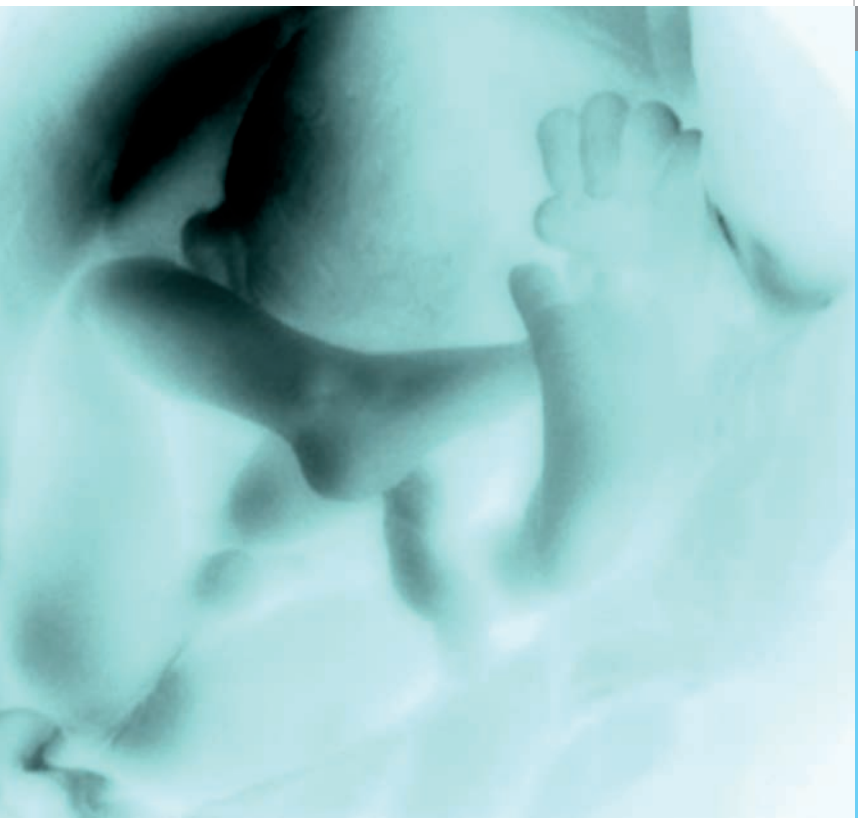
SWISS SOCIETY OF NEONATOLOGY

Severe consequences of illicit drug consumption during pregnancy



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This male infant was born to a 38-year-old HIV positive G2/P2 after 39 weeks of gestation by elective Cesarean section. Ten years ago, when she had already been infected with HIV, she had given birth to a baby girl who has remained seronegative ever since. During this pregnancy, treatment with zidovudine (AZT) and lamivudine had been started in the 32nd week of gestation and at the time of birth her viral load was < 50 copies/ml.

The mother reported that she had smoked 1-2 packs of cigarettes a day and drunk an occasional glass of wine during this pregnancy. However, she denied the consumption of any illicit drugs, although she had a prior history of cocaine abuse. Her drug history had lasted for eight years and she claimed having been „clean" for the last two years.

The infant boy adapted well with Apgar scores of 3, 8 and 9 at 1, 5 and 10 minutes, respectively. The arterial umbilical cord pH was 7.33. He presented as asymmetrical growth restriction with a body weight of 2410 g (P<10), a birth length of 44.5 cm (P<10) and a head circumference of 33.5 cm (P10-50). Because of respiratory distress, he required nasal CPAP support for the first 2 days of his life. Clinical examination was otherwise unremarkable. Oral therapy with AZT was started.

