

## IDIOPATHIC NEONATAL AORTIC ARCH THROMBOSIS: A CASE REPORT

Ignazio Lofù <sup>1</sup>, Antonio Di Mauro <sup>2</sup>, Antonio Di Coste <sup>3</sup>, Egisto Scalini <sup>1</sup>,  
Vincenzo Basile <sup>1</sup>, Daniela Codazzi <sup>4</sup>, Nicola Laforgia <sup>2</sup>, Mariano Manzionna <sup>1</sup>

### SUMMARY

**Background:** Neonatal aortic arch thrombosis is a rare but life threatening condition. A correct diagnosis and an appropriate therapeutic approach are fundamental to prevent death or severe injuries.

**Case presentation:** we report a case of spontaneous aortic arch thrombosis in a term newborn, who presented with suggestive signs of aortic coarctation immediately after birth. Despite the initiation of anticoagulant therapy, a massive increase in size of thrombus with evidence of coronary involvement was noted. Thrombolytic treatment was performed with thrombus resolution. Death occurred after a few days due to widespread brain haemorrhage.

**Conclusion:** To date, no definitive guidelines have been published for the treatment of neonatal aortic arch thrombosis, and only anecdotal reports are available. A multidisciplinary approach is fundamental in order to evaluate the risk:benefit ratio of proposed medical and surgical interventions. Further studies are needed to improve consensus evidence based guidelines and ensure appropriate approaches to this condition.

### Introduction

Neonatal aortic thrombosis is an extremely rare event with a generally poor prognosis. Due to its rarity, knowledge about its pathogenesis is quite limited. Although various studies have shown an association with acquired and inherited predisposing conditions (Tab. 1), most cases remain idiopathic [1].

Depending on the thrombus location, degree of aortic occlusion and involvement of other organs, aortic thrombosis clinical signs range from a completely asymptomatic presentation to a life threatening neonatal emergency [2]. Recently, The Italian Society of Neonatology has developed recommendations for the diagnosis and treatment of neonatal thrombosis [3]. However, these have been drawn from trials in adult and paediatric patients without rigorous evaluation of their efficacy and safety in newborns. Available options include anticoagulation with heparin, thrombolysis with tissue plasminogen activator (tPA), surgical embolectomy, and finally, watchful waiting [4]. An early diagnosis is mandatory for the initiation of treatment without delay.

Here we describe a fatal case of severe aortic arch thrombosis in a term newborn without any identifiable predisposing conditions, treated with anticoagulation and thrombolysis

### Address of the authors

1. Pediatric Unit, Maternal and Child Health Department "S. Giacomo" Hospital, ASL BA, Monopoli (Bari), Italy

2. Neonatology and Neonatal Intensive Care, Unit Department of Biomedical Science and Human Oncology, University of Bari "Aldo Moro", Bari, Italy

3. Pediatric Heart Surgery Unit, Giovanni XXIII Pediatric Hospital, Bari, Italy

4. Pediatric Intensive Care Unit, Giovanni XXIII Pediatric Hospital, Bari, Italy

**Send correspondence to:** Mariano Manzionna, [mariano.manzionna@alice.it](mailto:mariano.manzionna@alice.it)

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who died due to a widespread brain haemorrhage and myocardial ischemic damage. The authors wish to emphasize the clinical presentation and the diagnostic approach in order to guide other physicians during the management of this potentially catastrophic condition.

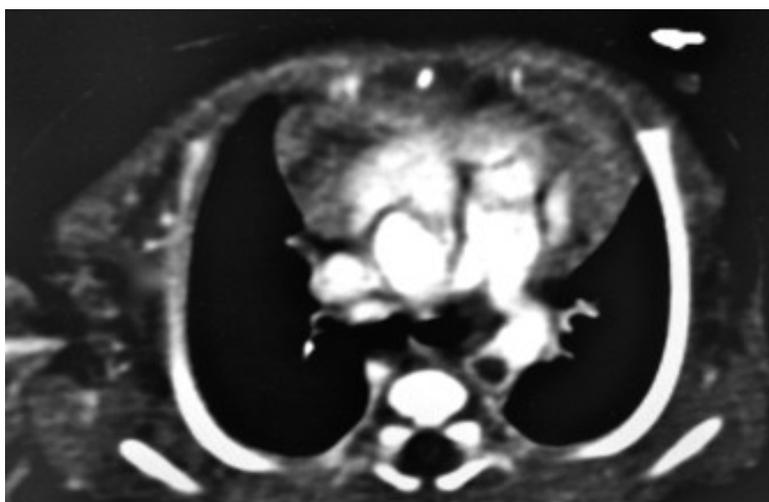
#### Clinical report

A term male neonate was born by normal vaginal delivery. After birth, he presented with acutely pale and cold legs, weak femoral pulse and right arm oedema. Arterial pulse oximetry screening revealed significant difference between a preductal oxygen saturation of 98% and a postductal oxygen saturation of 85%. Because a duc-

