few small skin-damaged areas and scabs were noticed initially and subsequently converted into IAOP lesions (Figure 3). In all presented cases, the permanent IAOP changes developed in the form of atrophic hypopigmented regions surrounded by hyperpigmented edges. On follow-up examinations, which were performed until the age of 12-30 months, IAOP lesions remained unchanged, with a slight increase in size parallel to infant body-growth.

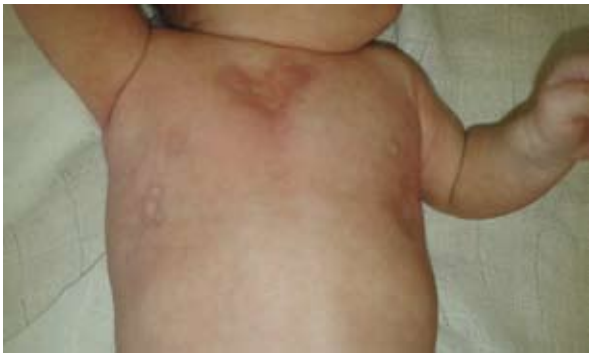

**Figure 1.** Extensive atrophic skin changes in patient No 2.

**Table 1.** Perinatal and neonatal characteristics of presented infants diagnosed with iatrogenic anetoderma of prematurity

| | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 |
|---|---|---|---|---|---|
| Gestation (weeks) | 25 | 24+5 | 24+5 | 25+4 | 30 |
| Birth weight (grams) | 780 | 750 | 680 | 670 | 1270 |
| Appropriate for gestational age | yes | yes | yes | yes | yes |
| Sex | girl | girl | boy | girl | girl |
| Mechanical ventilation | yes | yes | yes | yes | yes |
| Bronchopulmonal dysplasia | yes | yes | yes | yes | yes |
| Late-onset sepsis | yes | yes | yes | yes | yes |
| Treated patent duct | no | yes | yes | yes | / |
| Severe intracranial hemorrhage | yes | no | yes | no | no |
| Severe retinopathy of prematurity | no | yes | yes | yes | no |
| Congenital malformations | no | no | no | no | Pentalogy Fallot |
| Length of primary hospitalization (days) | 108 | 96 | 174 | 222 | 149 |

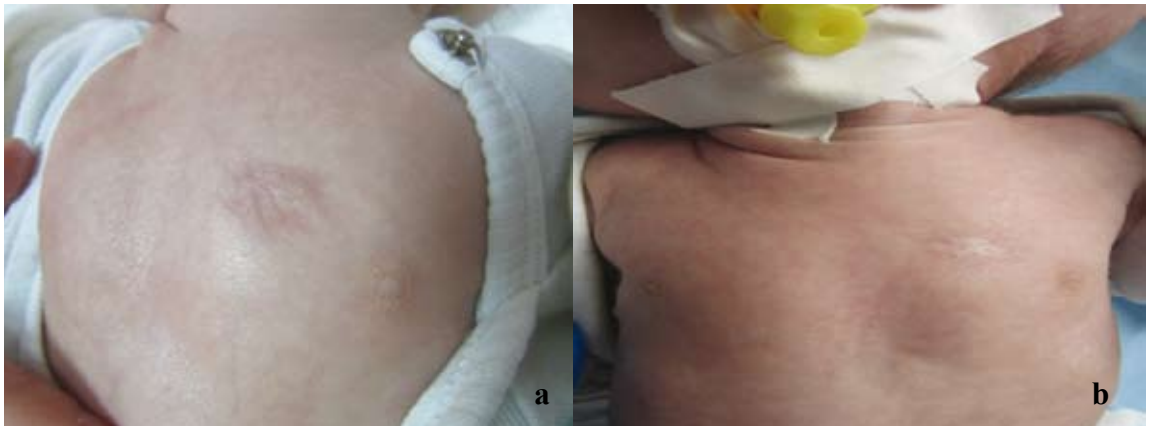


**Figure 2.** Round telangiectatic area on a previous electrode site (a) which was gradually transformed into an atrophic lesion (b) in patient No 3.

During the 3-year study period, 239 very and extremely preterm infants, i.e. with less than 32 GW of age, were discharged from our hospital. Since 5 of them developed IAOP, the frequency of this type of skin lesions was 2.09% among infants in this subpopulation.

