

Association between neonatal Volkmann's syndrome and perinatal ischemic stroke: review of the literature

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Summary. *Background and aim:* Neonatal forearm compartment syndrome, also known as neonatal Volkmann's syndrome, is an uncommon condition for which the pathognomonic finding is the presence of a forearm skin lesion. Stroke in newborns occurs in about 1/1600-5000 births. Aim of the present review is to highlight the possible association of these two conditions. *Methods:* We performed a review concerning the association of both these conditions. *Results:* We found only few reports on the association of an ischemic limb injury and a perinatal stroke combined in the same newborn. *Conclusions:* In light of the high percentage of delayed diagnosis of perinatal stroke, we recommend to perform an accurate neurological evaluation and eventual neuroimaging studies in order to investigate for a cerebral vascular damage and, furthermore, to rule out thrombophilic conditions in infants with signs of a neonatal ischemic limb and/or Volkmann's syndrome. (www.actabiomedica.it)

Key words: neonatal forearm compartment syndrome, neonatal ischemic limb, neonatal compartment syndrome, perinatal ischemic stroke, cerebral infarction

Introduction

Neonatal Volkmann's syndrome is an uncommon condition due to an acute compartment syndrome leading to a prolonged ischemia, and for which the pathognomonic finding is the presence of a forearm skin lesion (1). Stroke in the perinatal period occurs in 1/1600-5000 births and in about 1/4000 full-term neonates (2,3), however the incidence is probably underestimated due to the high percentage of delayed diagnosis. Here we have searched the case reports which have presented the association of these two conditions, highlighting the potential role of a peripheral/cutaneous lesion as an indicator of central nervous system damage.

Methods

Literature searches were performed in Pubmed, using the following search terms: (neonatal Volk-

mann's syndrome OR neonatal forearm compartment syndrome) AND (perinatal stroke OR cerebral stroke OR cerebral infarction OR neonatal stroke OR cerebral stroke). We also reviewed all the cases of neonatal Volkmann's syndrome in the literature and included secondary sources of data, such as reference lists of articles reviewed.

Results

In the literature there were only three reports about the association of neonatal Volkmann's syndrome and ipsilateral cerebral stroke (4-6) and only few further reports about the association of an ischemic limb or extremity gangrene and cerebral stroke (7-13). The main characteristics of these reports are reported in Table 1. In most cases the upper limb was involved (10/12), with a slight right side predominance (6/12). As the perinatal stroke was mostly ipsilateral to

Table 1. Main findings of previous reports found in literature

References	Risk Factors/ coagulation findings	Upper/ Lower limb	Limb side	Limb signs	Doppler ultrasound scan	Stroke side	Stroke side vs limb side	Neuroimaging	Neonatal Sz	Outcome
Perricone G & Granata C 1982 (4)	Prolonged and difficult labour/ n.r.	U	L	VS (cutaneous lesion, pale and edematous hand/ forearm)	n.p.	L*	Ipsi	n.r.	-	R He
Asindi AA et al. 1988 (7)	Incomplete placenta with ragged membranes/ low platelet count.	U	R	IL (fingers cyanosis, limitation of movements, no pulses, decreased arm/forearm circumferences; muscle wasting)	+ Normalization within 72 hours of birth.	R	Ipsi	cystic lesion in the area of the right middle cerebral artery with shrinkage of the right hemisphere (CT scan)	-	L spastic He, L hemianopia HC<10°p
Raine J et al. 1989 (8)	-/-	U	R	IL (pale and cold arm; faint/absent pulses)	n.p.	B (R>L)	Ipsi- Contra	Diffusely increased echodensity of the cerebral hemispheres and small/compressed ventricles (cranial US), Bilateral middle cerebral artery and R posterior cerebral artery infarction (CT scan).	+	Hypertonia (L>R) HC<3°p
Gudinchet F et al. 1991 (9)	Prolonged delivery due to shoulder dystocia/-	U	R	IL (no spontaneous movements, cyanosis, no pulses)	+	R	Ipsi	hypodense lesion in the area of the R middle cerebral artery with calcification and atrophic aspect (CT scan)	-	L He
Guajardo L et al. 1994 (10)	Fetal intolerance to labor and 3+ meconium stained fluid/-	U	L	IL (blanching/pallor, ecchymotic area with blistering; no radial artery pulsation)	+	L	Ipsi	WM edema due to ischemic changes (CT scan). L hemispheric infarction (MRI)	(apnoeic episodes. EEG n.p.)	n.r.

