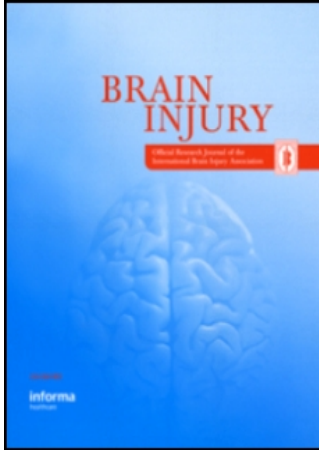


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The association between developmental handicaps and traumatic brain injury during pregnancy: An issue that deserves more systematic evaluation

V. LEROY-MALHERBE¹, C. BONNIER², E. PAPIERNIK³, E. GROOS⁴, & P. LANDRIEU¹

¹Service de Neurologie Pédiatrique, CHU KREMLIN-BICETRE, LE KREMLIN-BICETRE 94275, France, ²Service de Neurologie Pédiatrique, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium, ³Maternité de Port-Royal-Hôpital Cochin, Université René Descartes, Paris 75014, France, and ⁴Centre Ressources pour l'enfant avec lésion cérébrale acquise, Hôpital National de Saint-Maurice, Saint-Maurice 94275, France

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Abstract

Aims: Trauma during pregnancy is commonly viewed as benign for the foetus when the delivery occurs normally. This study revisits that point of view.

Method: We included eighteen patients having a neurological handicap with an anamnesis of an accident during pregnancy and a follow-up sufficient to determine a definite outcome.

Results: *Pregnancy outcome and observed management.* Foetal abnormalities were detected in six cases between the first and the thirteenth day after the trauma. Emergency delivery or rapid birth after signs of foetal distress occurred in five cases. One baby died soon after birth. One-third of cases were not submitted to any investigation.

Various neurological handicaps were recorded: Congenital microcephaly (three patients), congenital hydrocephalus (three), Infantile cerebral hemiplegy (six), quadriplegy with severe encephalopathy (four), diplegy (one), clumsiness with cerebellar atrophy (one), Moebius syndrome (one), mental retardation with autistic features (two), learning disability (one) auditory agnosia (one).

Cerebral imaging showed macroscopic abnormalities in fourteen patients, evoking various pathogenetic hypotheses.

Conclusion: The association between maternal trauma and foetal brain lesions lacks sufficient investigation in many cases. Prospective studies are needed to clarify both medical and legal issues. Guidelines are proposed for obstetrical and paediatric management after significant maternal trauma.

Keywords: *Fetus, brain injury, developmental handicap*

Introduction

Accidents occur in 6% of all pregnancies [1] and are the main cause of death among women of reproductive age. In industrialized countries, approximately two-thirds of all traumas during pregnancy result from motor vehicle accidents. Other causes include falls and domestic violence (resulting in repetitive traumas) [2–5] reports that 75% of injured women who were hospitalized twice during

pregnancy had domestic abuse. Trauma occurs more commonly during the third trimester than at any other time of a woman's life [6, 7]. More than 90% of all injuries result from minor trauma, so hospitalization represents only 0.4% of pregnant women [8]. Although the risk of foetal death could be as high in an apparently trivial trauma as in a major accident [3, 9, 10], most pregnancies continue to term with relatively little intervention and are not

followed up [11, 12]. The currently dominant attitude is to consider that relative risk of having a cerebral-palsied child after exposure to trauma is not significant [7] and the outcome of the pregnancy is normal when no early-warning symptom is registered [13].

The present study examines this attitude and describes a significant number of cases for which information could be collected about the trauma, the outcome of pregnancy and the child's follow-up. In many cases, clinical and morphological data allowed us to substantiate the traumatic origin and to raise physiopathological hypotheses. A protocol of surveillance for the foetus and the child's development is suggested.

Patients and methods

Population

Eighteen patients having both a neurological handicap and a history of accident during pregnancy where identified. For these patients, a causal relationship was judged possible from the chronology of the events and from the observed clinical and radiological abnormalities. Twelve children were admitted between 1997 and 2006 in a network associating a department of child neurology and a rehabilitation centre dedicated to childhood victims of acquired lesions of the CNS. Six other children were identified in a university hospital in Brussels known to admit very young brain-injured children. The median follow-up was five years after birth (range: 6 months–10 years). Six children had been followed since birth, three came later in childhood for a neurological diagnosis, three came for learning disabilities and six for help in medico-legal litigation.