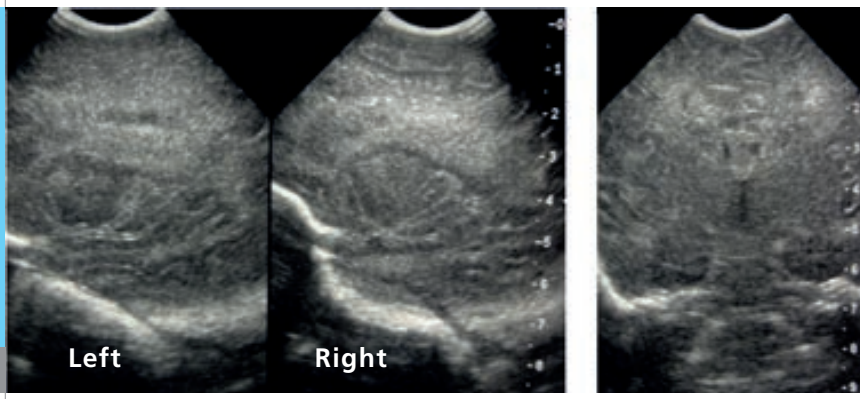

Fig. 1

Cranial ultrasound on day 2 of life: parasagittal and coronal views showing periventricular hyperechogenic areas

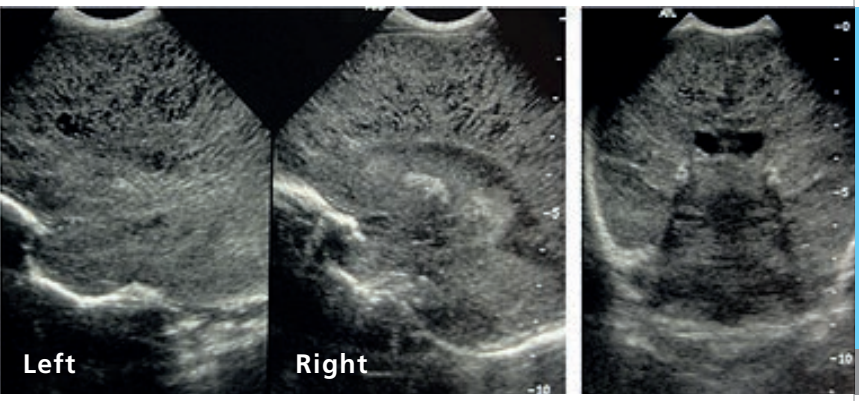

Fig. 2

Cranial ultrasound at 3 weeks of life: parasagittal and coronal views showing transformation into periventricular microcystic lesions.

From the second day of life, generalized muscular hypertension, tremor, uncontrollable crying, sucking weakness and a lack of coordination were noted. These were felt to represent possible drug withdrawal symptoms and monitoring with the modified Finnegan score was started. Drug testing for exposure to illicit substances was positive for opiates and benzodiazepines (he had received meperidine and midazolam because of agitation prior to urine collection) and for cocaine. Cranial ultrasound revealed bilateral periventricular hyperechogenicity and a poorly demarcated corpus callosum (Fig. 1).

When confronted with the results of the infant's toxicology results, the mother admitted that she had consumed cocaine regularly after discovering her pregnancy; she also reported that she had taken a final large dose of cocaine with the onset of labor.

Three weeks later, cranial ultrasound demonstrated transformation of the previously observed hyperechogenic areas into microcystic lesions (Fig. 2). Cranial MRI obtained at this time confirmed diffuse damage of both cerebral hemispheres and of the basal ganglia, primarily attributable to ischemic injury (Fig. 3). On EEG, there was suppression of background activity with subclinical seizures (Fig. 4).

In the following months, repeat cerebral ultrasound examinations demonstrated diffuse, large, cystic

changes in both cerebral hemispheres (Fig. 5) and follow-up EEG recordings continued to show severe disturbance of background activity. At the age of 3 months, the EEG was diagnostic for a epileptic encephalopathy (Fig. 6). Over the years, the boy developed severe hypertonic-dystonic tetraparesis with scoliosis (Fig. 7). He exhibited profound mental retardation with secondary microcephaly (IQ < 20), and suffered from pharmacoresistant epilepsy and a cortical visual impairment.