(continued)

Table 1. Main findings of previous reports found in literature

References	Risk Factors/ coagulation findings	Upper/ Lower limb	Limb side	Limb signs	Doppler ultrasound scan	Stroke side	Stroke side vs limb side	Neuroimaging	Neonatal Sz	Outcome
	History of herpes genitalis in the mother/-	U	B	IL (blanching/pallor of upper extremities, no pulses)	+	B	B	Extensive areas of decreased density involving both hemispheres (CT scan). Extensive bilateral infarction (MRI). Multiple intracranial major vessels occlusions (MRA).	+	n.r.
Carr M et al. 1996 (11)	3 previous spontaneous abortions; prematurity; multiple infarcts in the placenta/-	U		Ga (large necrotic area on the ulnar border of the forearm and hand)	+	R	Ipsi	Multiple large cystic lesions in the R cerebral hemisphere suggesting massive intrauterine infarction in the R anterior and middle cerebral artery distribution (CT scan).	-	L He
Léauté- Labrèze C et al. 1998 (pt 2) (5)	Co-twin death/ n.r.	U	R	VS (unilateral cutaneous defect, wrist flexion, ulnar and median nerves paralysys)	n.p.	L	Ipsi	L emisphere atrophy (CT scan).	-	R arm Mp; focal Sz
Long DK et al. 2002 (12)	Mother's diabetes; vacuum assisted delivery; Apgar score 1 min=5; anticoagulation IgG in the mother/ decreased plasminogen activity	Lo	L	Ga (necrosis below the knee)	n.p.	R	Contra	a small R thalamic infarct with intraventricular and periventricular blood. No evidence of a sagittal sinus thrombus (CT scan and MRI).	(apnoeic episodes. EEG n.p.)	n.r.

(continued)

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References	Risk Factors/ coagulation findings	Upper/ Lower limb	Limb side	Limb signs	Doppler ultrasound scan	Stroke side	Stroke side vs limb side	Neuroimaging	Neonatal Sz	Outcome
Salama H et al. 2003 (13)	Birth trauma/ low level of serum protein C and S and of AT III	U	R	IL (cyanosis, no pulse, Erb's palsy)	-	R	Ipsi	infarction of the territories supplied by the R middle cerebral artery (MRI). No evidence of thrombus formation (MRA).	+	L, spastic He
Pavlidis E et al. 2013 (6)	Maternal ge- stational diabe- tes/ low level of serum protein C and S and of antithrombin III; prolonged PT and PTT times	Lo	R	IL (cold and pale, poor pulsation)	n.p.	R	Ipsi	Subarachnoid hemorrhage. Mixed density areas within the R temporal lobe representing infarction (CT scan).	+	L He
Pavlidis E et al. 2013 (6)	Oligohy- drannios/ -	U	L	VS (unilateral lesion, wrist flexion, distal hypomobility, normal pulses)	-	L	Ipsi	Extensive L hemisphere encephalomalacia in the frontal and temporo-parietal regions-areas supplied by L middle cerebral artery- (MRI).	-	Signs of R He
Total	Risk factors= 11/12 Coagulation anomalies= 4/10	U= 10/12 Lo= 2/12	R= 6/12 L= 5/12 B=1/12	IL = 7/12 Ga = 2/12 VS = 3/12	+ = 5/7 - = 2/7	R= 6/12 L= 4/12 B=2/12	I = 10/12 C = 2/12 B = 1/12		+ = 4/12 - = 8/12	He/CP = 9/9 Sz = 1/9 Mi = 2/9

