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The pathology and aetiology of subcortical clefts in infants

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ABSTRACT

In infants, traumatic surface contusions of the brain are rare but subcortical clefts or cysts, variously labelled "contusional tears", "contusional clefts", "cortical tears" or "parenchymal lacerations" have been ascribed to trauma, and are even said to be characteristic of shaking and abuse.

We describe the pathology of subcortical clefts or haemorrhages in seven infants. In none were the axonal swellings characteristic of traumatic axonal injury seen in relation to the clefts. Subpial bleeding was associated with clefts in all the cases of recent onset. We hypothesize that subcortical clefts are not due to direct mechanical forces of trauma but are part of a secondary cascade caused by impaired venous drainage which may or may not follow trauma. The finding of subcortical and subpial haemorrhages should prompt a search for CVT. We consider the term "contusion" is not accurate and is misleading.

1. Introduction

Contusions of the brain are regarded as one of the hallmarks of head trauma in adults. The term contusion (usually used synonymously with bruising) is taken to imply mechanical tissue damage and by definition includes bleeding from small blood vessels. Several types of contusion are described in the adult brain; surface contusions which typically involve cortical gyral crests of the under surface of the frontal- or temporal lobes, and gliding contusions which are subcortical in location and associated with diffuse axonal injury.

In infants the incidence and patterns of contusions are different. Surface contusions are extremely rare in infants. Instead subcortical clefts or cysts, historically considered to be the result of trauma, have been described in infants under the age of 5 months [1–4]. These subcortical lesions, which have sometimes incorrectly been labelled contusions or contusional tears, are found beneath an intact cortex, particularly bilaterally in the frontal lobes and in the temporal lobes. In a seminal paper Lindenberg and Freytag [2] described the early microscopic appearances of subcortical clefts as hardly differentiated from artefacts except for bleeding into them. In some cases, they described associated microscopic tears in the outer layer of the cortex, parallel to its surface. Although they ascribed these lesions to blunt trauma the diagnosis was not clearly established clinically and in some cases, was based solely on the presence of meningeal bleeding. Furthermore, they specifically noted that the histological hallmark of traumatic axonal injury, axonal swellings, were not seen in relation to these lesions; axons simply terminated at the margin of the clefts. Calder et al. [5] described "contusional tears" in 7 infants under 5 months of age and similarly noted the absence of axonal injury or retraction balls. In 3 of these 7 cases no trauma was described. Vowles et al. [6] used additional specific axonal staining methods but also failed to identify axonal swellings in relation to subcortical clefts.

Neuro-imaging studies have described these subcortical lesions as "contusional tears", "contusional clefts", "cortical tears" or "parenchymal lacerations" [7–10], which again have historically been accepted as the result of trauma, including the consequence of instrumental delivery in childbirth [11]. Some have suggested these lesions are characteristic of shaking or abuse [7,9,10] but neuropathology does not support this suggestion; subcortical lesions are either very rare or not seen at all in babies thought to have been shaken [3,4,12].

The lesions in question are specifically located just beneath the cortex in infants who are usually less than 5 months of age. In the immature brain this zone is defined as the subplate; a transient zone and the most prominent architectonic compartment in the late fetal period. It is considered to be the site of the earliest synaptogenesis and a waiting compartment for afferents growing into the cortex [13–15]. One of the characteristics of the subplate is its hydrophilic extracellular matrix, remnants of which persist into the second year of life, [16]. This and the loose plexiform arrangement of fibres may favour oedema and bleeding into the

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subplate in the same way as has been suggested for subcortical cystic leukomalacia in infants [17]. The subcortical white matter may be particularly vulnerable in infants while remnants of the subplate persist.

The subplate area is the endzone for the superficial venous system [18] and subcortical haemorrhage has been described as a radiological marker for occult cerebral vein thrombosis in adults [19]. Ultrasound, pathological and radiological studies have shown that in infants, subcortical lesions may develop after mechanically difficult delivery and suggested venous obstruction as the cause [11,20,21]. Infants with cerebral vein or sinus thrombosis (CVST) may develop parenchymal lesions in the subcortical white matter of the frontal, parietal and temporal lobes [22,23].

While trauma is undoubtedly associated with subcortical clefts in some cases, the inability to establish this as a clear clinical diagnosis in all cases, together with failure to demonstrate the pathological characteristics of trauma form the rationale for our study. We question the specificity of the pathology and whether it may result from the secondary effects of trauma or even from altogether different aetiologies. We describe the pathological findings in the brains of seven infants, all with subcortical clefts or haemorrhages. We hypothesize that subcortical clefts and haemorrhages are not due to direct mechanical forces of trauma but are part of a secondary cascade caused by impaired venous drainage with or without trauma. Any event causing outflow obstruction of the superficial venous system, including trauma, surface venous compression by displaced skull fragments or venous or sinus thrombosis with local oedema may lead to this pathology.

We suggest that an association between subcortical and subpial bleeding supports a venous origin, and we consider the term “contusion” is inappropriate for these lesions.