Magnetic resonance imaging at 3 weeks of life: T1-weighted coronal and transverse views showing diffuse damage with loss of white matter and cystic transformation of both hemispheres including the basal ganglia.

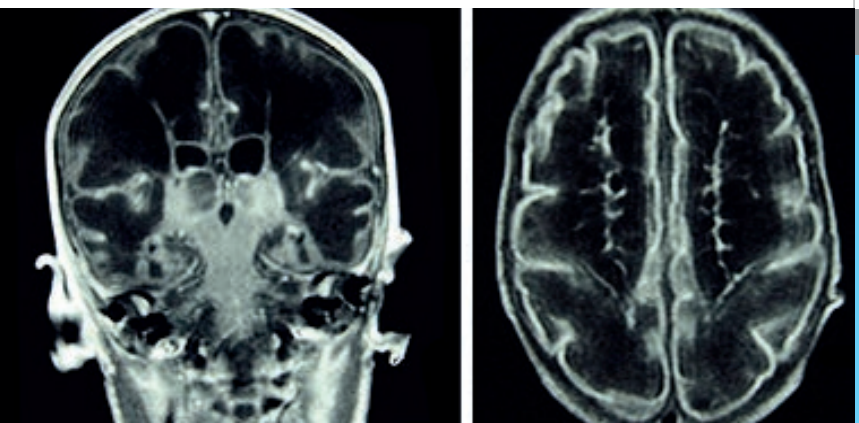

Fig. 3

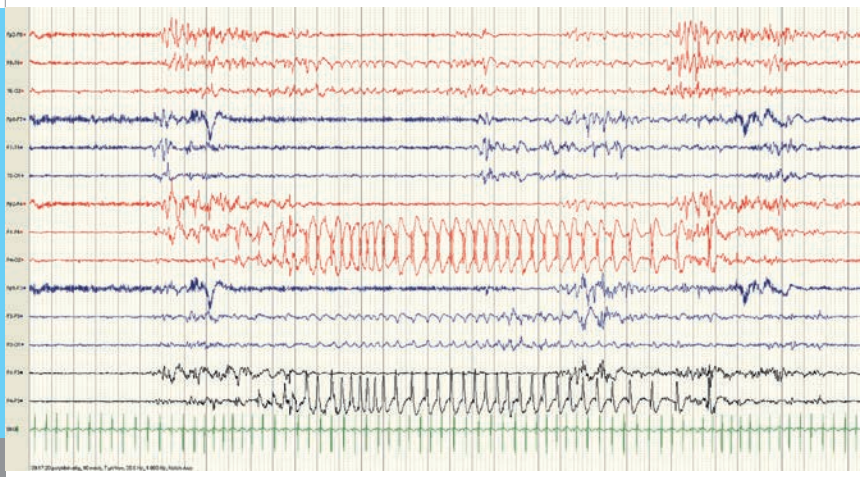

Fig. 4

First EEG at 42 weeks postmenstrual age: severely disturbed background activity with depression and asynchrony between both hemispheres, multifocal spikes, right parietal subclinical seizure with repetitive discharges - indicating severe bilateral brain dysfunction and poor prognosis.

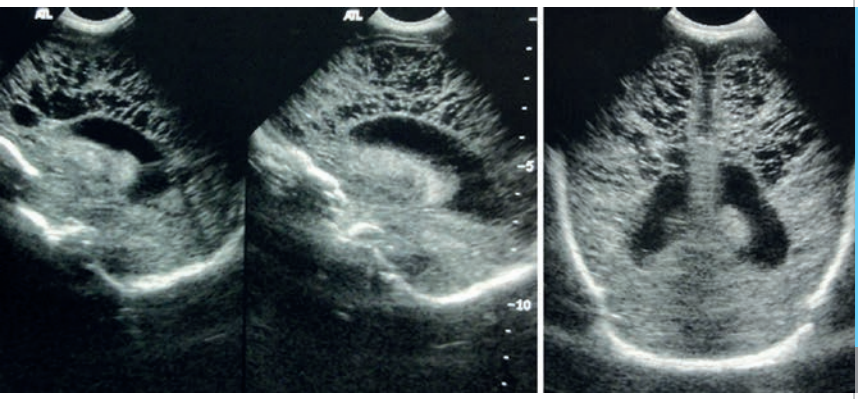

Fig. 5

Cranial ultrasound at 3 months of life: diffuse cystic lesions in both hemispheres.