AT III = antithrombin III; B = bilateral; Contra = contralateral; CT = computed tomography; Ga = gangrene; HC = head circumference; He = Hemiplegia/ hemiparesis; IL = ischemic limb; Ipsi = ipsilateral; L = left; Lo = lower; Mi = microcephaly; Mp = monoparalysis; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging; n.p. = not performed; n.r. = not reported; pt = patient; R = right; Sz = seizures; U = upper; US = ultrasound scans; VS = Volkmann's syndrome; * = not reported, assumed in light of the patient's clinical history.

the limb lesion, this little sample of subjects presented, differently from the current knowledge on perinatal stroke (14), an unusual right prevalence of cerebral infarcts. Whereas some Authors argued that a right upper limb predominance of the ischemic lesion could be due to intrauterine fetus position (15), it was otherwise suggested that this side prevalence for both peripheral and cerebral ischemic lesions could be explained by an embolus migrating from the umbilical vein or placenta, via the foramen ovale, into the arterial circulation, to the right cerebral system and right ulnar artery via the brachicephalic artery (8,11). However, the minority of cases with left-sided lesions are possibly ascribable to similar pathogenic mechanisms as the ones involved in typical perinatal stroke. Abnormalities in coagulation profile were evident in 4/10 subjects in whom these laboratory analysis were performed. Thus, we suggest performing an accurate work up to rule out such conditions, and to exclude the risk of thrombotic events recurrence. Doppler ultrasound scan abnormalities were found in 5 out of the 7 newborns in whom it was performed (71.4%). In some case reports with negative findings it is plausible to think that they could have already normalized at the time Doppler scan was done, because of the high plasma fibrinolytic activity in newborns, as previously suggested by other authors (7). Neonatal seizures are reported in only four subjects (33.3%), whereas two further neonates had apnoeic episodes. Thus, only half of the newborns showed systemic or neurological signs/symptoms, leading to an early diagnosis of the associated stroke. In the large majority of neonatal Volkmann's syndrome cases described in the literature, neuroimaging studies are not reported in the diagnostic assessment (1,4,15-25).

Discussion

Neonatal forearm compartment syndrome is best known by the name of its sequelae: Volkmann's syndrome or Volkmann's ischemic contracture. Recently Ragland et al. performed a review of the existing literature on this syndrome (1). The authors found 24 newborns with this syndrome. They were variously reported, focusing on skin lesions -sometimes misdiagnosed with aplasia cutis congenita- or on nerve palsy. Other

reports underlined the association of nerve palsy and subcutaneous fat necrosis (26-29). Although a precise estimation of incidence/prevalence of this condition is still not available, the increasing number of reported patients led the authors to conclude that this condition is not as rare as initially asserted. Recent data indicated an incidence of one in 4500 births per year for neonatal limb ischaemia (30). Volkmann's syndrome was first described in 1881 as the association of an ischemic muscle paralysis and contracture (31), due to an acute compartment syndrome leading to a prolonged ischemia. In adults and older children this condition is mostly caused by traumatism/fractures and external injury/compression (16), whereas in children displaced supracondylar fracture of the humerus with or without an associated displaced forearm fracture is frequently reported (32). Nevertheless, neonatal Volkmann's syndrome is a peculiar condition, related to specific mechanisms of the pre- and peri-natal period (such as amniotic band syndrome, umbilical cord entanglement, twin pregnancies, malposition of the upper limb, cephalopelvic disproportion, operative delivery, oligohydramnios) (17). Coagulation disorders are also reported (1). Fundamental pathogenic mechanisms can be essentially summarized in trauma, coagulation disorders, and infectious causes (15). Interestingly, the same pathogenetic mechanisms seem to be involved in other clinical conditions such as ischemic limbs and extremity gangrene (11), leading the author to speculate that we are facing a spectrum of conditions with different degrees of severity (from subcutaneous fat necrosis and nerve palsy to gangrene) rather than different clinical entities. To properly classify these conditions, some authors referred to skin lesion as a steady finding consistent with neonatal forearm compartment syndrome, being a larger lesion related to a greater injury and a more severe loss of function (1). Perinatal stroke incidence is about 1/1600-5000 births (3). The most affected areas are those vascularized by the middle cerebral artery, with a left hemisphere predominance (33). The main clinical presentation during neonatal period consists of clonic or tonic (mostly focal) and/or apnoeic seizures, possibly associated with other systemic neurological signs/symptoms (ipo-/a-reactivity, lethargy, tone abnormalities) (14,34,35). However, about 40% of perinatal strokes are clinically