## DISCUSSION

Anetoderma can generally occur at any age. The occurrence of anetoderma in infants can be congenital (present at birth), familial (present in family members, immerged at birth, or presenting spontaneously during first decade of life), or acquired at an early age in very and extreme preterm infants (2,3). The latter refers to IAOP as a specific consequence of iatrogenic application of various medical adhesives and electrodes in modern neonatal intensive care units (NICU) (1).

IAOP is rarely reported in literature. The first report of two cases of IAOP, though under a different name ("skin craters") was published in 1981 by Golden (4). The term "anetoderma of prematurity" was first introduced by Prizant *et al*. (5) in 1996, when the authors reported a series of 9 cases of IAOP. Subsequently, 5 more cases of IAOP were published before 2010 in a total of three papers (Todd (6) in 1997, Coldítz *et al*. (7) in 1999, and Ben-Amitai *et al*. (8) in 2008). In 2010 Goujon *et al*. (9) reported the largest series of IAOP cases. They described 11 patients born at 25-30 weeks of gestation, with skin lesions on the ventral side of the trunk associated with prolonged usage of ECG electrodes. In 2014, Maffeis *et al*. (10) gave a detailed description of an IAOP lesion on the chest in an extremely preterm girl. Finally, in 2016 Glauser *et al*. (11) reported 4 cases of IAOP changes in extremely preterm infants associated with ECG electrodes and CO2 leads. That makes a total of 32 literature cases of IAOP until our report.

IAOP is characterized by well-demarcated areas of changed skin texture and/or coloration (1). These areas may be flat or below the level of surrounding skin. Additionally, (usually in later course, with the child's growth) they may emerge as pouch-like herniation of atrophic skin (1,10). The skin changes are

**Table 2**. Summarized perinatal and clinical characteristics of all infants with iatrogenic anetoderma of prematurity reported so far, including our clinical cases

| | |
|---|---|
| **Gestational age (weeks) (n=37)** | 24-32 GW (up to 30 GW in 34=91.89%) |
| **Birth-weight (g) (n=37)** | 440-1640 (< 1500g in 33 =89.19%) |
| **SGA status (n=37)** | 8 (21.62%) |
| **Single/twin (n=28)** | Twins 9 (32.14%) |
| **Sex – male (n=26)** | 13 (50%) |
| **Mechanical ventilation (n=37)** | 33 (89.19%) |
| **Electrodes (n=37)** | 35 (94.59%) |
| **Morbidity (n=37)** | BPD: 27 (72.97%)<br>PDA treatment: 17 (45.94%) |

BPD – Bronchopulmonary dysplasia
PDA – Patent ductus arteriosus

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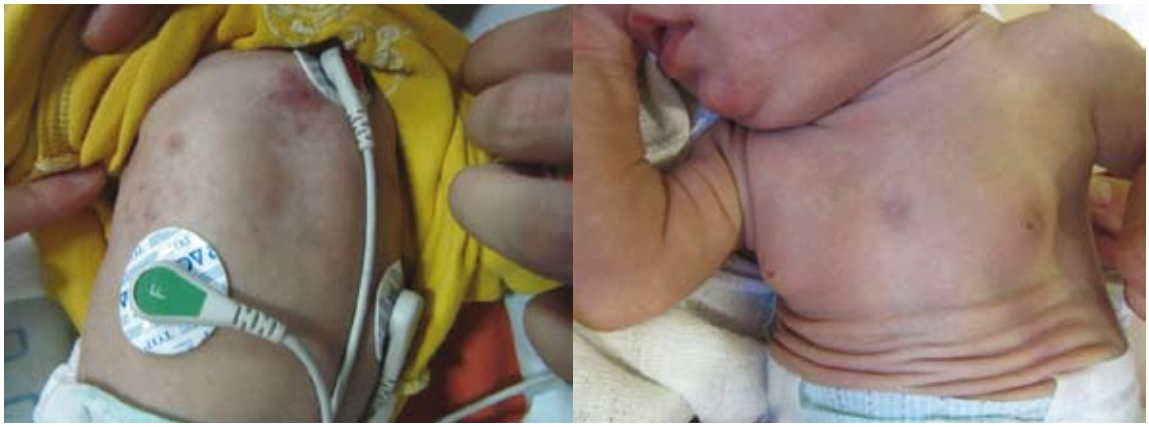

