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Surgical Treatment in a Case of Neonatal Fulminant Purpura

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Authors' contributions

This work was carried out in collaboration among all authors. Author THG designed the study, prepared the presentation of the case, selected the most illustrative photographs and wrote the first document of the manuscript. Authors MAAG and YTSÁ reviewed the manuscript and translated it from Spanish to English. Author ALMH managed the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

The literature is reviewed and a clinical case is presented in which a severe protein C deficiency was diagnosed and presented a flowery picture of the disease. The surgical treatment of the girl required the performance of gradual necrectomies, the amputation of the hand, the forearm of the right upper limb and some fingers and distal phalanges of the left hand, in addition to daily dressings with the application of temporary cutaneous covering of skin of lyophilized pig (heterograft-xenograft). Definitive closure of the lesions occurred by spontaneous epithelialization and the placement of living donor skin homografts obtained in this case from the father. The recovery of the grafted areas and of the limb amputations was favorable.

Conclusion: Due to the severity and torpid evolution of the disease, at the age at which it appears that makes the small caliber and difficult access of the blood vessels produce the gradual loss of accesses for the administration of essential medications, to the serious consequences left in organs

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and systems due to thrombotic events and finally to the lack of early availability and high cost of Protein C Concentrate; the prognosis for this disease is extremely bleak, leading to death in the majority of neonates who suffer from it.

Keywords: Fulminant Neonatal Purpura; necrectomy; amputation; heterograft-xenograft; homograft.

1. INTRODUCTION

Purpura fulminans has been associated with congenital and acquired diseases. Congenital abnormalities are secondary to coagulation disorders and are the main cause of purpura fulminans in the neonatal period [1].

The relationship between protein C deficiency and this nosological entity has been described. [2] Mutations in the PROS gene for protein C and the PROS1 gene for protein S are the most frequent and known, and the decrease in protein C activity the most commonly related. The heterozygous mutation of the PROS gene has an incidence of 1 / 200-500 inhabitants / year, associating a partial protein C deficiency and behaving as a risk factor for thromboembolic disease in children and adolescents. However, the homozygous mutation of the PROS gene, which associates a much lower incidence, around 1 / 40000-250000 inhabitants per year, presents a serious deficiency of protein C [2,3]. In Cuba, only the history of a case of neonatal age [4,5].

The clinical picture of these patients, at the level of the skin and subcutaneous cellular tissue, is related to a Spontaneous Blood Extravasation Syndrome associated with thrombosis of the dermal plexuses, severe peripheral ischemia and gangrene at any level but especially of the limbs and fingers, which can lead to multiple necrectomies and amputations. The surgical treatment of these children usually requires making difficult decisions, since the multidisciplinary group and the family members must consider the possibility of continuing with an aggressive line of treatment that can leave multiple mutilating and disfiguring sequelae that add to the severity of the condition and to the damage produced by the disease in organs and systems.

2. CASE PRESENTATION

The case is a female patiet newborn from a euthotic birth, with Apgar 8/9, maternal history of moderate toxemia at the end of the third trimester of pregnancy and birth for which he required admission and treatment with antihypertensive medications achieving total control after delivery; paternal health history. Before 48 hours after birth, the girl is transferred from the conventional ward to the neonatology unit of the Camilo Cienfuegos Provincial General Hospital of Sancti Spíritus because she begins with hemorrhagic manifestations on the skin (ecchymosis) at the level of the upper limbs, especially the right, left lower limb and right lumbar and perineal region; once in the unit, she presented signs of intraparenchymal hemorrhage that was corroborated by Computed Tomography. The evaluation of the case begins immediately by a multidisciplinary group.

It was first interpreted as Neonatal Allogeneic Thrombocytopenia and Tissue Necrosis Syndrome due to Spontaneous Hematic Extravasation. The lesions were observed closely and with expectant behavior until within the purpuric-hemorrhagic spots, large areas of tissue necrosis were delimited that apparently affected skin and subcutaneous cellular tissue. The most compromised area was the Right Upper Limb in its entirety, which over the days began to manifest a clinical picture of Compartment Syndrome, for which it was decided to perform the first emergency surgical intervention: escharotomy and fasciotomy of the arm and forearm. With some necrotic areas defined and others still in the form of ecchymosis and the presence of blisters and the bloody area left by the fasciotomy, it was decided to initiate local occlusive cures with antibiotic cream (Nitrofurazone) and request the tissue bank of the Frank País Surgical Hospital de la Habana Freeze-Dried Pigskin as skin covering for future surgical interventions (Fig. 1).

