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Abstracts

Neurosurgery Session 2

Hydrocephalus based procedures in an adult/ transition Spina Bifida Clinic: a 5 year experience

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Background There are more adults than children living with Spina Bifida yet there are limited resources and clinics to support their unique needs. To address this need in our region we initiated an Adult Spina Bifida Clinic in 2010 and report here a 5-year experience with the management of hydrocephalus in this cohort.
Methods Retrospective review of a prospectively collected institutional database. IRB approval obtained. Shunt procedures were stratified into single revisions (shunt revision with 1 year of revision free survival) and those which occurred in clusters (those procedures requiring multiple revisions and prolonged hospitalization) and were evaluated by age.
Results Since 2010 198 unique adult (age >= 18 years) patients with a past medical history of open Myelomeningocele or Occult Spinal Dysraphism (Lipomyelomeningocele, Split Cord Malformation or Dermal Sinus Tract) were evaluated in our adult Spina Bifida Clinic (ASBC). From this group we identified 61 patients who underwent 176 Neurosurgical procedures. All procedures not related to hydrocephalus management were excluded to yield a cohort of 51 adult patients who underwent a total of 151 procedures for hydrocephalus. The average number of procedures was 2.04 (STD = 1.9) but those occurring in clusters ranged from 2–11 shunt revisions. Clustered events tended strongly to occur in younger patients. Patients 25 and under demonstrated an 85% rate of clustered procedures whereas only 1 patient over 35 had a cluster of shunt procedures. The inflection point occurred around age 25.
Conclusions In this cohort of adult SB patients younger patients exhibited a higher rate of complex clustered shunt procedures compared with older patients. If corroborated at other centers these data may impact clinic choices of the age for transition. Procedures for shunt intervention occur throughout the life span but decrease in frequency.

Long-Term Clinical Outcomes of Terminal Myelocystocele

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Background Myelocystocele is a rare, skin-covered form of spinal dysraphism. This condition may also be associated with cloacal anomalies, imperforate anus and spinal defects. We present long-term outcomes for the largest cohort of patients with myelocystocele described in the literature.
Methods All patients presenting to a single institution between 1982 and 2014 with myelocystocele were identified. Out of 58 patients, 3 were excluded due to lack of follow up, 55 were reviewed for operative and clinical outcome measures.
Results We reviewed 55 patients (60% male). 47 (85%) had a primary untethering at our institution (median age 2.3 months). 38% of our cohort had an associated cloacal anomaly (CA) (20 cloacal exstrophy, 1 cloacal malformation). In the non-cloacal anomaly (NCA) cohort, 27 (79 %) presented with a fatty mass, sacral dimple, skin tag or hemangioma, 6 (18%) with

urinary symptoms and 1 (3%) with a combination of these. Of those that had their primary repair at our institution, 16 (34%) required a second untethering, and 3 (6%) required a third untethering procedure.
25% had a lumbar drain placed. The average estimated blood loss was 37 ml, with 1 patient requiring a postop transfusion. Fifteen patients (27%) had 24 postoperative complications, including cerebrospinal fluid leak (11), wound dehiscence (5), wound infection (3), pseudomeningocele (2), meningitis (2) and wound revision (1).
Long-term continence was assessed in 53/55 patients who had follow up $>$ 6 months. Of those, 12/28 (43%) in the NCA group were continent vs.
1/20 (5%) in the CA group ($p = 0.0683$). In the NCA group 31/32 (100%) were ambulators vs 15/21 (71%) in the CA group ($p = 0.0066$). One patient, age 9 years, died from severe pulmonary hypertension.
Conclusions We present the largest study of patients with myelocystocele with a median follow-up of 12.0 years (1–27 range). Myelocystocele without cloacal anomaly demonstrated better long-term urological and ambulatory outcomes.