Obstetrical history

Trauma of the mother was evaluated on records for 83% of subjects (fifteen) and was analysed retrospectively on cross-examination during evaluation of the child for 17% (three). Time and mode of the accident and general symptoms in the pregnant woman were collected. Automobile accidents were responsible for 72% of the situations (thirteen), domestic accidents for 17% (three) and domestic abuse for 11% (two). All the women had a gynaecological examination within 24 hours of the trauma, except in cases of domestic abuse. The obstetrical work-up included ultra-sonographic (US) imaging for 55% of subjects (ten) and foetal heart rate for 66% (twelve, both investigations for nine). No initial foetal assessment was performed for 27% (five). Subsequent clinical and ultrasound follow-up was regularly repeated for 39% (seven),

once during the third trimester for 27% (five) and unknown for 33% (six). Mode of delivery and neonatal symptoms were obtained from delivery records.

Child assessment

Final status was estimated by the Glasgow outcome scale adapted for children by Ewing-Cobbs et al. [14]. Good recovery (GOS = 1) refers to age-appropriate or pre-injury levels of functioning; moderate disability (GOS = 2) to a significant reduction in cognitive functioning from estimated normal levels, to motor deficits interfering with daily living activities or to recourse to an outpatient rehabilitation service; severe disability (GOS = 3) is assigned to cognitive scores in the deficient range, to severe motor deficits, such as lack of appropriate postural control or ambulation, and to recourse to an inpatient rehabilitation centre; persistent vegetative state (GOS = 4) is defined as total dependency; death is recorded as GOS = 5.

Neuro-imaging was performed for 94% of subjects (seventeen): 5% (one) had a cerebral computerized tomography scan (CT Scan); the others had a CT Scan and cerebral magnetic resonance imaging (MRI) with T1- and T2-weighted axial, coronal and sagittal sections. Neuro-imaging was performed for 27% of subjects (five) within the first three months after birth. Late neuro-imaging was performed for 94% (seventeen) in a median delay of one year after birth. All images were reviewed by an independent investigator, who was asked to detect developmental abnormalities and scars of hemorrhagic or malacic lesions (including localization to an arterial territory).

One deceased patient had had a pathological examination. Four patients with developmental dysmorphic features on brain imaging had a normal karyotype.

Results

General results

Type and timing of the accident, general symptoms in the pregnant woman, observed management, signs of transient foetal repercussions, outcome of pregnancy (timing, mode of delivery), neonatal symptoms, the child's neurological follow-up, score of handicap and imaging of cerebral lesions are summarized in Table I. Neonatal death occurred in 6% (one) and prematurity in 27% (five). The Apgar score was normal in 38% (seven), low in 44% (eight), low but secondarily normalized in 18% (three). Birth weight was significantly low in 17% (three). Microcephaly was present at

Table I. General results.

Patient	Time of accident (mode)	General symptoms in parturient (delay from the accident)	Signs of foetal distress (delay from the accident)	Time of birth (mode)	Neonatal symptoms	Neurological picture (Glasgow outcome scale) [age of confirmed diagnosis]	Cerebral imaging
1	22 W (MVA)	Short initial loss of consciousness Abdominal pain, vaginal bleeding and regular uterine contractions (immediately) No hospitalization	Rare foetal spontaneous movements (Day 1) Acquired microcrania (Month 3)	40 W	Apgar 10; 2770 gr Microcephaly (Cranial circumference: 27 cm)	Quadriplegic; Mental retardation; Major microcephaly (GOS = 4) [3 months]	Multiple porencephalic cavities
2	27 W (F)	Voluminous abdomen and loss of amniotic liquid (Day 13)	Hydrocephalus (Day 13) Slowing down foetal cardiac rhythm (Day 13)	31 W (breech birth; forceps)	Apgar 3/5/6; 1045 gr Hydrocephalus (ventricular haemorrhage)	Deceased at 2 hours (GOS = 5)	<i>Post-mortem examination:</i> Dilatation of both ventricles with haemorrhage; No evidence of parenchymal brain damage
3	40 W (MVA)	Haematoma on a cheek and the scalp, right lumbar pain and haematuria Numbness and weakness of the right side for 15 minutes (immediately) No hospitalization	Non reactive tachycardia at 160/min (the first two days and during delivery on the third day)	40 W	Apgar 3/5/7 3,160 gr; Hypotonia; Partial seizures	Infantile hemiplegia; Epilepsy; Microcephaly; Low developmental state (GOS = 3) [6 months]	Hyposignal on axial T1 weighted section in the occipital, parietal and temporal region, respecting the frontal and internal part of the basal ganglia
4	39 W (MVA)	Several bone fractures, haematuria (immediately) Hypotonia; Secondary intracranial hypertension (meningeal haemorrhage)	Slowing foetal cardiac rhythm at 60/min (Day 5)	40 W (emergency caesarian for foetal distress)	Apgar 1/3/6; 3220 gr	Tetraplegic; Microcephaly; Epilepsy (GOS = 4) [8months]	Porencephalic lesions on both temporal and parietal hemispheres with enlargement of pericerebral spaces
5	36,5 W (MVA)	Vaginal bleeding (immediately)	Low foetal heart rate at 70/min (immediately)	365 W (emergency caesarian for abruptio placenta)	Apgar 0/6/9; 3200 gr	Hemiplegic Cognitive impairment Epilepsy (GOS = 3) [6 months]	Hyperdensities of bilateral basal ganglia, enlargement of ventricles, thin corpus callosum
6	8 W (MVA)	Coma, hypovolemic shock (immediately) Several months-hospitalization	None	40 W	Apgar 7/8/8; 4,330 gr Pierre-Robin anomaly [neonatal]	Mental retardation; Moebius syndrome (GOS = 3)	Normal

