

Aplasia cutis congenita and central nervous system malformations on a multiple pregnancy with fetus papyraceus: Case report

Laura Carolina Cardenas Moron ^{1,*}, Myriam Patricia Casas Villate ², Jorge Esteban Lopez Mora ² and Carlos Rivera Hernandez ²

¹ Department of Pediatrics, Faculty of health sciences, Militar Nueva Granada University, Hospital Militar Central, Bogota, D.C, Colombia.

² Neonatal Intensive Care Unit, Hospital Militar Central, Bogota, D.C., Colombia.

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Abstract

A fetal death in utero causes a prothrombotic environment due to abnormal placental anastomoses with hypoperfusion, which determines multisystem malformations, including dermal and subcutaneous involvement such as aplasia cutis and a central nervous system (CNS) abnormalities. We present the case of a quadruple pregnancy with death of a fetus at week 16, from which 3 live newborns were obtained, twin #1 with aplasia cutis type V. Twin #2 who did not present complications or associated malformations and twin # 3 with radiological documentation of dysgenesis of the corpus callosum. Based on literature, there is a relationship between chorionicity and the history of a papyraceous fetus and the multisystemic congenital malformations.

Keywords: Vanishing twin syndrome; Fetus papyraceus; Aplasia cutis congenita; Multiple pregnancy; Fetal death; Prematurity.

1. Introduction

Intrauterine demise of one fetus occurs in 0.5 to 6.8% of cases in multiple pregnancies. ¹ This event triggers the release of thrombotic material from the dead twin, leading to abnormal vascular placental anastomoses, hypovolemic state and, consequently, hypoperfusion periods^{1,2}. Chorionicity plays a major role since it has been documented that monochorionic pregnancies have a 6-fold increased risk of mortality after an intrauterine demise with associated multisystem malformations^{4,5}.

It has been found to be associated to aplasia cutis congenita, which is characterized by the localized absence of skin, subcutaneous cell tissue and even bone tissue in the most severe cases. It may occur as an isolated defect or be associated with cranial and cerebrovascular disorders with high morbidity and mortality⁶.

2. Case Report

Extremely preterm 29-week newborns, the result of a triamniotic, monochorionic, multiple pregnancy of a 31-year-old mother with one fetus dead at week 16, G3P2V2, non-primipaternity, spontaneous pregnancy. Table 1 shows the twins characterization.

* Corresponding author: Laura Cardenas

2.1. Case 1

Upon physical examination, some findings were noteworthy: absence of skin, subcutaneous cellular tissue and cranial bone in the midline at the level of the sagittal suture, at the frontal, temporal, parietal, coronal and occipital region, left flank, and atrophic skin defect and generalized erythroderma at the posterior level of the left thigh. Dermatology and plastic surgery evaluated the case and considered it to be Type V aplasia cutis (Figure 1, 2).

On the eighth day of life, she underwent washing and debridement + skin graft placement + amniotic membrane placement. On the second postoperative day, with 10 days of life, showed marked clinical deterioration, massive hemorrhage, with hemodynamic, respiratory instability and died.