tus dependent heart disease was suspected, infusion of  $E_2$  prostaglandins (0,01 $\mu$ g/kg/min) was started, and the baby was moved to the nearest paediatric Cardio Surgery Centre for further investigations. A Color Doppler echocardiogram excluded congenital heart disease and showed an echo-dense sub-occluding mass in the aortic arch (Figure 1). Thrombus was strongly suspected and confirmed by high-resolution angiography computed tomography (ACT). It extended from the patent ductus arteriosus to the innominate artery (23 mm), partially occluding the aorta and left carotid (Figure 2). Diffuse ground glass pulmonary opacity was also detected on CT scanning of the chest.



**Figure 1:** Bidimensional Color Doppler Echocardiogram: Aortic arch thrombus with sub-total lumen occlusion.



**Figure 2:** Cm CAT: Absence of contrast medium in the aortic lumen isthmus, caused by a circular thrombus; visible the patent arterial ductus.

Complete blood count with platelet, clotting and thrombophilia screen (factor V Leiden mutation, MTHFR, and protein C and S deficiency) were all within the normal range for term neonates. No family history of thrombophilia was reported. No evidence of sepsis was found. A diagnosis of an idiopathic neonatal aortic thrombosis was made. Due to the extension of the thrombus, surgical removal was not considered as a valid therapeutic option. On the basis of input from neonatologists, cardiologists and haematologists, anticoagulant therapy with standard heparin was started according to the Italian Society of Neonatology Recommendations for diagnosis and treatment of neonatal thrombosis [5]. The baby underwent a daily echocardiogram and monitoring of coagulation parameters.

Echocardiography on day 5 showed persistence of thrombus in the aortal arch and presence of a new thrombus in the descending aorta.

In a scenario of acute life threatening vessel occlusion with immediate impact on cardiac, renal and limb functions, an urgent thrombolysis with t-PA (0,1 mg/Kg/h) was carried out successfully according to the Italian Society of Neonatology Recommendations (Figure 3).

A few hours later the baby showed a sudden desaturation followed by bradycardia, which required intubation with mechanical ventilation.

There followed a progressive worsening of the baby's general conditions resulting in coma. CT head imaging revealed multiple haemorrhages and multiple ischemic infarcts in both cerebral hemispheres. Death occurred on day 8 of life.

In addition to massive haemorrhages and multiple ischemic infarct of the brain, autopsy showed left ventricular myocardial ischemic necrosis caused by coronary embolism, and presence of small aspecific lymphoid aggregates in the lung, probably related to a misleading interstitial pneumonia.

### Discussion

Newborns are susceptible to thromboembolic accidents due to an immature haemostatic system [6].

Arterial thrombosis represents nearly 30% to 50% of thromboembolic complications and approximately 4% to 30% of these are related to aortic thrombosis[7,8,9].

Based on a recent review by Wieland et al, only 21 reports deal with neonatal AAT [10]. Including our patient, the mortality rate is 60% (13/22).

Neonatal AAT can be most insidious and can occur, as in our and other reported cases, mimicking aortic coarctation [11] or congenital heart disease [12,13]. A neonatal partially occlusive thrombus does not represent a severe emergency if systemic circulation is maintained through patent ductus arteriosus with prostaglandins



**Figure 3:** Cm MPR CAT: Total resolution of thrombus in aortic arch after thrombolytic treatment.

infusion. Color Doppler Echocardiography is the most commonly applied diagnostic method to differentiate and diagnose aortic thrombosis. However, despite its advantages as point of care testing, ultrasound provides imprecise anatomic feature information and other imaging techniques could be more useful (ACT or Magnetic Resonance Angiography).

Although the correct management of arch aortal thrombosis remains controversial and the risk:benefit ratio of treatment needs to be considered individually in each case, the Italian Society of Neonatology recommends anticoagulant therapy with standard or low-molecular weight heparin in the absence of organ or life threatening ischemia, and thrombolytic therapy with t-PA or surgical thrombectomy in thrombus showing a massive organ or limb ischemia. Our case was unsuccessfully treated at diagnosis with standard heparin and, although t-PA was effective in lysing thrombosis, a fatal bleeding complication occurred. Medical interventions should be undertaken with caution because of significant risks of major bleeding and, moreover, prior to administering thrombolytic agent to a neonate, it is mandatory to exclude a pre-existing intracranial haemorrhage. Probably had the thrombolytic therapy been administered with caution as an initial therapeutic approach it may have been resolute. However, this is purely speculation.