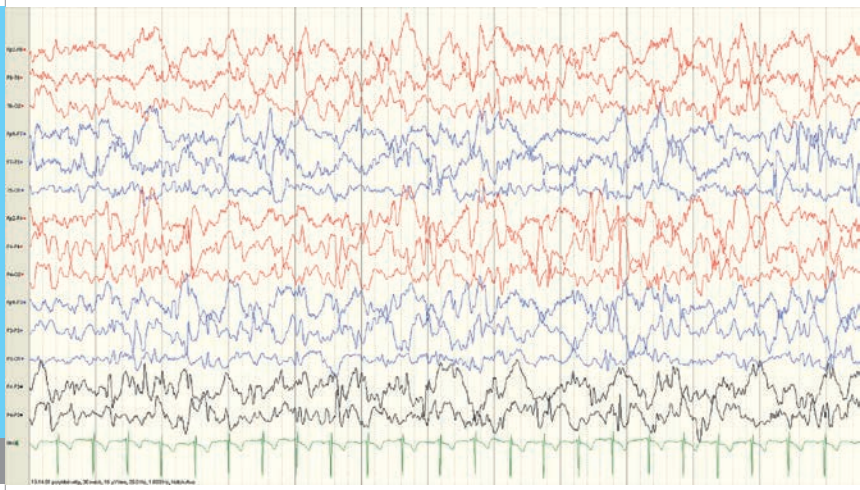

Fig. 6

EEG at 3 months of age with slowing of high voltage background activity and multifocal spiking indicating severe epileptic encephalopathy.

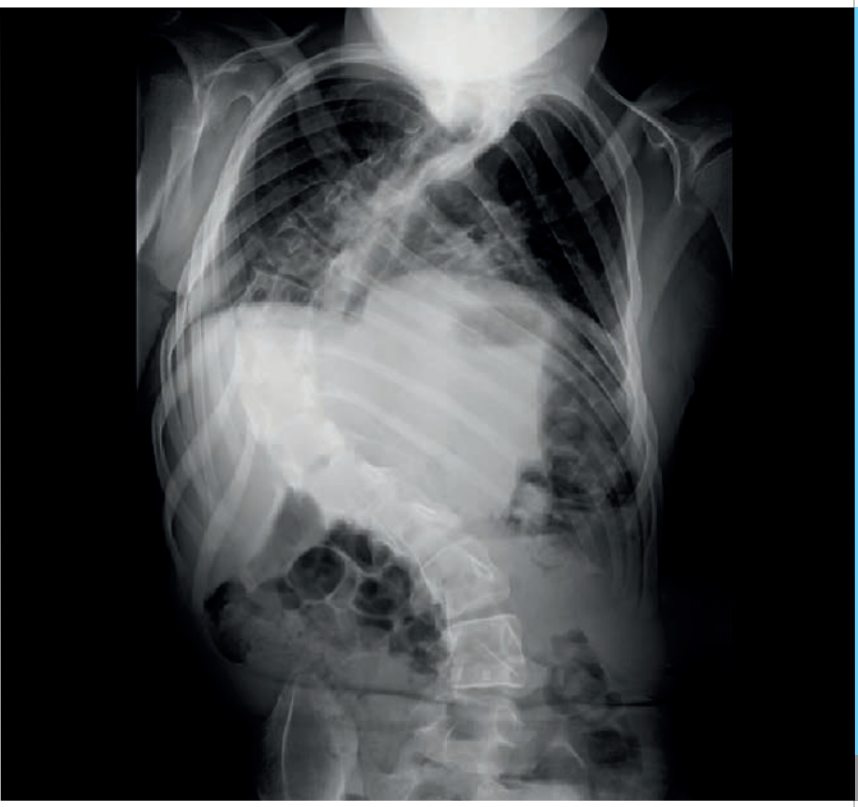

Fig. 7

Conventional X-ray of the spine documenting severe scoliosis.