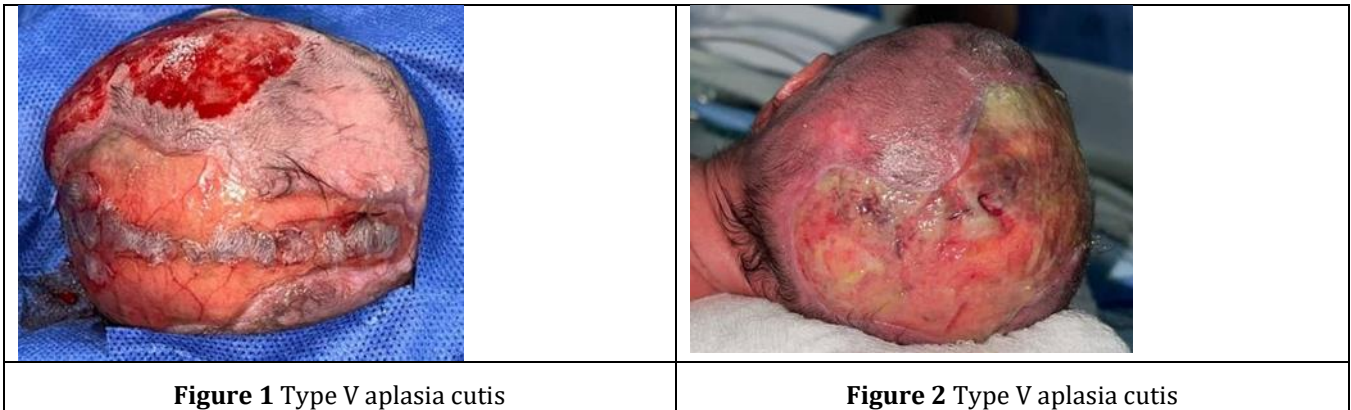


Figure 1 Type V aplasia cutis

Figure 2 Type V aplasia cutis

* Authorization of images by consent signed by the parents

2.2. Case 2

CNS ultrasound showed ventricular system dilation with images of periventricular echogenicity suggestive of periventricular leukomalacia and narrowing vs. dysgenesis of the corpus callosum. Renal ultrasound showed left pyelocalyceal ectasia. Brain Magnetic Resonance Imaging reported a maturity and furrowing pattern of the cerebral hemispheres, slight to moderate supratentorial ventriculomegaly with posterior predominance consistent with colpocephaly, potentially related to neuronal migration disorder, in which the prognosis is uncertain.

Table 1 Subjects characterization

Characteristic	Twin 1	Twin 2	Twin 3
Birth weight	915 g	1055 g	925 g
Birth height	36 cm	33 cm	35.4 cm
APGAR	5-7-8	5-7-8	5-7-8
Orotracheal intubation	Yes	Yes	Yes
Lung surfactant	Yes	Yes	Yes
PAD	No	No	Yes

PAD: patent ductus arteriosus

3. Discussion

In multiple pregnancies, with intrauterine demise of one fetus, there are significant consequences for the survivor, particularly in monochorionic pregnancies due to the development of ischemic lesions in vital organs such as the brain and even increased mortality itself [1,2].

A recent systematic review assessed the risk of mortality in the surviving twin in monochorionic and dichorionic pregnancies, finding 12% vs 4%, respectively, with a 6-fold increase in the risk of mortality after intrauterine demise for monochorionic pregnancies [3]. This is similar to the findings of Ward et al. who described that the greatest predictor for the survivor is chorionicity [4]. They also highlighted the importance of the ultrasound study in twins resulting from monochorionic pregnancies, since those without ultrasound signs of brain lesions had a better neurological prognosis.

Hillman's systematic review had similar findings: mono chorionic twins have 3.25-fold increased risk of imaging alterations than dichorionic twins, with a 7.57-fold higher risk of neurological morbidity at week 28-33 of gestation compared to dichorionic twins [5].

Aplasia cutis congenita, in turn, is a part of a heterogeneous group of conditions defined as the absence or scarcity of skin, with lesions at different depths, including the epidermis, dermis, and often, subcutaneous tissue and even bone tissue [6]. The lesion is non-inflammatory in nature, well demarcated with shape variation. At birth these defects may be covered by a thin transparent membrane [7].

By 2021, an incidence of 3 in 10,000 live births was reported, [6, 7, 11] with approximately 500 cases described in the literature [6].

Frieden classification for aplasia cutis is a method by which clinical diagnosis is currently established worldwide [8]. (Table 2).

Type V Aplasia cutis has been reported in monozygotic and dizygotic multiple pregnancies with papyraceous fetuses secondary to abnormal vascular placental anastomosis leading to placental infarcts [6, 9]. Fetal demise is thought to create thromboplastic material that spreads across vascular anastomoses, causing subsequent DIC in the surviving fetus due to an immature fetal fibrinolytic system, antithrombin III deficiency, and produces characteristic lesions secondary to abnormal skin development caused by those thrombotic events [9].

This type of aplasia often has a symmetrical bilateral distribution (Table 3) with variable size, and is considered the one that leads to the largest defects [10]. This is related to the distribution of the watershed areas that are more likely to undergo ischemia-induced damage [6].

Table 2 Frieden’s classification [8].

Type	Localization
1	Located on the scapula without other abnormalities
2	Located on the scapula but with abnormalities of the limbs such as: malformations of the limbs (Adams-Oliver syndrome), hypoplasia or aplasia of the distal phalanges, vascular malformations, fibromas, abnormalities of the nipple and hair
3	Located on the scalp along with epidermal nevus, neurological and ophthalmic abnormalities (such as seizures, mental impairment, corneal and eyelid lesions)
4	Accompanied by embryological deformities: such as omphalocele, leptomeningeal angiomas, cranial stenosis, porencephaly, meningomyelocele, spinal dysraphism, or gastroschisis
5	Associated to papyraceous fetus, placental infarction; extensive aplasia cutis of the trunk or limbs
6	Aplasia cutis and epidermolysis bullosa affecting the lower limbs
7	Aplasia cutis without epidermolysis bullosa involving the limbs
8	Associated to teratogens: intrauterine infections by herpes simplex and varicella-zoster virus, as well as intake of drugs during pregnancy such as methimazole or carbimazole
9	Associated to congenital malformations (Patau syndrome (trisomy 13), Wolf-Hirschhorn (4p deletion), Setleis syndrome, Johanson-Blizzard syndrome, Goltz syndrome, ADAM complex, Kabuki syndrome, Delleman syndrome, Finlay- Mark, XY gonadal dysgenesis)

Between 15 to 30% of cases are associated with cranial or underlying dura mater defects, with consequent exposure of brain tissue and sagittal sinus, increasing the risk of infection, thrombosis, and hemorrhage [7, 9, 10].