(continued)

Table I. Continued.

Patient	Time of accident (mode)	General symptoms in parturient (delay from the accident)	Signs of foetal distress (delay from the accident)	Time of birth (mode)	Neonatal symptoms	Neurological picture (Glasgow outcome scale) [age of confirmed diagnosis]	Cerebral imaging
7	20 W (MVA)	Fracture of the pelvis (immediately) Feeding problems Few days-hospitalization	None	40 W (caesarian for transversal position)	Apgar 10; 3600 gr	Bucco-facial apraxia; Infantile hemiplegia (GOS = 2) [3 years]	Medial septum agenesis, asymmetric brainstem and basal ganglia
8	25 W (MVA)	None	None	41 W	Apgar 7/9/10 3260 gr	Pseudobulbar syndrome; Auditive agnosia; Infantile hemiplegia (GOS = 3) [1 year]	Bilaterally dysplastic and microgyric central sulcus; Sylvian fissure extended vertically in the opercular region
9	25 W (MVA)	Multiple fractures of the legs (immediately) Few days-hospitalisation	None	41 W	Apgar 10 Right arm monoplegy	Infantile hemiplegia; Bilateral pyramidal signs (GOS = 2) [6 months]	Thalamostriatal hypoplasia; Dysplastic sylvian fissure
10	28,5 W and 30 W (DA)	Repeated blunt abdominal trauma	None	32,5 W (Caesarian for premature breech birth)	Apgar 6/8/8 1790 gr	Spastic diplegy (GOS = 2) [9 months]	Periventricular leucomalacia
11	29 W (MVA)	Brain injury, coma = 1 1/2 month (immediately) 6 months hospitalization	No reactive foetal cardiac rhythm (immediately)	29 W (emergency Caesarian); micro-thrombi on the placenta	Apgar 6/7/8 1240 gr	Autistic symptoms; Global backwardness (GOS = 3) [4 years]	Atrophy of the posterior part of the corpus callosum
12	22 W (MVA)	Pelvic fractures Loss of consciousness several days (immediately) 6 months hospitalization	None	41 W (Caesarian section)	None 3580 gr	Autistic symptoms; Global backwardness (GOS = 3) [22 months]	Normal