2. Case histories

2.1. Case 1

Male baby delivered via emergency lower segment caesarean section (LSCS) for presumed foetal distress following prolonged rupture of membranes at 40 + 1 weeks gestation. Apgar scores were 0, 3 and 4 at 1, 5 and 10 min respectively. At 5 min of age he was bradycardic and had no respiratory effort so was intubated and ventilated, following which he was cooled. At 2 h of age, he was given blood products for a severe coagulopathy. He continued to be hypoxic and hypotensive, requiring inotropes and subsequently became profoundly acidotic which failed to respond to corrective measures. Due to continued deterioration, supportive care was withdrawn and he died day 1 post-delivery. At autopsy right parietal skull fracture and thin linear bilateral parietal subcortical bleeding were identified.

2.2. Case 2

Male baby delivered at 40 gestational weeks via emergency caesarean section due to fetal distress. There was no respiratory effort, the baby was severely hypoxic and developed abnormal blood clotting secondary to the HII. He died at 1 day of age. At autopsy a right parietal skull fracture and sub aponeurotic haemorrhage were discovered. The venous sinuses were normal. There were linear and cystic bilateral frontal subcortical clefts.

2.3. Case 3

Female born at 41 + 5 weeks gestation by emergency lower segment caesarean section (LSCS) for presumed foetal distress during a prolonged labour. She required forceps lift out. There was no respiratory effort or palpable heart beat following delivery (Apgar score 4 at 1 min). Cardiac output was recovered 20 min post-delivery, but she began fitting 5 h post-delivery. Antibiotics and cooling were commenced. CT identified numerous bilateral parenchymal contusions. Autopsy demonstrated bilateral parietal bone fractures, bilateral fronto-parietal subcortical clefts and subgaleal haemorrhage. She died on day 5.

2.4. Case 4

At 9 weeks old, this male infant was taken to his doctor with a three-day history of coryza and fever. On the day of presentation, he had cried out suddenly, clenched his mouth shut and his body tightened for 10 min. Following this, he was irritable, pyrexial and refusing further feeds. He was transferred to hospital where he had a generalized tonic-clonic seizure lasting 45 min. Approximately 8 h later, he fitted again (despite loading with phenytoin), became bradycardic and developed unequal pupils. There were no external injuries and no scalp bruising. He was sedated, intubated and ventilated and transferred to the paediatric intensive care unit (PICU). CT scan showed extensive brain swelling and no parenchymal lesions. He continued to deteriorate and died 6 days later. Autopsy showed recent bilateral subcortical haemorrhages in the frontal parasagittal regions and the parietal lobes. Later review of the scans showed thrombosis of the superior sagittal sinus associated with a small linear fracture traversing the overlying parietal bones. Further history was sought and revealed that the baby had rolled off a bed onto a carpeted floor four days prior to presentation but had no apparent ill effects. The fall was observed by his mother. The child welfare team investigated but there were no concerns of abuse and there was no prosecution.

2.5. Case 5

Male baby born via normal vaginal delivery at 41+3 weeks gestation following an uneventful pregnancy. He was well until 11 months of age. He fell over backwards from a standing position on to a carpeted floor during the afternoon. This was witnessed by his mother and a visiting friend. Later that day his mother witnessed him fall backwards from a bed onto a thinly carpeted floor. He cried immediately but his arms then ‘seized’, following which he became blue and floppy. On admission no scalp abrasions or bruises were noted and there were no skull fractures. Computed tomography (CT) identified a left-sided subdural haemorrhage with brain swelling and midline shift but no parenchymal lesions. The baby underwent surgical decompressive craniectomy. He died fifteen hours after admission. At autopsy post-surgical scalp haemorrhage was noted. Left parasagittal subcortical clefts were identified underlying the subdural haemorrhage. A diagnosis of inflicted shaking and impact injury was made. There was police investigation and prosecution, but charges were dropped before trial.

2.6. Case 6

Female delivered at 40 + 2 weeks via normal vaginal delivery following an uneventful pregnancy. Apgar scores of 9 at one and five minutes. Mild neonatal jaundice resolved spontaneously after 3 days. At 4 weeks of age, the baby was seen by a doctor because she was irritable, colicky, arching her back while feeding and vomiting after feeds. A diagnosis of gastro-oesophageal reflux was made. At 4 months of age the baby was vaccinated and a few days later her parents reported the baby to have blank staring spells which were interpreted as seizures. At 4 $^{1}/_{2}$ months the baby was brought to hospital unresponsive and not breathing after being accidentally dropped from a height of approximately one metre from the father’s arms on to a wooden floor. The father was the

only witness. She had a left parietal scalp haematoma and diffuse right head swelling and a full anterior fontanelle. She had contusions on the chest and trunk. She was intubated and ventilated and maintained spontaneous circulation. CT and MRI scans showed bilateral temporo-parietal and right occipital skull fractures, parafalcine and intraventricular bleeding and an old lesion in the left parietal lobe with associated leucomalacia. She died the following day. At autopsy epidural, old and recent subdural and subarachnoid bleeding was described. There was old parasagittal haemorrhagic infarction involving cortical, but predominantly subcortical, tissue of the brain. The original autopsy conclusion was homicide and was followed by police investigation and prosecution.