DISCUSSION

In 2006-7, 5.2% of all American pregnant women aged 15 to 44 years exposed their fetus to illicit drugs. In the same population, 11.6% reported alcohol consumption and 16.4% smoking of cigarettes. Even though smoking of cigarettes and drinking of alcohol are legal, use of these substances in pregnancy is at least hazardous (1). Although there are no precise statistics about illicit drug use in pregnancy, alcohol and tobacco use are a common problem in Switzerland with up to 10% of pregnant women admitting to smoking and 30% consuming alcohol even after recognizing that they are pregnant (2).

From the mid-1980s into the early 1990s, many reports raised concerns about the potential toxic impact of fetal cocaine exposure during pregnancy. Cocaine impairs the reuptake of norepinephrine, epinephrine and dopamine and it affects serotonin homeostasis, causing pronounced effects on both the peripheral and central nervous systems. Increasing concentrations of catecholamine occur both in the mother and in the fetus. On the maternal side, this leads to a reduction of placental blood flow and, because of increasing uterine contractility, placental abruption can occur. Cocaine use during pregnancy is associated with prematurity.

Direct effects on the fetus are even more deleterious: increases in fetal catecholamine concentrations lead to generalized vasoconstriction, increase in blood

pressure and decreased organ blood flow. As a consequence, the CNS lesions associated with intrauterine cocaine exposure are ischemic and hemorrhagic. Hemorrhage results from the abrupt increase in fetal blood pressure and hypoxemia, whereas the ischemic lesions are caused by cocaine-mediated vasospasms similar to what has been described in ischemic coronary (myocardial) and cerebral vascular events in adults. Altered levels of monoamines in the CNS can lead to excitotoxic injury and impaired neuronal development (3). Cocaine-induced vasoconstriction may also impair the perfusion of other organs. In this context, an increased risk of necrotizing enterocolitis has been well documented.

Interestingly, there are only a few reports of cocaine-associated periventricular leucomalacia (PVL) or other cerebral abnormalities such as subependymal cyst (4). Behnke et al, in their prospective, longitudinal study of 154 cocaine users matched with 154 control subjects, found that cocaine-exposed infants were significantly growth restricted (including head circumference), but did not find any significant difference in the type or number of cerebral abnormalities between the two groups assessed by cranial ultrasound (5,6). Magnetic resonance imaging analyzes the brain structures more precisely. Roussotte et al. showed subtle dysmorphic patterns in the striatum and changes in the volume of the frontal lobes (7) among infants born to cocaine-dependent mothers. Because these abnormalities are

too subtle to be detected by ultrasound, some authors feel that routine cranial ultrasonography is not warranted in this population (8).

Our patient developed catastrophic cystic PVL with severe long-term consequences. Factors that have been reported to be associated with PVL and white matter abnormalities especially in preterm infants include early-onset sepsis, hypocarbia, early neonatal hypotension, delayed surgical closure of a hemodynamically significant patent ductus arteriosus and necrotizing enterocolitis (9-11). These risk factors were not present in our patient. We speculate that the mother's last dose of cocaine taken shortly before birth may have resulted in vasospasm of the carotid arteries and/or other major cerebral vessels resulting in the observed ischemic damage of both hemispheres. This is comparable to another case report where cocaine exposure led to hydranencephaly, i.e., severe destruction of cerebral hemispheres after occlusion of the middle and anterior cerebral arteries (3).

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