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BACKGROUND: Cerebellar mutism syndrome (CMS) is the commonest and most serious complication of posterior fossa tumour surgery with life-long consequences on speech and motor function. Despite previous identification of pre-operative clinical and radiological predictors of CMS, a unifying pre-operative risk stratification model for use during surgical consent is currently lacking. The aims of the project are to develop a simple pre-operative risk scoring scheme to stratify patients in terms of post-operative CMS risk. METHODS: Pre-operative radiological features were recorded for a retrospectively assembled cohort of 89 posterior fossa tumour cases from two major UK treatment centres aged 2–23 years: gender; 28M,61F; diagnosis: 38 pilocytic astrocytoma, 32 medulloblastoma, 12 ependymoma, 1 high grade glioma, 1 pilomyxoid astrocytoma, 1 atypical teratoid rhabdoid tumor, 1 hemangioma, 1 neurilemoma, 2 other histologies. Twenty-six (29%) were post-operative CMS. Based upon results from univariate analysis and C4.5 decision tree, step-wise logistic regression was used to develop the optimal model and generate risk scores. RESULTS: Univariate analysis identified five significant risk factors and C4.5 decision tree identified six predictors. The final model had an accuracy of 88.8% (798/89). Using risk score cut-off of 203 and 238 allowed discrimination into low (38/89, predicted CMS probability < 3%), intermediate (17/89, predicted CMS probability 3–52%) and high-risk (12/89, predicted CMS probability > 52%). CONCLUSIONS: We will continue to work with leading neurosurgical centres in Europe and North America to expand the cohort and organise an international workshop in Nottingham to (1) validate and/or modify the preliminary model; (2) compare our findings through joint discussion, and (3) develop a simple and useful risk stratification tool that can inform early decision-making and support information exchange to establish a stratified approach to cerebellar mutism risk reduction. Following further multi-centre validation, this tool could be of value in providing CMS risk during the consent procedure and for stratifying patients in terms of CMS risk in trials of therapeutic strategies.

TRTH-25. REDUCING TIME TO DIAGNOSIS OF PAEDIATRIC BRAIN TUMOURS IN THE UK – HEADSMART AWARENESS CAMPAIGN

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BACKGROUND: Public and professional concern about delays in diagnosis of childhood brain tumours has led to a clinical referral guidelines and the Headsmart campaign to raise awareness of the early features of brain tumours and the need for timely imaging. As part of the outcome evaluation, we have collected data on total diagnostic intervals (TDI): i.e. intervals between symptom onset to diagnosis through a national service evaluation. The aims of the project are to (1) report the most recent TDI; and (2) identify the subgroup(s) with the longest symptom interval. METHODS: Paediatric brain tumour cases (aged 0–18 years) diagnosed between June 2014 and May 2015 were identified through a network of Headsmart clinical champions. Age at diagnosis, dates of first symptom onset, first presentation to healthcare and diagnosis, tumour site, diagnosis were collected thorough electronic record systems. RESULTS: Data of 334 eligible cases, representing over 75% of incident cases in the UK of that year were recorded. TDI showed a right skewed distribution with a 90th percentile of 48 weeks and maximum of 313 weeks. Group median TDI had reduced significantly over time: 13.4 weeks in 2006 to 6.7 weeks in 2014. CONCLUSIONS: Time to diagnosis for paediatric brain tumour patients up to two years after diagnosis. The risk was greatest (6.0%) in 0–5 year-olds and lowest (1.5%) in 19–25 year-olds. Tumours above the tentorium (5.1%), cranial nerve (4.5%) and in the midline (4.2%) pose the highest diagnostic challenges. Planned post-operative CMS. Higher age at diagnosis, medically unexplained symptoms and lower performance status were associated with longer TDI. Further subdivision according to tumour site and histology revealed significant differences, but only the analysis of medulloblastoma was statistically significant. Tumours below the tentorium (6.7%) had the longest TDI. CONCLUSIONS: Brain tumour was the commonest cause of blindness certification in England in 2011 affecting 6% of children aged 0–18 years. It was most common in benign / slow growing tumours affecting midline structures. The proportion with blindness certification has fallen between 2007–2012, coinciding with the reduction in reported TDI since the launch of referral guideline, which was the focus of the Headsmart campaign. Headsmart Certifications data was collected through the information exchange to establish a stratified approach to cerebellar mutism risk reduction. Following further multi-centre validation, this tool could be of value in providing CMS risk during the consent procedure and for stratifying patients in terms of CMS risk in trials of therapeutic strategies.

TRTH-26. PRIMARY BRAIN TUMORS – A POPULATION LINKAGE STUDY

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BACKGROUND: Histone deacetylases (HDACs) are crucial regulators of epigenetic and posttranslational modifications and therefore represent a promising therapeutic target in cancer cells that harbor distinct epigenomes from normal cells. To exploit the therapeutic potential of HDAC inhibitors (HDACIs) we synthesized a unique in-house library of more than 200 inhibitors. For the evaluation of the antitumor effects of the compound library in brain tumor cell lines, we successfully established an optimal screening workflow. METHODS: The screening procedure was streamlined by automated dispensing of cell lines, reagents and inhibitors into 384-well plates. The drugs were evaluated for their effect on tumor cell viability in a panel of cell lines derived from different brain tumor entities (8 glioblastoma, 10 medulloblastoma and 6 atypical teratoid/rhabdoid tumor cell lines) and compared to 5 normal control cell lines. Correlation between dose-response profiles were generated using an optimized bioinformatics workflow. In addition to our in-house library commercially available and clinically used HDACi (e.g. Vorinostat) were included. RESULTS: The generated datasets contained targeted antitumor profiles in 384-well plates. In combination with additional modifications, a remarkable increase of the overall throughput was realized, while generating accurate and reproducible results. Based on this workflow, we created a unique and comprehensive data set and could thereby identify various HDACi acting universally across brain tumor cell lines or being with cellular activity on distinct cell line subtypes.