2.7. Case 7

Female born at 39 + 0 weeks via ventouse delivery due to failure to progress. Polyhydramnios was noted but the pregnancy otherwise uneventful. At day 4, neonatal jaundice was noted which resolved spontaneously. The baby was brought to hospital aged 27 days with a 24-h history of respiratory difficulties on lying flat or feeding, with two witnessed apnoeic attacks. There was no history of trauma. A diagnosis of staphylococcal pneumonia was made based on biochemical, chest radiograph and microbiology swabs and antibiotics commenced. No external injuries were identified, there was no scalp bruising. Despite this, she deteriorated and required intubation and ventilation. CT identified bilateral fluid filled cysts in the frontal lobes with hypoxic areas posteriorly. The lesions were documented as "Jaspan lesions" please cite reference 9 here and a diagnosis of shaking assumed. The baby survived with severe brain damage for 16 months.

3. Materials and methods

Seven cases of infants with subcortical clefts were reviewed. All cases were referred to the Department of Ocular Pathology and Neuropathology at the Oxford University John Radcliffe Hospital.

Sections were sampled as part of routine diagnostic autopsy examination. Six of the cases were reviewed with additional reticulin and βAPP immunostaining of brain sections. In one case there were no blocks available for these further stains. All samples have consent for teaching and research with ethical approval of the Oxford Biobank Generic Research Tissue Bank (The Oxford Brain Bank HTA licence number is 12217, the Research Ethics number is 15/SC/0639).

Tissue samples were taken from brains fixed in 10% formalin (fetal tissue for a minimum of 7 days and all other samples for up to 3 weeks) and processed to paraffin wax. Six-micron sections were cut and mounted on SuperFrost® Plus slides and dried overnight at 37 °C. Sections were stained with H&E, Retic (Gordon and Sweet's method) and with βAPP antibody (Invitrogen, Cl: LN27). The following immunostaining protocol was used for βAPP antibody. βAPP sections were dewaxed and the endogenous peroxide activity blocked by treating with 10% hydrogen peroxide for 30 min. Heat-induced epitope retrieval (HIER) was carried out by microwaving the sections in 0.1 M citrate pH6 buffer (2 x 5 min cycles). The presence of non-specific staining was blocked with 10% foetal calf serum in TBS-Triton (30 min). The primary antibody was diluted (βAPP, Invitrogen) with 5% FCS in TBS-Triton and incubated for 1 h at room temperature. The Dako REAL™ EnVision™/HRP, Rabbit/Mouse (ENV) detection kit was used as per the manufacturer's recommendations. The reaction product was visualised using Dako REAL™ DAB + Chromogen. The sections were lightly counterstained with haematoxylin, dehydrated, cleared and mounted in DPX mounting medium.

Sections were independently examined by two pathologists (WS, KBL).

4. Results

Clinical details are summarised in Table 1.

Five babies were under the age of 5 months, one was aged 11 months and one 18 months at the time of death (but the primary subcortical lesion was described on a MR scan at the age of 29 days). All of the seven cases had normally developing brains with clefts or haemorrhages located in the subcortical zone of the white matter, in either the frontal or parietal lobes.

In five cases (cases 1–5) subcortical lesions were recent. In all of these there was massive venous congestion in the superficial venous system (Fig. 1). In one case (case 4) sinus thrombosis was identified radiologically and histologically where thrombus was also seen in a dural vein (Fig. 1f). Microscopically, the subcortical lesions varied from foci of perivascular bleeding to tissue clefts with or without a thin rim of bleeding within them and with or without discrete perivascular bleeding around them. In one case there was massive parenchymal bleeding. In a few cases bleeding extended into the adjacent cortex. There were no macrophages or gliosis around the fresh bleeds, but some white matter gliosis and siderophages surrounded the older lesions. Axonal swellings were not identified in the walls of the clefts with H&E or Beta APP immunostaining (Fig. 3). The cortex overlying subcortical bleeding was generally intact apart from a thin film of superficial, subpial haemorrhage which was identified in all 5 recent cases (eg. Fig. 1c, e and 4 a–e).

The subpial haemorrhages were macroscopically difficult to distinguish from subarachnoid bleeds, but for their limited extent and discrete margin. With the reticulin stain the blood was seen to

Table 1
Clinical details.