13	26 W (F)	None	None	38 W	Apgar 9/ 3030 gr Microcephaly (Cranial circumference: 33 cm); Intracranial hypertension	Tetraplegy; Microcephaly; Epilepsy (GOS = 4) [3 months]	Encephalomalacia with a thin coat of greymatter, presence of cere- bellum, brainstem, medial septum and basal ganglia
14	12 W (MVA)	Leg weakness during a few hours (immediately) No hospitalization	Unknown	41 W	Hypotonia	Clumsy child; Language impairment (GOS = 2) [9 years]	Small ventricle dilata- tion; Cerebellum vermis hypoplasia
15	26 W (K)	None	Unknown	40 W	None	Infantile hemiplegia; Epilepsy (GOS = 2) [6 months]	Enlargement of the left ventricle with thin cortical coat; Thin corpus callosum
16	35 W (MVA)	Fractured ribs (immediately) No hospitalisation	Unknown	41 W (breech birth)	Apgar 9/10 3,100gr	Right hemiplegy; Pseudobulbar syndrome (GOS = 2) [1 year]	Bilateral and asy- metric hypersignal of white matter on T1 and T2 weighted section
17	Unknown (DA)	Repeated blunt abdominal trauma	Unknown	36 W (Caesarian for loss of amniotic liquid)	None	School learning disabilities (GOS = 1) [6 year]	Normal
18	37 W (MVA)	Transient facial palsy and right hemiplegy and aphasia for 3 weeks (immediately) Few weeks hospitalization	Unknown	40 W (forceps)	Apgar 10/10 2,320 gr; Microcephaly (Cranial circumference: 33 cm)	Quadriplegic Mental retarda- tion; Microcephaly; Stereotypies (GOS = 4) [4 months]	Diffuse cortical and white matter atro- phy; Thin corpus callosum

MVA, motor vehicle accident; K, knock; DA, domestic abuse; F, fall; GOS, Glasgow outcome scale; GOS 1, good recovery; GOS 2, moderate disability; GOS 3, severe disability; GOS 4, persistent vegetative state; GOS 5, deceased; APGAR, at one, five and ten minutes.

birth in 17% (three) and macrocephaly reflecting hydrocephalus in 17% (three).

Neonatal neurological impairment was suspected clinically in 55% of subjects (ten). Eleven per cent (two) suffered neonatal convulsions. Neurological impairment was suspected during the first year of life in 17% (three) and later for 27% (five). The clinical picture consisted of cerebral palsy in 73% (thirteen), autism in 11% (two) and cranial nerve palsies in 6% (one). Twenty-seven per cent (five) developed epilepsy, 66% (twelve) delayed cognitive development. The score on Glasgow outcome scale showed good recovery in 6% (one), moderate disability in 34% (six), severe disability in 34% (six) and persistent vegetative score in 20% (four).

Cerebral imaging was normal in 17% (three) and showed lesions in 77% (fourteen). Focal ischemic lesion with congenital abnormalities was seen in five patients whose accidents happened between 8 weeks and 25 weeks. Ischemic lesions restricted to a vascular territory were suspected in two patients whose accidents happened around 25 weeks. Diffuse ischemic lesions were detected in three patients whose accident happened between 22 weeks and 36.5 weeks. Periventricular leucomalacia was detected in two premature patients. Diffuse white matter abnormality was present in one patient. One patient had diffuse cortical and white matter atrophy. One deceased patient had hemorrhagic lesions on pathological examination.

Further analysis of the lesions in relation with the timing of the trauma, its immediate consequences, the course of the pregnancy and the child's follow-up led us to propose four distinct situations, each one illustrated below by an example.

(1) Foetal and newborn distress shortly after the trauma – Rapid consequences on the course of pregnancy and on foetus health were observed in five cases (patients 2–5, 11). Signs of foetal distress, i.e. anomalies of foetal heart rate with or without anomalies of spontaneous movements, manifested during the first day in four cases and on day 5 and day 13 for two others. A fatal consequence on the pregnancy was suspected for three of them, leading to emergency Caesarian section. For two other patients, abnormalities not considered to be fatal resulted in spontaneous delivery a few days later.

Patient 3: The car collision occurred after 40 weeks of a normal gestation. The mother had haematomas on the scalp, right lumbar pain, microscopic haematuria and numbness of her right side for 15 minutes. Fever was present for two days, without detectable infection. US scan showed slight echogenicity in the placenta but no foetal anomaly. Disorganized uterine contractions with increased tonus and foetal tachycardia with few oscillations