This condition can be documented before birth by means of ultrasound detection of an amniotic fluid index >20 cm and a relatively small abdominal wall circumference and with positive maternal alpha-fetoprotein [12, 13, 14].

Efforts to establish clinical and imaging findings relative to cerebrovascular involvement have been made. A study, comprised of 90 cases with a 7-year follow-up, found that the location of the lesion (vertex), the presence of the hair

collar sign, vascular spots, a lesion >5 cm were strong clinical indicators of cranial or cerebrovascular involvement [12, 13].

The management of this entity is controversial, with two major variants: conservative and surgical. Conservative management, that includes change of dressings and topical antibiotics, in order to keep the wound moist enough to create an optimal healing environment, [6, 7] exposes the patient to the risk of desiccation and necrosis of the wound bed, as well as associated morbidities, such as sagittal sinus thrombosis, hemorrhage and infection [6]. The surgical approach with skin grafts considered in large defects entails risks from anesthesia, massive hemorrhage, necrosis of the scalp flap, loss of the skin graft, morbidity at the donor site and infection [7, 10, 15].

Table 3 Frequency of locations of type V aplasia cutis [10].

Locations of type V aplasia cutis	Frequency
Chest	70%
Buttocks	60%
Abdomen	33%
Scapula	26%
Arms	21%
Back	16%

The mortality due to associated congenital defects, meningitis or bleeding from the sagittal sinus, surgical complications and infection has been estimated to range from 20 to 55% [7].

On the other hand, most congenital alterations of the nervous system are secondary to the disruption in the development of these structures due to genetic, infectious and/or toxic causes [16]. Some of them, such as agenesis/hypoplasia of the corpus callosum, may occur as an isolated condition or associated with other malformations. In a cohort of 225 newborns with this diagnosis, 42% occurred isolated, however 11% were associated with malformations at different levels, such as in the musculoskeletal and cardiovascular systems in 35 and 24% respectively [16].

The association that may exist between alterations of the central nervous system in the multiple pregnancy setting, mainly severe interventricular hemorrhage, encephalomalacia and ventriculomegaly, has been described [3].

The alterations in the CNS caused by multiple pregnancies with intrauterine demise have been explained by the occurrence of a disseminated intravascular coagulation status as a result of the release of thrombotic material from the dead twin. This is associated with unstable blood pressure and hypovolemia with severe hypotension secondary to placental anastomoses that allow blood transfer from the surviving twin to the dead co-twin, leading to periods of hypoperfusion and neurological damage [2, 3, 18].

Another systematic review of 28 studies assessed the presence of neurological alterations in the surviving twin, and found that the risk was 18% in monochorionic pregnancies, with a 4-fold increased risk than dichorionic ones [3]. A study performed in 2017 on 143 surviving twins of monochorionic multiple pregnancies with a mean gestational age of 29 weeks, found that the fetal loss rate is higher before 24 weeks with a greater association with perinatal mortality. It also highlighted the importance of the weight at birth, since this value affects newborn mortality by 50% [17] and earlier gestational age resulted in greater neonatal morbidity. It is important to consider the latter fact since monochorionic pregnancies have a 68% risk of preterm labor compared to dichorionic pregnancies with a 54% risk [5].

This is how Pharoah et al., in their study consisting of 524 newborns with long-term follow-up, found an association between cerebral palsy in the surviving twin of multiple monochorionic pregnancies, [2] highlighting the importance of early screening of patients to perform early obstetric interventions and have an impact on the multidisciplinary management required. Their approach included questioning why some monochorionic pregnancies are not affected and they concluded that it is due to the different types of placental anastomoses, it varies depending on whether it is arterioarterial, arteriovenous or venovenous. It was not possible to identify the association of severity for each one, [2] but the scope of ultrasound or diagnostic methods to establish this degree of circulatory exchange and the impact of new technological studies that lead to the development of appropriate strategies was highlighted.

4. Conclusions

The association between the various clinical, systemic manifestations was found in both cases presented in relation to chorionicity and history of a papyraceous fetus. Currently, with increasingly frequent incidence reports of multiple pregnancies, the papyraceous fetus is probably more common than it is recognized, so perinatal follow-up is critical to guarantee early detection of this type of congenital malformations.

Type V aplasia cutis is a rare entity. Diagnosis is based on clinical findings and history of the papyraceous fetus and the management depends on the extent and severity of the lesions. CNS malformations lead to significant morbidity and are typically associated with other systemic disorders. These entities require multidisciplinary management from genetics, neurology, psychiatry and neonatology.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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