Case number	Age at collapse	Survival post collapse	Cause of collapse	Subcortical bleeding	Forensic consideration
1	0 h	24 h	Birth trauma	Thin linear bilateral parietal	Abuse not considered
2	0 h	24 h	Birth trauma	Linear and cystic bilateral frontal	Abuse not considered
3	5 h	5 Days	Birth trauma.	Bilateral fronto-parietal	Abuse not considered
4	9 weeks	7 Days	Sagittal sinus thrombosis 4 days after fall from bed on to carpeted floor.	Bilateral frontal parasagittal and parietal.	Abuse considered but dismissed without prosecution following family review
5	11 Months	15 hours	Two falls, from standing and from bed, both onto carpeted floor.	Fresh left parasagittal beneath the SDH	SBS prosecution dropped prior to trial
6	4 Months	1 Day	1 metre fall on to wooden floor	Old bilateral parasagittal parietal, predating fall.	SBS conviction.
7	27 Days	17 Months	Staphylococcal pneumonia	Old bilateral frontal cysts	SBS conviction

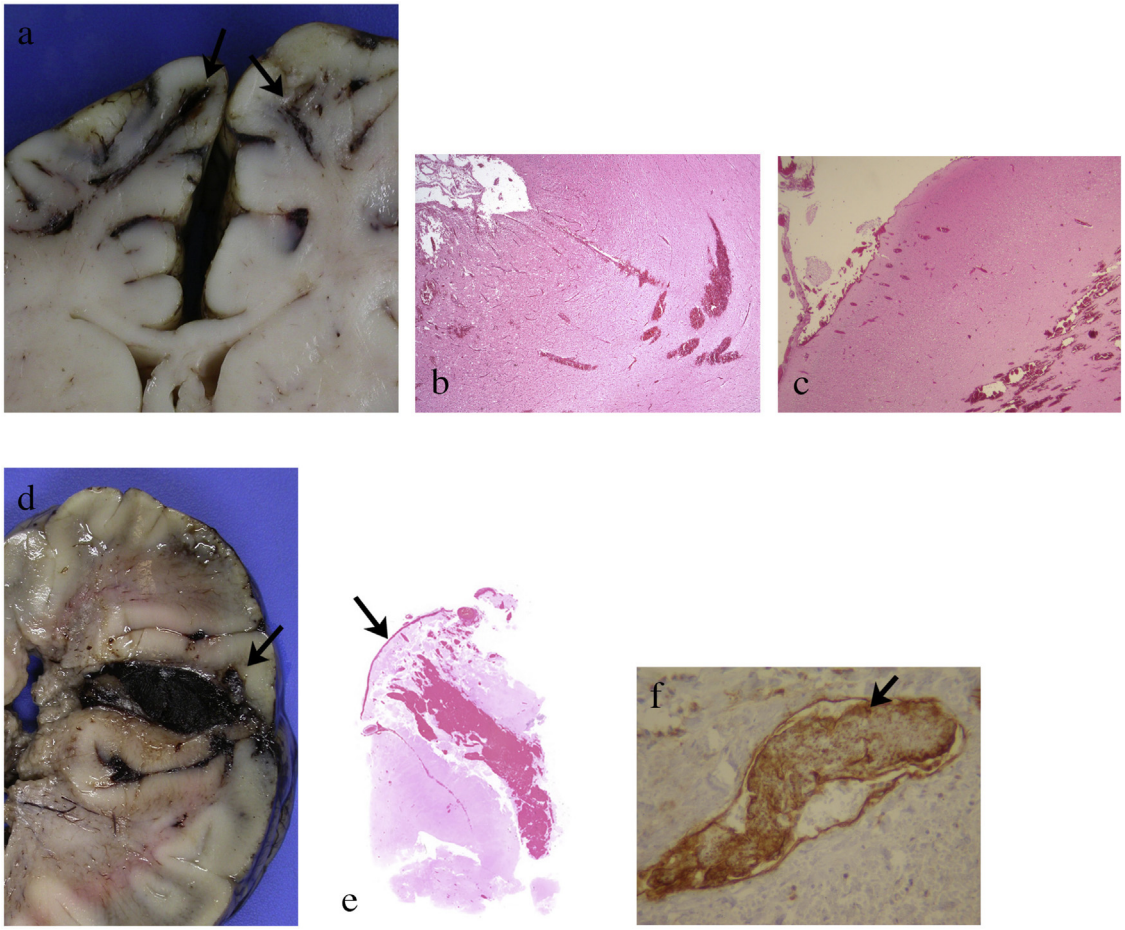

Fig. 1. (a) Case 3: Formalin fixed brain with subcortical bleeding and cysts. (b) Case 3: The histology confirms subcortical bleeding predominantly around blood vessels running parallel to the deep cortex at its junction with the white matter. (c) Case 2: Histology showing bleeding in the subcortical zone close to the deep cortical border. Note also a small bleed in the upper subpial surface of the cortex. (d) Case 4: At autopsy a large blood clot occupies much of the subcortical white matter in the parietal lobe. The overlying cortex is relatively well preserved. (e) Case 4: Histology confirms subcortical bleeding associated with a thin layer of subpial blood (arrow). (f) Case 4: CD31 stain showing a thrombus in a dural vein.

form a layer which lifted the pial basement membrane; in some cases, the bleeding appeared to split the superficial cortical cell layer leaving a small rim of superficial cortical tissue attached to the pia (Figs. 1c, 4 c). The underlying cortex was generally intact apart from irregular cuffs of red cells around venules beneath the subpial blood (Fig. 4e).