At 20 days after birth, the diagnosis of Fulminant Neonatal Purpura was raised, the patient maintained systemic treatment with maternal platelets, fresh frozen plasma and low molecular weight heparin (fraxiheparin), achieving improvement but not stabilization of the results of the complementary ones. The parents are studied and the results show a slight protein C deficiency in both.

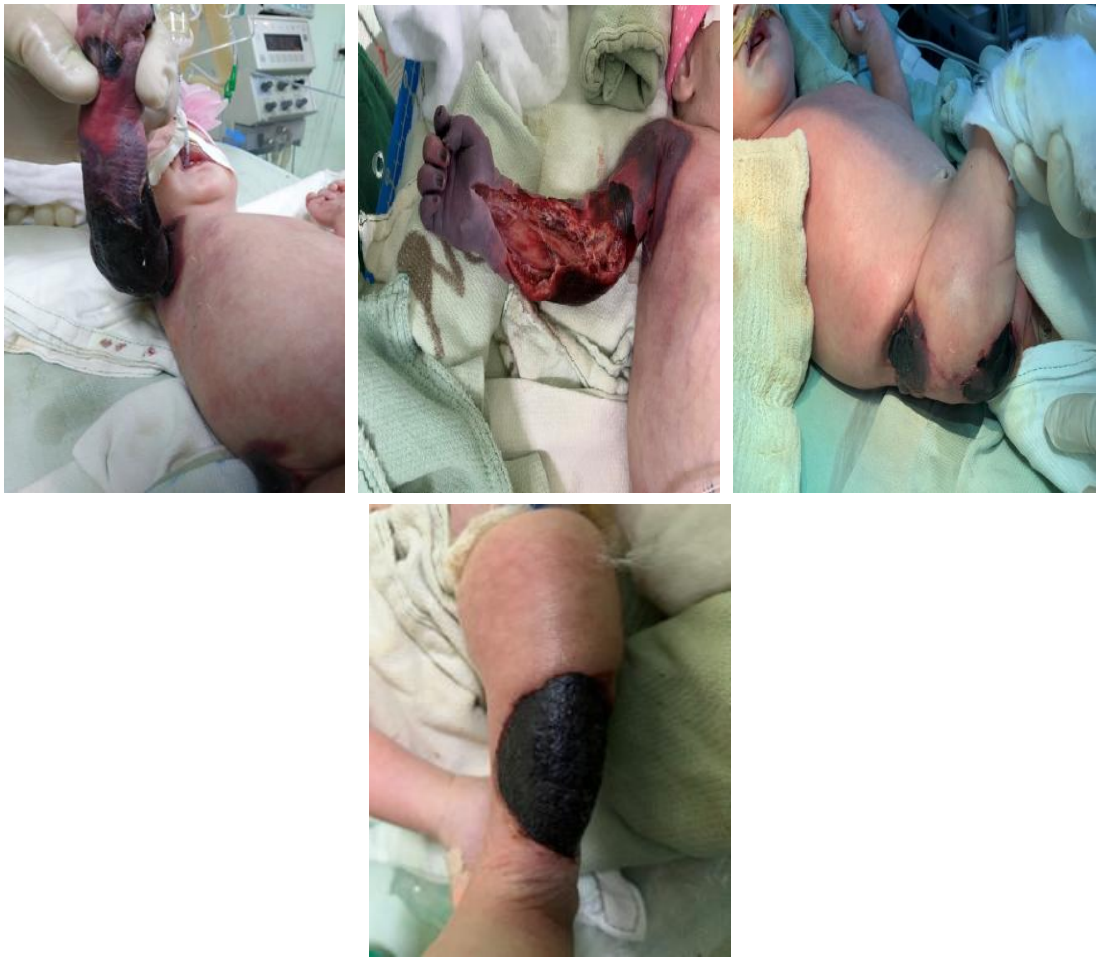

Fig. 1. Skin necrosis and fasciotomy of the right upper limb

On day 28, during healing, urgent surgical treatment for amputation is indicated, since the right hand was not viable as well as all the skin and subcutaneous cellular tissue of the limb, in the same intervention the areas of necrotic tissue would undergo necrectomy from other locations. The team meets to assess the level of amputation, the hand is completely unviable and with a poor prognosis from the functional and aesthetic point of view of the entire limb. Amputation is considered from the view point of the state of the limb, also total amputation at the thoracic level would be ideal, but the clinical state of the girl with low platelet counts, in addition, with necrotic tissue at the thorax level in the area of the flaps used for closing is evaluated as well, this dangerous option is made to protect the patien´s life and the success of the intervention. Amputation is considered at the level of the forearm; this option would eliminate the devitalized hand but would leave a large area of a limb that would not be functional without skin coverage and with exposed muscles. After exhaustive analysis, the consensus was reached to perform amputation at the elbow joint that would eliminate the devitalized hand, an uncovered and dysfunctional arm and the surgical intervention would undoubtedly be of a lesser scope as it moves away from the thoracic cavity, the bloody left area by arm necrectomy would undoubtedly means less bloody body surface to treat (Fig. 2).