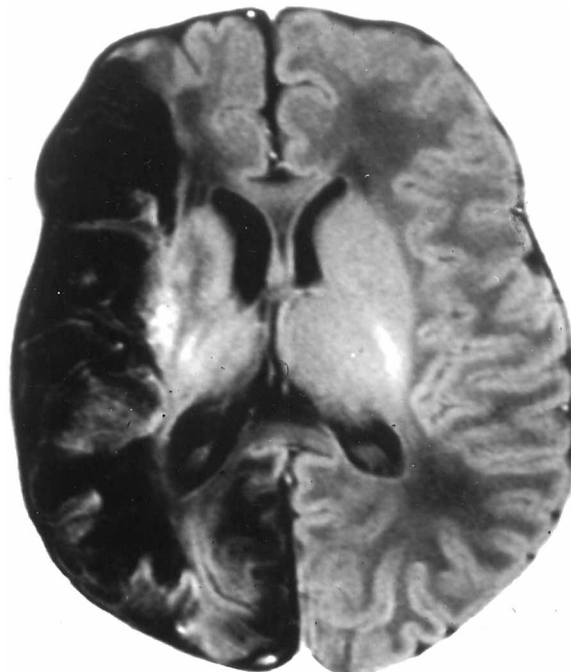


Figure 1. MRI patient 3: large hypointense in the right hemisphere, respecting the frontal and the internal part of the basal ganglia (axial T1 sequence).

returned to normal within two days. Birth occurred spontaneously three days after the traumatism. Non-reactive foetal tachycardia was noticed during delivery. The baby girl was normotrophic but hypotonic (Apgar 3/5/7). Partial seizures on her left side occurred 3 days later. Later, hemiplegy was associated with spatial and motor neglect. Cranial circumference was -2 SD. IQ (Intelligence Quotient) was 66. A neonatal CT scan showed hypodensity of the right hemisphere with contrast diffusion in the thalamostriatal structures, suggestive of a recent ischemic lesion in the carotid territory. At day 13, MRI showed a hypointense on the axial T1 and hypersignal on axial T2-weighted sequences in the right hemisphere, respecting the frontal and the internal part of the basal ganglia (Figure 1). A later CT scan showed atrophy of the right hemisphere.

(2) Premature birth (<38 weeks) shortly after the trauma, without other evidence of foetal distress. This was observed in cases 10 and 17.

Patient 10: The mother had repeated blunt abdominal trauma during pregnancy. She came to hospital for domestic abuse at 28.5 and 30 weeks but sustained no apparent injuries. Immediate course was normal, but a Caesarian was decided at 32.5 weeks because of a premature breech. Birth weight was 1790 gr, Apgar score 6/8/8. The child developed spastic diplegy and visual agnosia. MRI at 1 month showed bilateral periventricular leucomalacia. The EEG was normal.

(3) US observation of foetal brain changes without former signs of foetal distress (one case).

Patient 1: A motor vehicle accident happened after a 22-week normal gestation. The mother complained of abdominal pain. A transient diminution of foetal movements was considered as a purely subjective phenomenon. Vaginal bleeding and regular contractions were revealed by examination and uterine monitoring. Foetal heart rate was normal, as well as placental and foetal morphology on ultrasound examination. Three months later, the echography showed a microcrania. Genetic and infectiologic investigations were normal. After 40 weeks of gestation, the baby was born with microcrania (HC = 27 cm) and abnormal tonus. At 3 years of age, he was severely handicapped. HC was -8 SD. CT Scan showed multiple porencephalic cavities respecting the territory of anterior right cerebral artery.

(4) Neonatal or postnatal revelation of a handicap after uneventful foetal follow-up and birth – In five cases (patients 6–9, 12), foetal investigations showed no anomalies and there was no special care after the accident. In three cases (patients 13–15), in the absence of abdominal symptoms and of maternal demand, no foetal investigation was performed. In two others (patients 16, 18), the foetal work-up after the trauma was undetermined.

(4a) After a trauma early in gestation

Patient 6: The mother had a car accident after an 8-week uneventful pregnancy. A spleen rupture led to emergency surgical investigation. Later in the pregnancy, glucidic intolerance was treated by diet. The baby boy was born after 40 weeks of gestation. Apgar score was 7/8/8, birth weight 4330 gr and HC 35.8 cm. Facial nerve palsy, palsy of oculo-motor nerves and Pierre-Robin anomaly led to the diagnosis of Moebius syndrome. At nine years, IQ was estimated to be 70. Growth and HC were normal, as well as Cerebral MRI.