In two cases (cases 6 and 7) the subcortical lesions were old; the infants survived more than a month after the event thought to have caused the subcortical bleeding. In case 7 the most prominent finding was of narrow slit-like cysts beneath thinned and gliotic cortex, located bilaterally in the frontal parasagittal region. There was Perls' positive material within the cysts, gliosis and increased density of capillaries were identified in the white matter surrounding the cysts (Fig. 2a–b). In case 6, the subcortical clefts were wide and contained many haemosiderin-containing macrophages. The overlying cortex was severely damaged and represented by thin band, or nodules, of gliotic tissue in thickened and vascular leptomeninges. Old thrombosed veins, some recanalised, were identified in the overlying leptomeninges (Fig. 2c–e). In neither case were there any axonal swellings.

Of the six cases where βAPP immunohistochemistry was performed, only weakly positive immunoreactivity was seen in two cases (Fig. 3). In one random scattered flecks of BAPP positivity was seen near to the cysts. Weak staining was identified at a distance from the lesions and interpreted as unrelated to them. There were no palisades of axonal swellings or varicosities in the walls of the cysts.

5. Discussion

In this study we describe seven infants with recent or old subcortical lesions. None had histological evidence of tissue shearing related to these lesions. They are not contusions and cannot be interpreted as a surrogate for trauma.

In assessing the pathology of brain trauma, it is important to distinguish between primary and secondary brain damage. Primary damage is that caused at the time of trauma by mechanical disruption of tissues. Secondary damage is the result of a progressive sequence of effects set in motion by trauma. The major mechanistic and pathological importance of recognising this principle is that the secondary effects of trauma including haemorrhage, hypoxia, ischaemia and brain swelling, are not unique to trauma; their identification cannot lead to an automatic assumption that trauma has taken place and alternative causes must always be considered. Failure to do this is not only too simplistic for biological systems, but may be misleading.

5.1. Pathological observations in subcortical clefts

The pathology we describe is consistent with that described in earlier reports [1–6,24]. There are several features which indicate

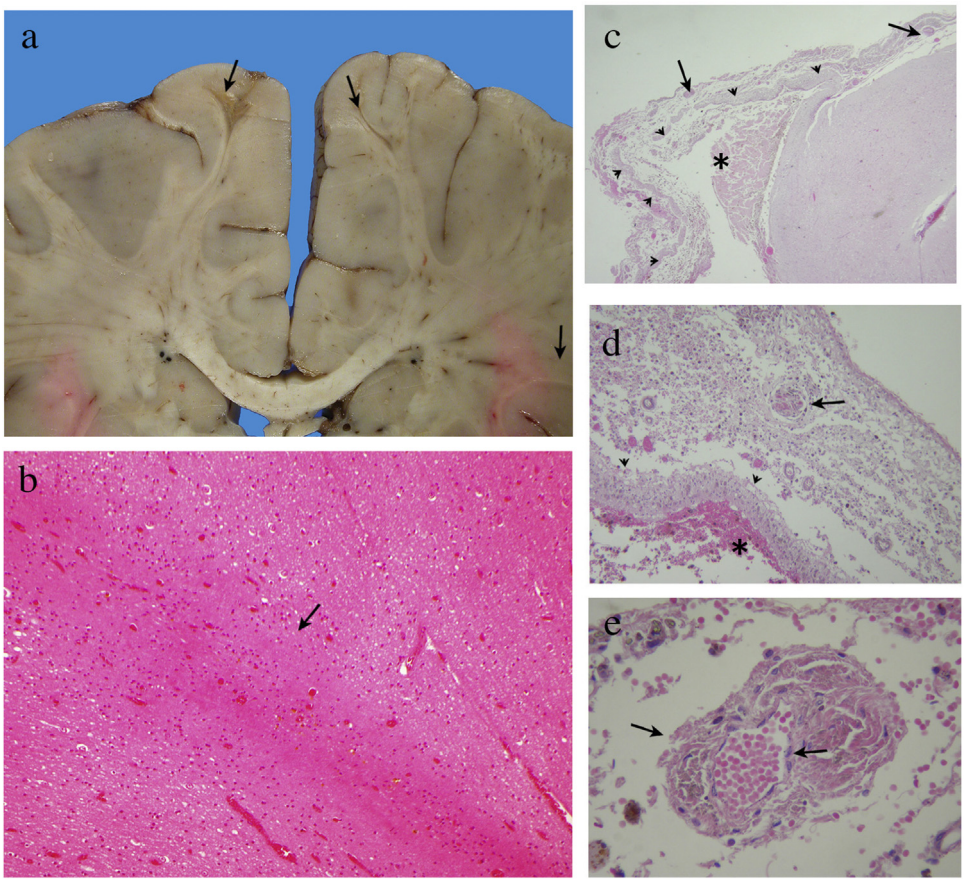

Fig. 2. (a) Case 7: Fixed brain slice showing a small cyst on the right and a thin glial scar in the subcortical white matter on the left. (b) Case 7: Histology confirms a glial scar (arrow) on the left containing hemosiderophages. (c) Case 6: Old subcortical cyst (*) with remnants of scarred cortex (arrowheads). Several old thrombosed veins are seen in the overlying leptomeninges (arrows). (d) Case 6: A thrombosed vein at higher power (arrow) in the subarachnoid compartment which is very cellular. It overlies the old subcortical cyst (*) and remnants of scarred cortex (arrowheads). (e) Case 6: Thrombosed subarachnoid vessel with recanalisation (arrow).