After this intervention, the vital and complementary parameters of the girl were stabilized by being subjected to another surgical intervention for necrectomy 10 days later, removing the devitalized tissue and maintaining occlusive cures and covering with lyophilized xenograft in the areas that were free of necrosis. The necrotic tissue on the stump of the right arm,

which was covered only by flaps of muscle tissue, was completed.

At 48 days after birth, it was decided to perform a skin homograft from a living donor, in this case it was decided to take skin from the father's thigh since it had to have certain compatibility and the girl was not in a position to provide her own donor areas for the autograft. Epithelialization of the bloody areas of the thorax and left lower limb had been achieved with heterologous skin coverage (porcine skin).

First, two sheets of skin were obtained from the father's right thigh, and then the girl was surgically treated with a wide toilette of the areas to be covered and stimulation of the granulation tissue, which was red, shiny, aseptic, and optimal for receiving the graft. The area of the stump of the right upper limb, the right lumbar and perineal area and the left arm are covered with sheets of the paternal homograft, during this surgical time the area of suffering delimited in the left forearm is necrectomized, which in the course of the successive days covered with xenograft. The final evolution of the surgical treatment at 83 days was the total epithelialization and graft seizure, which did not show signs of rejection (Fig. 3).

From this moment on, the girl maintained the treatment with fresh plasma, despite the fact that venous access for her transfusion was difficult after several catheterizations and venous dissections. There were no bloody areas and all regions were totally epithelialized.

Around day 90, the infant suffers a new thrombotic event. The patient died 4 months after birth.

