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Histological characterisation of segmental neuromuscular dysfunction in fetuses with spina bifida aperta

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Background

In spina bifida aperta (SBA), fetal leg movements caudal to the meningomyelocele (MMC) are quantitatively impaired and disappear shortly after birth. The time of initiation and the histological "substrate" for this motor dysfunction is still unclear. If motor dysfunction is primary related to the fusion defect, neuromuscular histological impairment would appear independent of gestational age or delivery. In contrast, if motor dysfunction were related to secondary damage, one would expect histological spinal detriment caudal to the MMC (such as apoptotic lower motor neurones (LMNs), infection and bleedings), especially at elder gestational ages. In the present study, we investigated segmental neuromuscular histology in SBA fetuses of various gestational ages.

Patients/methods

After informed consent by the parents, histological material of 8 SBA fetuses (median GA, 30 wks; range 16–40) was investigated. The MMC was at cervical (n = 1), thoracic (n = 5) or lumbar (n = 2) level. Pregnancies ended after abortion (n = 3, GA < 24 wks), abruptio placentae (n = 1), or delivery-related ventricular puncture (n = 4; in SBA fetuses with additional pathology: encephalocele, atrium septum defect, lung hypoplasia, palatoschisis and massive hydrocephalus). Histology was investigated in spinal segments (n = 8) and myotomes (n = 6) cranial, at and caudal to the level of the MMC. Histological and immunohistochemical staining was performed by HE and caspase-3. Prior to delivery, fetal ultrasound recordings were performed in 6 fetuses.

Results

In all (8/8) fetuses, spinal histological analysis indicated presence of LMNs and neural tracts cranial and caudal to the MMC. Caudal to the MMC, LMN quantity was reduced (compared to cranial to the MMC) without signs of ongoing apoptosis (caspase-3 negative in 8/8 fetuses). Spinal vascularisation caudal to the MMC appeared superfluously aberrant in 6/8 fetuses, compatible with abnormal mesenchymal migration. Fresh spinal haemorrhages appeared in all (8/8) fetuses. In all (6/6) fetuses, muscle histology was normal cranial to the MMC and abnormal caudal to the MMC (dystrophic and compensatory hypertrophic muscle fibres). All histological abnormalities were unrelated to gestational age and to prenatal presence of leg movements (observed in 5/6 fetuses).

Conclusion

In fetal SBA, segmental histological analysis caudal to the MMC shows presence of developmental abnormalities (i.e. quantitatively reduced LMNs, dystrophic/hypertrophic muscle fibres and aberrant vascularisation) throughout gestation. Superimposed on this, secondary

spinal haemorrhages are observed, which appear to be delivery-related. In neonatal SBA, we suggest that these spinal haemorrhages may contribute to the final disappearance of leg movements.