Limited Dorsal Myeloschisis' Association with Dermoids

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Background A histopathological hallmark of all limited dorsal myeloschisis (LDM) is glioneuronal tissue in the stalk, as it originates from undisjointed neuroectoderm during primary neurulation. The majority of LDMs have only the neuroglial tissue within the stalk but a small percentage will have elements of a dermoid cyst or a dermal sinus tract either separate from the LDM stalk or incorporated within its fibroglial matrix, explainable by the original continuum of cutaneous and neural ectoderms in LDM's embryogenesis. The dermoid elements can be microscopic and escape casual observation, but could grow to large intradural or intramedullar dermoid cysts when left behind.
Methods We present a pediatric series of 5 cases with LDMs associated with dermoid elements. We analyzed cutaneous stigmata, presenting neurological symptoms, initial complete removal of the LDM stalk, levels of laminectomy, histopathology, recurrence of dermoid elements and neurological outcome.
Results Two of 5 patients underwent revision surgery for symptomatic recurrence of dermoid tumours due to incomplete resection of the entire fibroneural stalk at initial surgery. Those cases with original complete removal of the fibroneural stalk and also the 2 patients with secondary complete resection had excellent outcome.
Conclusions The existence of dermoid cysts within the fibroglial matrix of a LDM stalk reflects the embryogenesis involving a continuum of cutaneous and neural ectoderms. We present our series of LDMs with associated dermoids and recommend excising the entire length of the intradural LDM stalk during the initial treatment to prevent recurrence of the dermoid remnants.

The Xiao Procedure did not Improve Continence or Voiding in Children with Spina Bifida: A Summary of Neurologic and Urologic Outcomes of a Randomized, Prospective, Double Blinded Surgical Trial

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Background Professor C.G. Xiao gave the keynote lecture at the first World Congress of Spina Bifida meeting in 2009, presenting outstanding results after an intradural somatic to autonomic (ex: L5 to S3/4) nerve transfer operation as a way to allow bladder emptying in response to cutaneous stimulation ("scratch and pee"). This reflex arc reportedly allowed spontaneous, controlled voiding in children with neurogenic bladder dysfunction, including children with Spina Bifida. Our multidisciplinary group embarked on a randomized, prospective, double blinded trial to study the Xiao Procedure in children with Spina Bifida undergoing spinal cord detethering shortly after his keynote speech.

Methods METHODS: Children with Spina Bifida and neurogenic bladder dysfunction were randomized between two groups: half of the patients underwent only a standard spinal cord detethering procedure (DT) and half underwent detethering plus the Xiao procedure (DT + X). Patients, families and study investigators, all of whom were blinded to the surgical details, analyzed the patients' results over a three year interval.
Results Ten children underwent only DT and the other 10 underwent DT + X. No patient in either treatment group, with or without the Xiao procedure, achieved continence or could void voluntarily or in response to scratching at any time during follow-up. Patients who underwent the Xiao procedure were more likely to have greater improvements in total bladder capacity, bladder over-activity and overall quality of life than patients who only underwent detethering. Detailed results will be presented.
Conclusions Until further peer reviewed research is performed, this study raises doubts about the clinical applicability of the Xiao Procedure for children with Spina Bifida at this time.

New Cellular and Molecular Aspects of "Symptomatic" Lipomyelomeningoceles (LMMC): Histological and Molecular Analyses of an Institutional Case Series

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Background Molecular and cellular mechanisms underlying symptomatic LMMC are hardly understood. We focused on specific inflammatory cascades potentially underlying symptomatic LMMC.
Methods Specimens obtained from LMMC-surgeries harboring neuroepithelial tissue were investigated. Clinical data were collected. Pre-surgical MRI was reevaluated (lipoma type, conus position, syringomyelia). Controls included normal adult spinal cords ($n = 4$). Sections were analyzed histologically and by staining with neuroglial, neural crest, mesenchymal and epithelial markers. Immunohistochemistry and real-time RT-PCR for IL-1b, IL-1R1, TNF-a, TNF-R1 were performed and analyzed qualitatively and semi-quantitatively. Cellular cytokine expression was confirmed via double-fluorescence-labeling with cellular markers. Hypoxia induced factors and cytokines (EpoR/Epo) were further analyzed.
Results Four transitional intraspinal lipomas, 4 transitional lipoma with extraspinal extension, and one chaotic lipoma were included into the study. In all 9 cases, GFAP and Vimentin exhibited significant induction in neural elements. IL1-1R, IL-1b, TNF-R1, TNF-a immunoreactivities (IR) were significantly elevated in all cases ($p < 0.05$ and $p < 0.001$ vs. control). These cytokines co-stained with neural and glial cell markers. Further, caspase-3 was found co-stained with these molecules. Also, hypoxia-induced factors were found on elevated levels in the majority of investigated cases.
Conclusions Our preliminary data provides hints for pro-inflammatory cytokines being potential mediators of pathophysiological cascades of neural LMMC structures. Their role as surrogated markers for symptomatic LMMC has to be proven with larger case numbers. Our data will serve as basis for a future multicenter study, which will be briefly outlined in the presentation (in case of interest, contact Gesa.Cohrs@uksh.de).