unrecognized in the neonatal period (35), because of scanty clinical signs/symptoms, inadequate early neuroimaging studies and precocious discharge from hospital (14,33). Both neonatal forearm compartment syndrome and perinatal stroke share a possible underlying risk factor in prothrombotic conditions. Risk factors for thrombophilia could be classified in maternal, prenatal, neonatal, and placental risk factors (for detail see (36)). Perinatal stroke can be an underestimated and harmful condition leading to long-term disability. Delayed diagnosis is not uncommon and is often achieved retrospectively due to the stroke sequelae. Thus, every sign/symptom that could help to discover such an injury has to be considered.

Conclusions

We suggest performing a detailed clinical neurological evaluation, cerebral ultrasound scans, and eventually cerebral magnetic resonance, in newborns with an ischemic limb or a neonatal forearm compartment syndrome, to bare a possibly associated perinatal stroke and to allow its prompt diagnosis.

References

- Ragland R 3rd, Moukoko D, Ezaki M, Carter PR, Mills J. Forearm compartment syndrome in the newborn: report of 24 cases. *J Hand Surg Am* 2005; 30: 997-1003.
- Lynch JK, Nelson KB. Epidemiology of perinatal stroke. *Curr Opin Pediatr* 2001; 13: 499-505.
- Lynch JK. Epidemiology and classification of perinatal stroke. *Semin Fetal Neonatal Med* 2009; 14: 245-9.
- Perricone G, Granata C. Volkmann's syndrome of the forearm in a newborn infant. *Chir Organi Mov* 1982; 68: 121-5.
- Léauté-Labrèze C, Depaire-Duclos F, Sarlangue J, Fontan D, Sandler B, Maleville J, et al. Congenital cutaneous defects as complications in surviving co-twins. Aplasia cutis congenita and neonatal volkmann ischemic contracture of the forearm. *Arch Dermatol* 1998; 134: 1121-4.
- Pavlidis E, Spagnoli C, Duca M, Ormitti F, Magnani C, Pisani F. Neonatal Forearm Compartment Syndrome: Look for Cerebral Stroke. *J Pediatr* 2014; 164: 427.e1.
- Asindi AA, Stephenson JB, Young DG. Spastic hemiparesis and presumed prenatal embolisation. *Arch Dis Child* 1988; 63: 68-9.
- Raine J, Davies H, Gamsu HR. Multiple idiopathic emboli in a full term neonate. *Acta Paediatr Scand* 1989; 78: 644-6.
- Gudinchet F, Dreyer JL, Payot M, Duvoisin B, Laurini R. Imaging of neonatal arterial thrombosis. *Arch Dis Child* 1991; 66: 1158-9.
- Guajardo L, Strauss A, Amster J. Idiopathic cerebral infarction and upper limb ischemia in neonates. *Am J Perinatol* 1994; 11: 119-22.
- Carr MM, al-Qattan M, Clarke HM. Extremity gangrene in utero. *J Hand Surg Br* 1996; 21: 652-5.
- Long DK, Lorant DE. Multiple arterial thrombi and in utero leg gangrene in an infant of a diabetic mother. *J Perinatol* 2002; 22: 424-7.
- Salama H, Rejjal A, Kattan A, Al-Mahmoud L. Neonatal cerebral infarction presented with limb ischemia. *Neurosciences (Riyadh)* 2003; 8: 191-4.
- Nelson KB, Lynch JK. Stroke in newborn infants. *Lancet Neurol* 2004; 3: 150-8.