that subcortical clefts are not the result of direct mechanical tearing of the subcortical white matter. The most obvious is the absence of axonal swellings around the clefts. Although axonal swellings are not by themselves specific for trauma and are seen after a variety of axonal injuries, including metabolic and ischaemic, they have been described within the margins of traumatic tissue tears [24]. Secondly, even when there were fractures overlying the part of the brain with subcortical clefts, the cortex was largely intact, as was the dura. Correlation with imaging in two of our cases (cases 3 and 5) showed no clefts or other parenchymal lesions on initial brain scans; these developed later indicating that they are not part of the initial traumatic insult. We have observed this in a third case, a toddler, following a fall but do not have consent to publish the details.

Even when subcortical clefts are associated with trauma the pathology and imaging show they are not characteristic of primary shearing and are more likely to be part of a secondary cascade involving brain swelling or hypoxic/ischaemic injury. In other cases, the aetiology may not be due to trauma at all. Lindenberg and Freytag [2] commented that the pathology of these cysts was the same as that described in circulatory disorders in infants.

5.2. Subpial bleeding

Subpial bleeding has been generally overlooked in the pathological and radiological literature; we found it in all five cases of recent subcortical bleeding. Friede [25] described subpial bleeding in a significant proportion of infants with perinatal intracranial haemorrhage. He hypothesized that subpial bleeding started in the parenchyma of the superficial glial cells of the molecular layer of the cortex and is facilitated by swelling of this cell layer. This corresponds with Lindenberg's description of superficial cortical "tears" [2]. We saw the same appearances in some of our cases but in others reticulin staining demonstrated clearly the pia lifted by the bleeding above an apparently intact superficial cortical layer. We observed minor irregular perivascular bleeding in the cortex below subpial haemorrhage. The perivascular compartment of the cortical veins, is in direct continuity with the subpial compartment [26]. We propose that subcortical haemorrhage from terminal vessels in the subplate can track along cortical veins into the subpial location. Spontaneous subcortical and subpial bleeding have been described radiologically in otherwise healthy neonates following normal vaginal delivery; all presented with apnoea or seizures. Local trauma and venous compression or obstruction was the suggested cause [21].

5.3. Aetiology — trauma?

Freytag [1] was the first to note that traumatic brain damage in infants presents a special and distinct picture; unlike adults, infants did not show haemorrhagic lesions on gyral crests but had slit-like non-haemorrhagic lesions in the white matter of the frontal or the temporal lobes. Lindenberg and Freytag [2] described 16 infants under 5 months with subcortical clefts which were usually frontal and bilateral. In nine there was evidence of trauma but 7 had no history of trauma but autopsy revealed "scalp bruises and skull fractures or meningeal haemorrhages or both", suggesting that in some cases the

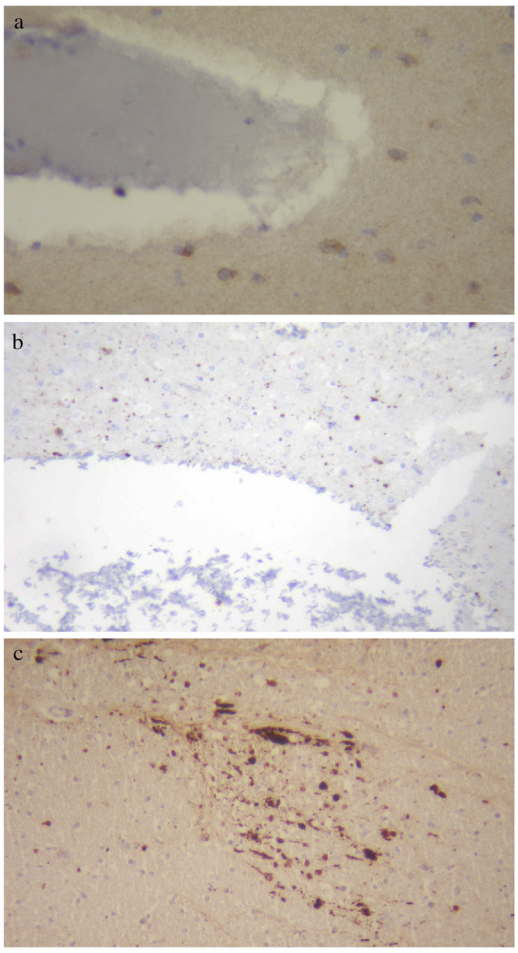

Fig. 3. (a) and (b) Case 5 and Case 3: βAPP staining shows weak positivity in a few cell bodies (a) and axons (b) around a subcortical cleft, but no axonal swellings are seen around the edges of the clefts. There is no bleeding in or around these clefts and no perivascular bleeing is seen close to them. (c) Case 5:In contrast, clusters of axonal swellings with βAPP positivity were demonstrated elsewhere in the deep white matter.

diagnosis of trauma rested on the presence of meningeal bleeding. The histology they described is very like that in our cases and, like them, we draw attention to the absence of axonal swellings around these cysts which distinguishes them from the white matter tears described in head trauma [24]. Calder et al. [5] described "contusional tears" in 7 infants thought to have been victims of non-accidental head injury. The diagnostic criteria are not set out; four had skull fractures but in 3 there is no description of trauma. Vowles et al. [6] added a further case with a skull fracture and, despite using additional axon staining methods, did not describe the axonal changes characteristic of traumatic axonal injury in the walls of the clefts.