Does Inflammation Play a Role in Tethered Cord Syndrome after MMC-repair Surgeries?

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Background Traction and hypoxia are considered main driving forces of Tethered Cord Syndrome (TCS). The aim of this study was to identify cellular and molecular mediators that may contribute to re-"tethering" of neural structures after MMC repair surgeries. Based on our recent findings on MMC-placodes the focus of this study was on inflammatory processes.
Methods Specimens obtained during surgery for symptomatic re-tethering after MMC-repair were investigated (12 cases). Clinical characteristics were obtained retrospectively. Normal adult spinal cords (sc) ($n = 4$) served as controls. Sections were immunostained with neuroglial, neural crest, mesenchymal, epithelial and inflammatory markers (GFAP, neurofilament, NeuN, synaptophysin, CNPase, Vimentin, CD68, CD11b). Immunohistochemistry and quantitative real-time RT-PCR for pro-inflammatory cytokines (interleukin-1beta (IL-1b), IL-1R1, tumor necrosis factor-alpha (TNF-a), TNF-R1) were performed. Induction of hypoxia inducible factors (HIF-1a/-2a) was confirmed. Based on our findings, PARP and Caspase-3 were stained to visualize apoptotic processes. Cellular expression patterns were confirmed by multiple-fluorescence-labeling.

Results All specimens contained neuronal, glial, and in part inflammatory cells. All TCS-cases exhibited significantly elevated GFAP- and Vimentin-immunolabeling (i.e. gliosis). IL-1b and TNF-a plus their receptors became detectable in cellular composites of intrathecal nervous structures on significantly elevated level. These cytokines were co-stained with NeuN (TNFa/TNF-R1), GFAP (IL-1b/IL-1R1), and inflammatory cellular markers. HIF-1a/-2a became detectible significantly elevated in all TC-cases. In these cases, Caspapse-3 and PARP labeled subsets of cells in neural tissues.

Conclusions Our findings indicate that, in addition to traction and hypoxia, pro-inflammatory and pro-apoptotic mechanisms may significantly contribute to TCS development.

Pro-Inflammatory/-apoptotic and Neuroprotective Mediators in the Myelomeningoceles (MMC) Placodes: Potential New Targets in Repair Strategies?

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Background Due to impaired neurulation MMC-neuroepithelium is prone to sustained injury. This may induce lesion-amplifying cascades that underlie progressive loss of function. We aimed to identify specific mediators of these mechanisms – also addressing neuroregenerative aspects – in placode tissues obtained during primary repair surgeries.

Methods Specimens of 17 cases (obtained during reconstructive surgery after birth) with sufficient neuroepithelial tissue were investigated. Normal adult and fetal spinal cord tissue served as controls. Neuroglial, neural crest and neuroepithelial marker expression profiles were established. CD11b, CD3, CD68 were used as inflammatory markers. Pro -inflammatory cytokines, their receptors (IL-1b/IL-1R1, TNF-a/TNF-R) and erythropoietin (EPO) plus its receptor EPOR were investigated by immunohistochemistry and real-time RT-PCR. Pro-apoptotic markers were investigated in selected cases (TUNEL; Caspase-3, PARP). Double-fluorescence-immuno-labeling was used for cellular localization Hypoxia inducible factors (HIF) 1 and 2 were investigated in the context of EPO expression.

Results All MMC-cases exhibited significant astrogliosis with inflammatory infiltrates throughout the neuroepithelial tissue. Multicellular IL-1R/IL-1b- and TNFa/TNF-R1-expression was significantly induced in all cases, accompanied by hints for apoptotic processes. Neuronal EPOR was found in most placodes, ignificantly induced in 8 cases. EPO was significantly elevated in 40% of the cases, co-labeling with HIF-2a IR, which was significantly induced in all MMC-cases.

Conclusions Like after spinal cord injury, inflammatory mechanisms became evident in MMC-placodes obtained after birth. Pro-inflammatory/- apoptotic and neuroprotective cytokine expression in mmc-placodes thereby offers potential targets for adjuvant treatment options in open neural tube defects.