In a small case series with evidence of AAT, Neal et al. [14] calculated survival rates for treatment options with 80% survival for anticoagulation therapy, 75% for thrombolysis and 67% for surgical thrombectomy. Due to the lack of large studies and only anecdotal evidence, there are not enough data to recommend any particular treatments, and each case has to be considered individually.

Despite various studies showing AAT association with acquired and inherited predisposing conditions, most cases remain idiopathic. In our patient, autptic study showed evidence of small aspecific lymphoid aggregates in the lung. We hypothesized a probable viral infection during the last days of pregnancy as a trigger cause of blood factor release leading to massive clotting. The role of virus-induced endothelium damage in the etiopathogenesis of neonatal arterial thrombosis has been

previously established[15].

### Conclusions

Neonatal AAT is a rare and often fatal event, which is extremely challenging for the medical team involved in its management. To date, no definitive guidelines have been published for the management of neonatal aortic arch thrombosis, and only anecdotal reports are available. Treatment is hampered by the lack of adequate clinical trials involving the neonatal population and a multidisciplinary approach is fundamental in evaluating the risk:benefit ratio of proposed medical and surgical interventions.

Further studies are needed to improve consensus evidence based guidelines to ensure appropriate approaches to this condition.

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### References

1. Saracco P, Parodi E, Fabris C, Cecinati V, Molinari AC, Giordano P. Management and investigation of neonatal thromboembolic events: genetic and acquired risk factors. *Thromb Res.* 2009 Apr;123(6):805-9.
2. Saxonhouse MA. Management of neonatal thrombosis. *Clin Perinatol.*2012; 39(1) 191-208
3. Raccomandazioni Diagnosi e Terapia delle trombosi neonatali. <http://www.neonatologia.it/show/Raccomandazioni%20SIN/4/>
4. Monagle P, Chan AK, Goldenberg NA, Ichord RN, Journeycake JM, Nowak-Göttl U, Vesely SK; American College of Chest Physicians. Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012 Feb;141(2 Suppl):e737S-801S.
5. Andrew, M., et al., Heparin therapy in Paediatric patients: a prospective cohort study. *Pediatr Res.* 1994. 35(1): p. 78-83.
6. Ignjatovic V, Mertyn E, Monagle P. The coagulation system in children: developmental and pathophysiological considera-

- tions. *Semin Thromb Hemost.* 2011 Oct;37(7):723-9.
7. Monagle P, Newall F, Barnes C, Savoia H, Campbell J, Wallace T, Crock C. Arterial thromboembolic disease: a single-centre case series study. *J Paediatr Child Health.* 2008 Jan;44(1-2):28-32.
8. Schmidt B, Andrew M. Neonatal thrombosis: report of a prospective Canadian and international registry. *Paediatrics.* 1995 Nov;96(5 Pt 1):939-43
9. Albisetti M, Schmugge M, Haas R, Eckhardt BP, Bauersfeld U, Baenziger O, Hug MI. Arterial thromboembolic complications in critically ill children. *J Crit Care.* 2005 Sep;20(3):296-300.
10. Wieland I, Jack T, Seidemann K, Boehne M, Schmidt F, Happel CM, Koeditz H, Bertram H, Sasse M. Neonatal aortic arch thrombosis: analysis of thrombophilic risk factors and prognosis. *Cardiol Young.* 2013 Jan 21:1-7.
11. Das BB, Sahoo S, Ivy DD. Neonatal aortic arch thrombosis masquerading as coarctation of the aorta. *Pediatr Cardiol.* 2004 Jan-Feb;25(1):80-3.
12. Kenny D, Tsai-Goodman B. Neonatal arterial thrombus mimicking congenital heart disease. *Arch Dis Child Fetal Neonatal Ed.* 2007 Jan;92(1):F59-61. Epub 2006 Jul 28.
13. Nagel K, Tuckuviene R, Paes B, Chan AK. Neonatal aortic thrombosis: a comprehensive review. *Klin Padiatr.* 2010 May;222(3):134-9.
14. Richard Neal, Katharina Mattishent, and Fiona Reynolds, "Aortic Arch Thrombosis Mimicking Interrupted Aortic Arch," *Case Reports in Critical Care*, vol. 2013, Article ID 948234, 3 pages, 2013. doi:10.1155/2013/948234
15. Lanari M, Lazzarotto T, Papa I, Venturi V, Bronzetti G, Guerra B, Faldella G, Corvaglia L, Picchio FM, Landini MP, Salvioli GP. Neonatal aortic arch thrombosis as a result of congenital cytomegalovirus infection. *Paediatrics.* 2001 Dec;108(6):E114