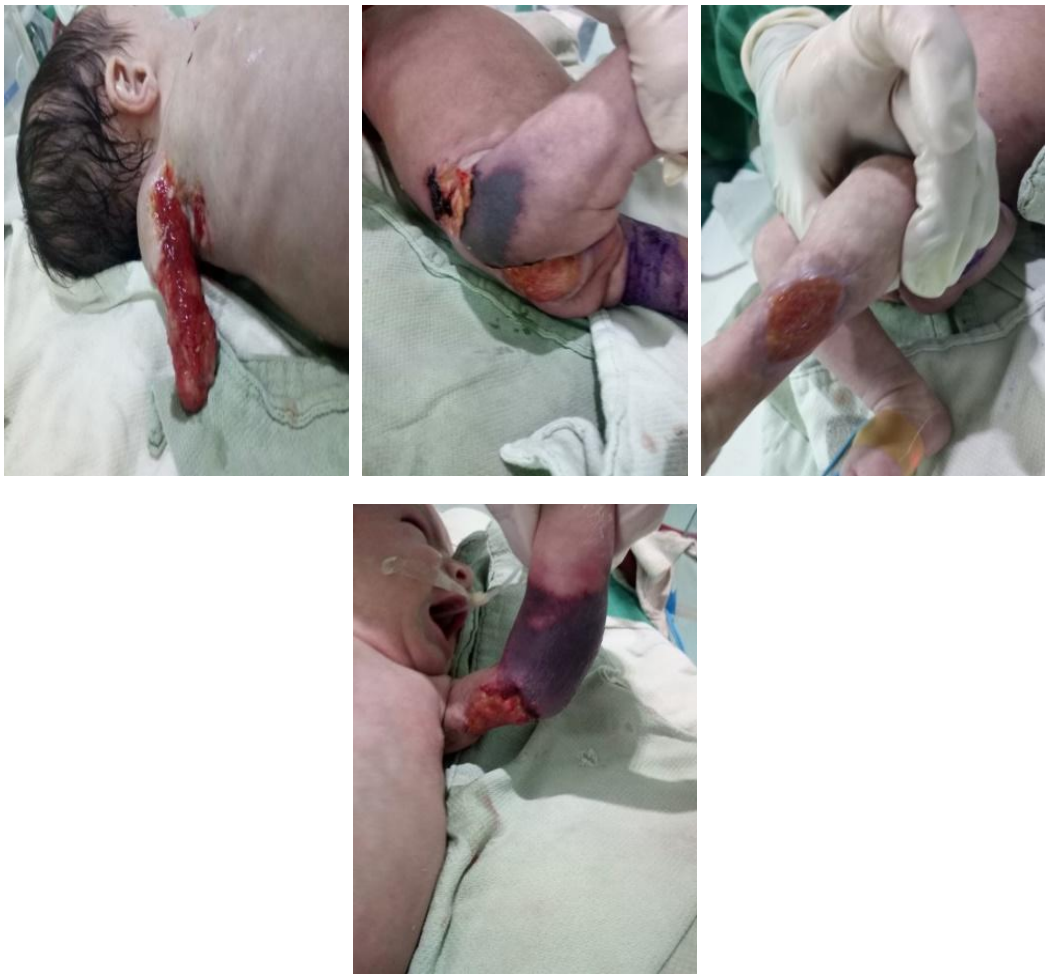

Fig. 2. Amputation of the right hand and forearm and necrectomy of the devitalized tissue

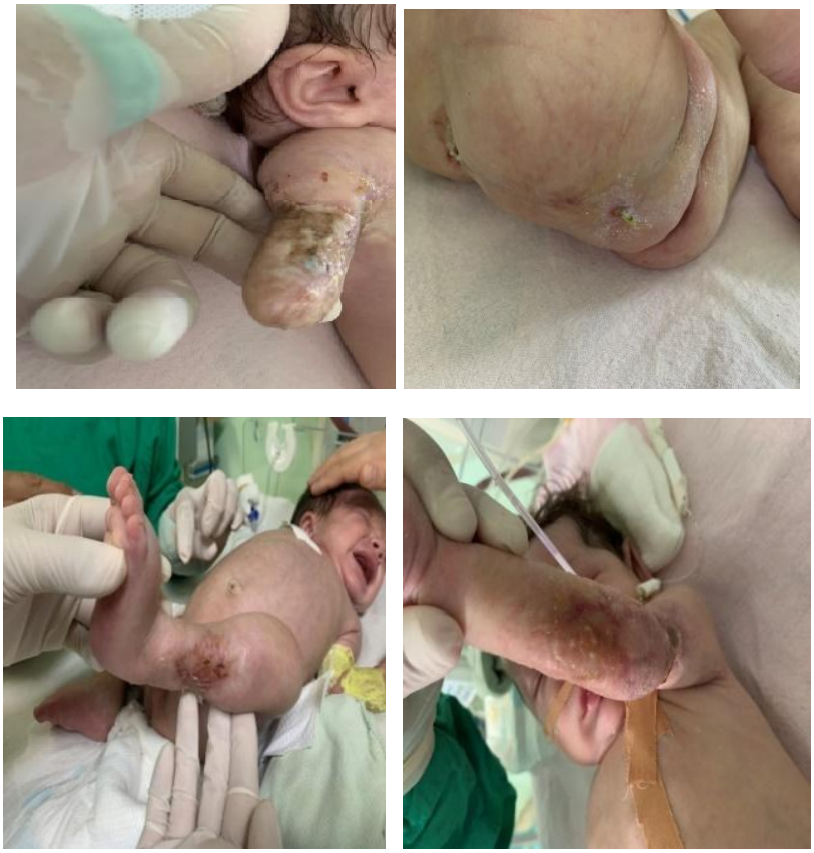

Fig. 3. Closure of bloody areas with paternal homograft and total epithelialization

3. DISCUSSION

Hereditary thrombophilia, entity that includes: Protein C deficiency, Protein S deficiency, Antithrombin III deficiency, Protein C resistance activated by mutation in factor V, Activated tissue plasminogen deficiency and Fibrinogen deficiency [6], in the General population has a frequency of 1: 25,000 to 1: 50,000.