Jaspan et al. [9] considered that subcortical clefts seen by ultrasound were pathognomonic of shaking injury. This study described six infants less than six months of age thought to have suffered inflicted injury. Subcortical clefts were identified by cranial ultrasound. Two of four cases had additional CT scans and/or MR scans which failed to identify these lesions. Two patients died and had pathological examination of the brain. In one, small slit-like cavities were present in the hemispheric white matter but no axonal swellings were described. The second patient who died some months later had severe cortical and white matter gliosis but subcortical clefts were not seen with the naked eye or with the microscope. Jaspan hypothesized that the subcortical lesions were the result of the cortex gliding over the white matter.

Palifka et al. [10] similarly described subcortical white matter clefts by MR imaging in babies which they considered had been abused. The criteria for diagnosis of abuse are not stated but appear to include subdural and subarachnoid bleeding. These authors were aware of bias in patient selection as a limitation of the study. The scans were reviewed unblinded and there was no pathological confirmation of their findings.

Most of the studies cited above described infants thought to have suffered trauma. The clinical history in some cases was consistent with trauma, but in others the criteria for diagnosis were not sufficient to ascertain the diagnosis with any certainty. Radiological studies lack the resolution to be reliable markers of mechanical tissue disruption or tearing.

5.4. Aetiology — a venous origin?

We suggest that that subcortical clefts and haemorrhages may be a consequence of obstruction of outflow in the superficial venous system. Occlusion of the superior cerebral veins during delivery was suggested as a cause of frontal atrophy and local scarring by Courville [27]. Similarly, venous damage was thought to cause parasagittal frontal lobe haemorrhages in adults "gliding contusions" [28]. Barnes [29] suggested that subcortical bleeding in CVST may be confused with traumatic shear injuries and misdiagnosed as "cortical contusions".

Neonatal CVST is increasingly recognised but is frequently underdiagnosed because of lack of clinical awareness or failure to use appropriate imaging techniques. The clinical presentation is non-specific and over 13% of cases are asymptomatic [22,30]. Associated parenchymal lesions are more common in neonates than older infants particularly in the frontal and parietal lobes [23]. The predominance of superior sagittal sinus thrombosis in neonates has been explained by compression of the sinus by the occipital bone close to the anterior fontanelle. This may occur during difficult delivery [22] or even by nursing in the supine position [31].

Compression or obstruction to the outflow of the superficial venous system of the brain leads to elevation of the hydrostatic venous pressure in its end-zone in the subplate [18,23,32,33] This results in vasogenic oedema and infarction; diapedesis of red cells causes bleeding in the majority of lesions which may transform into mass intraparenchymal bleeding in the subcortical white matter [34]. In 3 of our cases, both of whom had difficult forceps deliveries, there were parietal bone fractures overlying subcortical clefts or bleeding. The intervening cortex was, however intact. We suggest that pressure from forceps which caused the fractures, displaced bone fragments or associated soft tissue oedema led to transient venous outflow obstruction and subcortical damage. Parenchymal subcortical bleeds are also, in our experience, common in the temporal lobes, where they have been reported in radiological studies of spontaneous superficial bleeding in infants [21]. These authors suggested a venous origin, drawing attention to the immaturity of the venous drainage of the temporal lobe in term infants and its vulnerability to compression or injury during birth.

The site of parenchymal damage depends on venous anatomy and on the specific veins or sinuses which are occluded. An animal model of superior sagittal sinus occlusion caused bilateral subcortical haemorrhagic infarction in the frontal lobes in exactly the sites in which subcortical and gliding haemorrhages are described [35].

In infants, thrombosis of the superior sagittal sinus usually begins in the parietal region because the bridging veins enter the dura at a very acute angle here [22].

In a neuroimaging study Au-Yong et al. [11] describe "cortical tears" in 5 babies. However, careful examination of their report