(4b) After a trauma during mid or late gestation

Patient 9: The mother was 25-weeks pregnant when she had an automobile accident. Multiple fractures of the legs led to programmed surgical intervention. There was no direct abdominal collision, no clinical sign of foetal distress. After a routine follow-up, a full-term, normotrophic girl was born. A right cerebral hemiplegia was diagnosed when she was 6 months old. Head growth and cognitive development were normal. The Glasgow outcome scale score was 2. CT scan and MRI at 9 months showed dilatation of the ventricles on the left side. The left sylvian fissure appeared as a large cleft directed towards the lateral ventricle. The surrounding cortical ribbon was thick and interdigitations

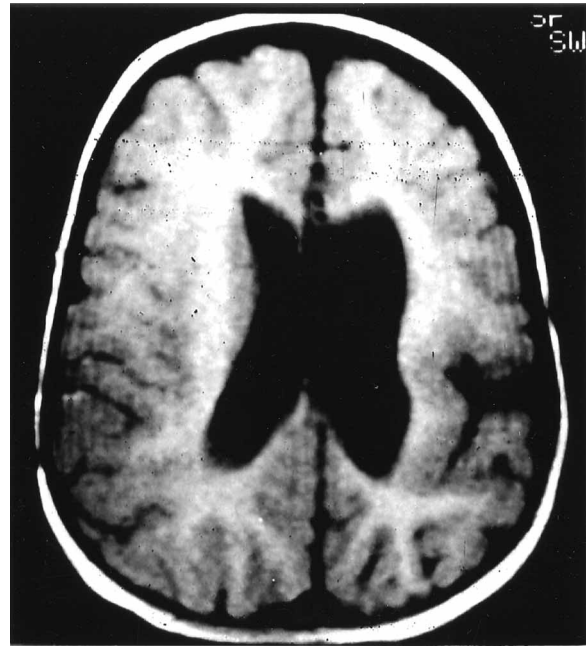


Figure 2. MRI patient 9: aspect of unilateral perisylvian dysplasia: the left sylvian fissure is enlarged and bordered by a thick cortex devoid of interdigitations with white matter (axial T1 sequence).

between grey and white matter were lacking. Thalamostriatal structures were restricted to the putamen (Figure 2).

Discussion

The present work supports the notion that foetal lesions do sometimes result from maternal trauma, suggests that they proceed from a large range of mechanisms and reveals that post-traumatic evaluation of the foetus is frequently incomplete or absent. Former work involved mainly isolated cases [15–20] or small series [21, 22] and also reported a variety of lesions which included leucomalacia, localized infarction, haemorrhage, hydrocephalus and cerebral atrophy. Probably four principal pathogenic conditions are involved:

Prematurity, foetal hypotrophy

Preterm labour associated with trauma appears to be frequent, although rarely reported in the immediate post-injury period [10, 11]. Direct rupture of the foetal membranes could lead to premature birth [23]. Injuries to the myometrial tissue could destabilize decidual lysosomes, thus releasing arachidonic acid and inducing uterine contractions. Cranial trauma of the mother could result in acute modifications in the balance of hormones controlling the initiation of labour. The contractions however are frequently not associated with dilatation of the

cervix [5, 17]. As in any pathological process occurring before 34 weeks of gestation, the two principal lesions at risk are periventricular leucomalacia and subependyma/intraventricular haemorrhage whether resulting or not in hydrocephalus [21, 34, present patient 10]. Intra-uterine growth retardation has rarely been reported [19], except in situations of domestic violence [7].

Arterial cerebral infarctus

In a subset of patients, an arterial ischemic accident appears to be the probable mechanism, both from clinical and morphological data. It can be explained by various mechanisms, such as asymmetric distribution of a low systemic blood flow resulting in a major hemispheric ischemia. Placental hypoperfusion can happen in situations of hypovolemic shock or of stress, especially when the adrenaline response results in peripheral vasoconstriction [24], as demonstrated in animal models [25]. As the uterine vascularity is maximally dilated in the resting physiologic state, any event that hampers the maternal haemodynamic stability can directly interfere with foetal blood-flow and oxygenation, especially in the brain [26]. However, no evidence of systemic shock was seen in most pregnant woman, thus other mechanisms are likely. Acute vascular changes in the placenta can result in localized formation of infarcts and clots, with subsequent migration in the foetal circulation. Direct trauma to the carotid artery by transmission of a shock wave could result in partial dissection and local formation of thrombosis.

The morphology of an arterial infarct depends mainly on the timing of the accident, the extent and the severity of ischemia and presence of haemorrhagic complications. During the first or second trimester of pregnancy, an acute vascular disorder not only produces destructive lesions but also interferes with development, leaving recognizable malformations such as porencephaly, schizencephaly, perisylvian polymicrogyria, septo-optic dysplasia [27–29]. If foetal injury is really most frequent in late pregnancy [6, 7], encephaloclastic lesions without disturbed gyral development and lesions similar to neonatal stroke will be more likely to occur. In the brainstem, when an ischemic process take place between the fourth week and the full term of gestation, it can be responsible for a Moebius syndrome [30], as presumed in patient 6.