- Silfen R, Amir A, Sirota L, Hauben DJ. Congenital Volkmann-Lesser ischemic contracture of the upper limb. *Ann Plast Surg* 2000; 45: 313-7.
- Caouette-Laberge L, Bartoluzzi P, Egerszegi EP, Marton D. Neonatal Volkmann's ischemic contracture of the forearm: a report of five cases. *Plast Reconstr Surg* 1992; 90: 621-8.
- Dandurand M, Michel B, Fabre C, Stoebner P, Meunier L. Neonatal Volkmann's syndrome. *Ann Dermatol Venereol* 2009; 136: 785-9.
- Nanda R, Kanapathipillai P, Stothard J. Selective growth disturbance of the hand following neonatal compartment syndrome: a case report. *J Hand Surg Eur Vol* 2009; 34: 813-4.
- Kline SC, Moore JR. Neonatal compartment syndrome. *J Hand Surg Am* 1992; 17: 256-9.
- Goubier JN, Romaña C, Molina V. Neonatal Volkmann's compartment syndrome. A report of two cases. *Chir Main* 2005; 24: 45-7.
- Tsujino A, Hooper G. Neonatal compression ischaemia of the forearm. *J Hand Surg Br* 1997; 22: 612-4.
- Bedbrook GM. Neo-natal Volkmann's syndrome. *Proc R Soc Med* 1953; 46: 349.
- Cham PM, Drolet BA, Segura AD, Esterly NB. Congenital Volkmann ischaemic contracture: a case report and review. *Br J Dermatol* 2004; 150: 357-63.
- Isik C, Demirhan A, Karabekmez FE, Tekelioglu UY, Altunhan H, Ozlu T. Forearm compartment syndrome owing to being stuck in the birth canal: a case report. *J Pediatr Surg* 2012; 47: e37-9.
- Raimer L, McCarthy RA, Raimer D, Colome-Grimmer M. Congenital Volkmann ischemic contracture: a case report. *Pediatr Dermatol* 2008; 25: 352-4.
- Lightwood R. Radial nerve palsy associated with localized subcutaneous fat necrosis in the newborn. *Arch Dis Child* 1951; 26: 436-7.
- Feldman GV. Radial nerve palsies in the newborn. *Arch Dis Child* 1957; 32: 469-71.
- Hayman M, Roland EH, Hill A. Newborn radial nerve palsy: Report of four cases and review of published reports. *Pediatr Neurol* 1999; 21: 648-51.

29. Ghinescu CE, Kamalanathan AN, Morgan C. Unilateral radial nerve palsy in a newborn. *Arch Dis Child Fetal Neonatal Ed* 2012; 97: F153.
30. Arshad A, McCarthy MJ. Management of limb ischaemia in the neonate and infant. *Eur J Vasc Endovasc Surg* 2009; 38: 61-5.
31. Volkmann R. Die ischaemischen Muskellähmungen und Kontrakturen. *Centrabl F Chir* 1881; 51: 801-3.
32. Stevanovic M, Sharpe F. Management of established Volkmann's contracture of the forearm in children. *Hand Clin* 2006; 22: 99-111.
33. Rutherford MA, Ramenghi LA, Cowan FM. Neonatal stroke. *Arch Dis Child Fetal Neonatal Ed* 2012; 97: F377-84.
34. Aso K, Scher MS, Barmada MA. Cerebral infarcts and seizures in the neonate. *J Child Neurol* 1990; 5: 224-8.
35. Chabrier S, Husson B, Dinomais M, Landrieu P, Nguyen The Tich S. New insights (and new interrogations) in perinatal arterial ischemic stroke. *Thromb Res* 2011; 127: 13-22.
36. Elbers J, Viero S, MacGregor D, DeVeber G, Moore AM. Placental pathology in neonatal stroke. *Pediatrics* 2011; 127: e722-9.

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