**Figure 3.** Erythematous area in the middle chest region on a previous electrode site (a) with later conversion into an IAOP lesion (b) in patient No 4.

usually located on the ventral side of the trunk at the sites where electrodes or adhesives were previously attached to the chest and/or abdomen (4-6,8-11), but in some cases were located on the back (4), thighs (4), proximal extremities (5), and forehead (7). In all our presented patients, IAOP changes were located on the chest – in the middle chest region, with additional bilateral changes in near-mamillar regions in the girl that has the greatest number of extensive lesions. Findings of IAOP above sternum might be associated with specific characteristics of the skin of this region – thin skin tightened over chest bone, with a scarce subcutaneous fatty tissue layer. As in most reported cases, these skin changes corresponded to previous ECG electrode sites. Most reported cases were also associated with the usage of different electrodes, either ECG (5,6,9-11), transcutaneous O2 and CO2 (4,11) or EEG electrodes (7). Usually, although not necessarily, different preceding skin changes can be seen on electrodes or adhesives sites. These take the form of hyperpigmentation, ecchymoses, hematoma, telangiectasia, or redness with or without additional skin damage and scabs. The lesions corresponding to fully developed IAOP are usually not noted immediately after specific skin injury, but rather after a period ranging from several weeks to several months (1).

The exact mechanism of developing IAOP skin changes, as well as anetoderma in general, has not yet been fully explained. Appearance of any type of anetoderma, i.e. loss of dermal elastic tissue, can be attributed to defects in synthesis and/or increased degradation of elastic fibers (8). In modern NICU, usage of medical adhesives, including different kinds of tapes, electrodes, dressings, and ostomy bags and pouches is an everyday necessity. At the same time, adhesives are the primary cause of a wide range of iatrogenic skin injuries (12-14), including IAOP. The proposed mechanism of occurrence of IAOP is hypoxia and inflammation of the local skin tissue as well as repetitive and long-term mechanical injury by pressure and traction caused by the presence and frequent replacement of medical adhesives (16). Preventive measures should include gentle care and manipulation of all medical adhesives, especially electrodes, avoiding positioning electrodes on cosmetically sensitive areas, minimizing pressure by preventing the infant from lying on electrodes, occasionally changing the position of the electrodes, and usage of hydrogel electrodes and silicone adhesives (1,9,15-17). Adherence to the abovementioned preventive measures is particularly important in infants with the highest risk of iatrogenic skin injuries, including permanent ones such as IAOP.

Using a summary of the characteristics of previously reported infants with IAOP (although some of the reports do not contain all information of interest) with the addition of clinical cases presented in this paper (37 cases in total), we have tried to present a profile of infants at particular risk of IAOP (Table 2).

Based on the IAOP cases published so far, we can conclude that the greatest risk for this type of skin lesions is present in infants born with very and extremely low gestation and BW and with unstable vital functions from birth, whose critical condition demands mechanical ventilation and long hospital stay, as well as prolonged continuous monitoring that involves the use of different electrodes.

Contemporary neonatology is not aimed at survival alone, but rather on the long-term quality of life even in infants born at the lower limit of viability. At first glance, IAOP changes can seem irrelevant in infants with such a high risk of mortality and different major morbidities. But more and more these infants not only survive but also have no major long-term

health and developmental consequences caused by prematurity. After the first several years of life, when the focus is on following up these major morbidities, more subtle complications can become important in later developmental stages, especially at school-age and in adolescence. IAOP changes are permanent, and for the time being there is no treatment other than surgery. IAOP can cause significant aesthetic and consequently psychological burden. For example, our patient 2 is a girl with rather extensive IAOP changes. She was followed during 30 months of postnatal age, and her psycho-motor development is even slightly above average compared with her term peers. But the aesthetic consequences of her IAOP are unavoidable. It is yet to be seen whether there may be skin outpouching in the near-mamillar regions during puberty with the onset of breast development, and how heavy a psychological burden will be created by those skin changes.

## CONCLUSION

IAOP is a benign but permanent skin injury, with a potentially considerable aesthetic and consequent psychological burden. It occurs in very and extremely preterm infants. Given the increasing survival of these infants, more and more often without major developmental consequences, milder complications like IAOP will become even more important. Different profiles of health workers should be familiar with IAOP in order to prevent, recognize, and provide proper advice to children with IAOP as well as their parents.

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