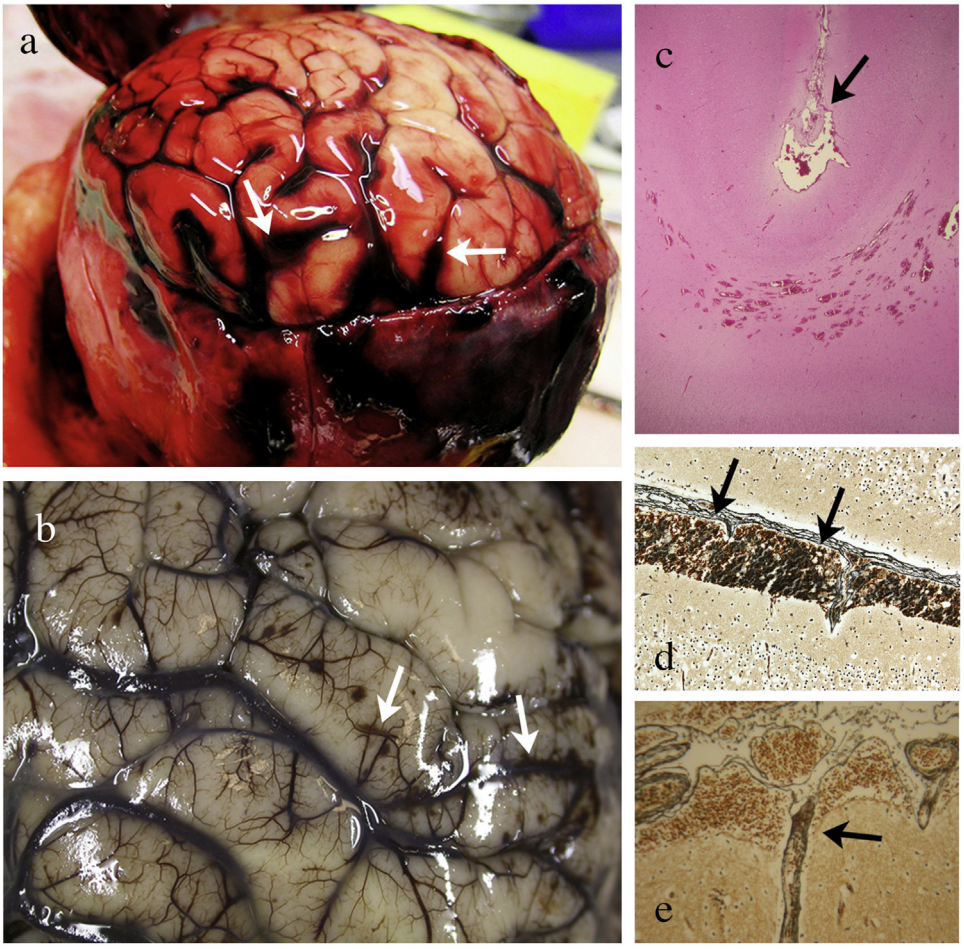

Fig. 4. (a) Case 3: Brain surface exposed at autopsy to show fresh subpial bleeding. The bleeding tends to be at the edges of gyri and has distinct borders (arrows). (b) Case 4: Fixed brain after baby spent 6 days on ventilator. Subpial bleeding marked by white arrows. There are also a number of small, distinct round perivascular bleeds. (c) Case 2: Histology shows subcortical congested vessels and perivascular bleeding and a cleft in the upper cortex, lifting a small layer of upper cortex (arrow). (d) Case 2: Reticulin stain showing a layer of fresh blood between the intact cortex and the pia and around superficial cortical vessels (arrows). (e) Case 2: A few red blood cells from a subpial haemorrhage are tracking around a venule passing from the cortex into the subarachnoid space.

indicates that the cortical "tears" were late developing and were not identified before 22 days of life. Three of the five specifically had no cortical tear on ultrasound scan at two and six days of life; the lesions were not identified until after 25 days of life. These "tears" may have developed secondary to subcortical damage. Pathology shows that it takes some 14 or more days for damaged tissue to become cystic following brain damage [36] which is consistent with the authors' conclusion that birth trauma was likely to be an important aetiology and due to venous compression. None of these babies was thought to have suffered inflicted head injury.

In our two cases with old subcortical cysts a birth-related cause is suggested. Case 7 died at 18 months of age. Although shaking injury had been proposed as a cause of collapse at 29 days of age MRI scan demonstrated that the cysts were already well-developed. There was no history of any event likely to cause these lesions and an origin at birth seems most likely. Case 6 similarly had no history of trauma prior to her admission to hospital following a fall although she had shown signs of cerebral irritation including seizures, which may have been due to the parenchymal lesions or to an associated old subdural haemorrhage. Again, an origin at birth or in the neonatal period seems most likely. The non-specific clinical history and presentation is consistent with reported cases some of whom present with apnoea or seizures but sometimes there are no neurological signs [11,21].

Venous oedema and haemorrhage would explain the pathology of the subcortical lesions we describe. They are often associated with only small amounts of bleeding as would be expected from diapedesis of red cells. The fact that they may become cleft like and split the white matter extending to the ventricular wall or rarely through the cortex may be due to the poor resistance offered by immature unmyelinated white matter with high water content.

6. Conclusion

While subcortical haemorrhages are undoubtedly seen in trauma, they are not pathognomonic for this aetiology and are not all due to trauma. Instead, subcortical and subpial haemorrhages may be one indicator of CVST and should prompt a search for this. The term contusion is not accurate and is misleading.

CRediT authorship contribution statement

Karen Bonde Larsen: Investigation, Writing - original draft, Writing - review & editing, Visualization. **Zoe Barber**: Investigation, Data curation, Writing - original draft. **Waney Squier**: Conceptualization, Investigation, Writing - original draft, Writing - review & editing, Supervision.

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