Direct impact

Pregnant women are more likely to suffer serious abdominal injury rather than other injury [12]. Direct impact through the uterine wall seems to be rare [11]. Compression of the foetal head against a

surrounding solid structure, such as the pubic symphysis, the pelvis, the spine or the sacral promontory, is probably necessary to produce head injury [31, 32]. This mechanism is suggested when other direct physical injuries are observed on the foetus, such as splenic rupture [33] or subpleural haemorrhages [34]. A traumatic origin is clear mostly for depressed skull fracture and cerebral haemorrhage. The evolution is spontaneously resolute [15] or leads to hydrocephalus or to death [34, our patient 2].

Indirect traumatic mechanisms

Transmission of the shockwave and rotational acceleration have been reported in experimental car crashes [32]. The sudden deceleration of the pelvis stopped by the lap belt leads to a first rise of intrauterine pressure. As the uterus continues to move forward, striking anterior abdominal wall, a second peak of uterine pressure is observed. Then the upper torso of the animal is thrown forward, resulting in a third elevation of pressure. As the amniotic fluid cannot be compressed, striking of the anterior uterine wall could cause elongation and narrowing of the uterus. Then, the fluid wave rebounds and expands horizontally, transmitting forces to the foetal brain. Moreover, as the amniotic fluid-to-foetus ratio decreases in late pregnancy, the 'cushion-effect' becomes less protective [33] and the shockwave more easily propagated. Diffuse axonal injury, as a consequence of strong accelerations/ decelerations in the foetal brain, could result in an arrest of head growth [16, 17, 19, present patients 1, 4 and 13]. On a model of newborn mice, brain damage appeared between day 13 and 31 post traumatism and was principally restricted to the white matter, either as focal haemorrhagic lesions evolving to cystic scars (especially in periventricular white matter, corpus callosum, brainstem and cerebellar white matter) or as a progressive atrophy resulting from axonal pruning [35].

Practical recommendations

Establishing the relationship between the accident and the handicap

Even if the juridical status of the foetus remains an unresolved issue, many of the families will ask more or less rapidly for medico-legal litigation. The difficulties are mainly related to the chronology of the trauma, to the execution or absence of foetal investigations immediately after the trauma, and the nature of the lesions observed on MRI. When combining all these parameters, a four-grade scale of likelihood could be considered (Table II).

Table II. Causal relationship between the traumatism and child's handicap: A four-grade scale of likelihood summarizing the most schematic situations.

	Timing of the accident	Foetal investigations after trauma	Course of pregnancy	Identified foetal/postnatal lesions
Highly probable	Second half of gestation	Signs of foetal distress Morphological changes after close interval	Foetal death/premature birth after close interval	Malacic/haemorrhagic
Plausible	Any	Not performed after close interval UC changes weeks after the trauma	Continuation	Malacic/Ischemic
Elusive	Early to mid gestation	Normal after close interval, then US changes (or not performed)	Continuation	Non-specific disorder brain development
Excluded	Second half of gestation	Performed or not	Continuation	Specific developmental nomal anterior to the time of accident

The relationship is highly probable when, after an uneventful pregnancy, the accident is rapidly followed by foetal investigations exhibiting signs of distress and by premature birth or foetal death (patient 2–5, 11). Here, the main difficulty is to evaluate to which extent the neurological consequences are related directly to the physical injury and to the prematurity. Conversely, a causal link can be excluded when the observed cerebral lesion is in relation with a developmental process initiated before the time of the accident: thanks to confrontations done by neuropathologists and by specialists of brain imaging, many recognizable cerebral malformations can be currently attributed to specific periods of development (for review see Barkovich [28]). Between the two extremes, whether a causal relationship is 'plausible' or simply 'elusive' will depend on various parameters, including recognition of additional risk factors (such as benign gestational diabetes in our patient 6). However, when medico-legal issues are involved, it is usual practice to consider that the doubt should benefit to the victim.

Investigations

Finally, the present data suggest that more systematic, prospective studies are needed. In addition to routine obstetrical examination, the following suggestions could be made.