Protein C is a serpin-type glycoprotein, produced by the liver that belongs to the group of proteins dependent on vitamin K [7]. Congenital protein C deficiency corresponds to a dominant inherited disorder with variable penetrance, the defect located on chromosome 2. Heterozygous people generally do not have symptoms until adulthood, but homozygous people have very low levels of protein C (<1%), and can develop severe purpura and thrombotic events, usually in the neonatal period it is rarer and can cause death.

To date, more than 160 mutations have been reported in the protein C gene [8]. The normal plasma concentration of protein C in newborns is 25 to 40 IU / dL, and it increases progressively until it reaches levels of a normal person at puberty. A mild deficiency is therefore considered to be one with values below 20 IU / dL, moderate from one to 20 IU / dL, and severe with values below one IU / dL [9]. The incidence in newborns is 1 / 1,000,000 births [10].

In the case presented, hemorrhagic skin manifestations constituted by ecchymotic spots located on the upper and lower limbs were evidenced from the first days after birth, traumatic injuries caused by a difficult fetal extraction were ruled out since the mother had a history of childbirth In addition, in these cases there are no complications and the damage gradually disappears during the first or second week of life [11].

In the clinical course of the condition that was presented, a rapid progression of the patient's cutaneous hemorrhagic picture was shown; during the second 24 hours of life, some blisters with serohematic content appeared in the lower limbs in the affected areas, which when

spontaneously ruptured They exposed areas of infiltrated underlying skin with hematic content that would evolve into areas of necrosis over the days, characteristics that agree with that reported in the literature [1-5,12].

Children with severe congenital protein C deficiency present with fulminant purpura with a very rapid onset of the clinical picture, usually within 2 to 12 hours after birth [9]. However, a delay in onset up to 6 and 12 months of age has been reported. They present an initial appearance of well-defined erythematous macules that evolve rapidly, with areas of necrosis and hemorrhage. Necrosis begins between 24 and 48 hours after the appearance of the first lesions, they are usually surrounded by a fine border of erythema, hemorrhage in the necrotic dermis causes the formation of vesicles or bullae with hemorrhagic content. Necrosis can involve soft tissues, requiring surgical debridement, fasciotomies, or amputation. Injuries occur at trauma sites and there is a predilection for the extremities [9].

The girl initially made an abrupt debut and most of the lesions evolved into an irreversible form. After establishing the diagnosis and starting the supply of Fresh Frozen Plasma and fraxiheparin, the successive episodes of lesions mostly remained in the first phase and they did not progress to necrosis, which stabilized in the short time that Protein C Concentrate could be prescribed.

Surgical treatment in this case was essential, due to the extensive areas of necrosis, mainly in the extremities. This treatment followed the consensus of the multidisciplinary group, focusing management on avoiding infections associated with hospital care and adequate nutritional support. As recommended, the debridement, graft and amputation that the patient underwent was performed until the infarcted areas were completely demarcated from the surrounding tissues, in addition to the administration of fresh plasma prior to the interventions, regardless of the periodic indications she received from This derived from blood. The recovery of the grafted areas and of the limb amputations was favorable.

4. CONCLUSIONS

According to the antecedents, the characteristics of the clinical picture of the case presented and the complementary studies carried out, the diagnosis of Fulminant Neonatal Purpura was made due to a hereditary and severe deficiency of Protein C in the girl. The surgical treatment of the case required the performance of gradual necrectomies, the amputation of the hand, the forearm of the right upper limb and some fingers and distal phalanges of the left hand, in addition to daily dressings with the application of temporary pig skin skin cover lyophilized (heterograft-xenograft). Definitive closure of the lesions occurred by spontaneous epithelialization and the placement of living donor skin homografts obtained in this case from the father. The recovery of the grafted areas and of the limb amputations was favorable. Due to the severity and torpid evolution of the disease, at the age at which it appears that makes the small caliber and difficult access of the blood vessels produce the gradual loss of accesses for the administration of essential medications, to the serious consequences left in organs and systems due to thrombotic events and finally to the lack of early availability and high cost of Protein C Concentrate; the prognosis for this disease is extremely bleak, leading to death in the majority of neonates who suffer from it.

CONSENT

As per international standard, parental written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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