- Cardio-tonic monitoring – Abruption placenta generally occurs within the first 48 hours after trauma [34, 36]. Foetal loss is mainly feared in the absence of foetal heart tone, at a gestational age less than 26 weeks [37], even if these elements are not definitely pessimistic [12]. Imposing foetal

monitoring can hardly exceed a few days post trauma, even if signs of foetal distress can be postponed up to the second week (our patient 2). An initial monitoring of 4 hours [11] then every 6 hours for a 4 or 5-day period could be reasonable [11]. However, the cardiac rhythm is regulated in the brainstem and can be normal in isolated hemispheric damage [19].

- Ultra-sound investigation determines foetal viability, gestational age, amniotic fluid volume, the integrity of the placenta and of the foetus cerebrum, with a special look for intrauterine blood clots (abruption placenta) and for foetal intracranial haemorrhage. The results can be hampered by the low position of the head in the pelvis, explaining that few data have been reported in the literature. An ultrasound scan should be repeated, because lesions consecutive to vascular dysregulation are visible a few days after the accident, both in clinical experience [17, 19, patient 3] and in animal models [35]. Another US one month later is aimed at detecting anomalies of biometry, especially in head growth.
- Systematic MRI of the brain has not been reported in foetus victims of trauma. Considering its sensitivity to show malacic and haemorrhagic lesions and the limited value of the other techniques, an MRI should be proposed at least in the following circumstances: on foetuses exceeding 24 weeks of gestation, whether or not signs of foetal distress or US anomaly have been registered; when the position of the head makes the US evaluation difficult; when the mother suffers a pelvic fracture; when a rotational mechanism is suspected (major injury of the mother, minor brain injury with subjective complaints); finally, when the context makes a

medicolegal issue likely. MRI can be done as soon as technically possible following the trauma. Slices in the three plans of space with basic sequences (T2 single shot) and axial and or frontal T1 should be used, as well as axial slices, gradient echo T2-weighted sequences for detection of haemorrhagic lesions. Diffusion sequences are probably indicated, but are still under evaluation in the foetus. If anomalies were identified on a first MRI, or if clear signs of transient foetal distress were registered, a second MRI should be done 2 weeks later. As for any highly sensitive technique, sufficient experience will be necessary before concluding about the specificity of abnormal signals observed in the foetal brain after a trauma.

- Toco-dynamic monitoring is not mandatory. Abnormal uterine activity is common immediately after a trauma, but is not usually associated with dilatation of the cervix and is not predictive of foetal death or of foetal sequelae. The usefulness of the technique long after the injury has never been demonstrated [12].
- The Kleihauer Blake assay has not been proved sensitive enough to show small foeto-maternal haemorrhages [5]. On the other hand, several authors recommend this to diagnose significant foeto-maternal haemorrhage, regardless of their Rh status [10, 32, 38, 39]. Foetal loss resulting from exsanguination into the maternal circulation is rare. Complications due to foeto-maternal haemorrhage are more likely to be detected through usual signs of foetal distress such as heart rate abnormalities. However, new molecular cytogenetic techniques, which make it possible to quantify precisely all foetal nucleated cells in maternal blood would be interesting to evaluate [40].

Provoking premature birth

In most situations at risk, maintaining the uterine environment should not be considered superior to delivery. Sixty per cent of foetal or neonatal deaths result from delay in recognition of foetal distress and in decision to carry out a Caesarian section, especially in mothers with minor injuries and no personal signs of distress [37]. Currently, we would suggest deciding on a Caesarean section in the case of clear signs of distress in a viable foetus of more than 22 weeks (defined by foetal heart rate of less than 100 [41], prolonged deceleration for more than 60 seconds or recurrent late decelerations [37]).

Neonatal and postnatal follow-up

A careful examination of the neonate should focused on several items [10, 42]: a low Apgar score, which

does not climb up to normal at 10 minutes, could be an after-effect of the trauma (our patients 2–6, 10–11), then should lead to a detailed neurological investigation. Abnormal biometry of Head (our patients 1–2, 4, 13, 18) should lead to cerebral imaging. Abnormalities rarely reported must be searched for, especially hearing loss or blindness [37]. Later on, surveillance of the developmental items of common use is recommended, including tests simplified from Gesell. Any anomaly would justify maintaining the follow-up to primary school level.

Conclusion

Whether rare or underestimated, maternal trauma is one of the environmental factors responsible for cerebral palsy and this should be known by gynaecologists and paediatricians. Prospective studies are needed, combining more systematic foetal investigation post-trauma and developmental follow-up on the long term.

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