given in 40% of cases and consisted primarily of colecalciferol, with daily doses ranging from 400 IU to 3000 IU. However, in 55% of cases there was no improvement in vitamin D levels following supplementation. This poor response to supplementation is likely to have a multifactorial aetiology, including inadequate/low dosing regimen, poor adherence and inconsistent follow up of vitamin D levels. Low bone density was confirmed in DEXA scans in 12% of cases. Seven children (28%) had fractures (clinical characteristics are summarized in table 1).

Subgroup analysis based on age showed that patients >10 years had significantly higher rates of fractures compared to patients <10 years (83% vs 11%, RR 7.9, p=0.001) as well as higher rates of vitamin D deficiency (83% vs 47% p=0.1).

Our paediatric physiotherapy team performed regular outpatient and/or inpatient reviews in 88% of our ALL cases; 41% had blocks of intensive physiotherapy treatment and 36% were provided with a home exercise program (HEP).

Abstract 579 Table 1

<table>
<thead>
<tr>
<th>Case</th>
<th>Age at diagnosis (years)</th>
<th>Gender</th>
<th>Mechanism of fracture</th>
<th>Vitamin D serum level at time of fracture</th>
<th>Position in treatment at time of fracture</th>
<th>Physiotherapy input</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>M</td>
<td>Pathological fracture</td>
<td>Nil</td>
<td>At diagnosis</td>
<td>Black of treatment</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>M</td>
<td>Injury</td>
<td>53 Colecalciferol 3000 IU UD</td>
<td>Maintenance</td>
<td>HEP</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>F</td>
<td>Minor Injury</td>
<td>57 Colecalciferol 400 IU UD</td>
<td>Maintenance</td>
<td>Black of treatment</td>
</tr>
<tr>
<td>4</td>
<td>11</td>
<td>M</td>
<td>Injury</td>
<td>118 Colecalciferol 3000 IU UD</td>
<td>Maintenance</td>
<td>Black of treatment</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>F</td>
<td>Injury</td>
<td>43 Colecalciferol 3000 IU UD</td>
<td>Maintenance</td>
<td>HEP</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>F</td>
<td>Stress fracture</td>
<td>40 Colecalciferol 3000 IU UD</td>
<td>Maintenance</td>
<td>Black of treatment</td>
</tr>
<tr>
<td>7</td>
<td>11</td>
<td>F</td>
<td>Stress fracture</td>
<td>38 Colecalciferol 3000 IU UD</td>
<td>Maintenance</td>
<td>Black of treatment</td>
</tr>
</tbody>
</table>

Conclusion Our results demonstrate that children undergoing treatment for ALL are at increased risk of fractures as well as vitamin D deficiency. We note significant variability in practices of diagnosing, treating and monitoring of Vitamin D deficiency in our unit, and targeted quality improvement projects should focus on standardising and optimizing these practices. This is particularly important to children >10 years, as this age group appears to be at an even higher risk of developing fractures and of responding less well to vitamin D supplementation. Finally, our study highlights the crucial role of paediatric physiotherapy in the POSCU multidisciplinary team, for prevention, early detection, treatment and follow up of the musculoskeletal morbidities of childhood ALL.

VITAMIN D LEVELS IN CHILDREN AND YOUNG PEOPLE DIAGNOSED WITH CANCER- A RETROSPECTIVE SINGLE CENTRE STUDY

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Abstracts


AN EXPLORATION OF EXISTING AND POTENTIAL NOVEL GFR MEASUREMENT AND NEPHROTOXIC BIOMARKERS IN PAEDIATRIC MEDULLOBLASTOMA
Stephanie Lyman, Newcastle University
10.1136/archdischild-2022-rcpch.495

Aims
1. To create a comprehensive database of all Medulloblastoma biomarkers currently described in the Medulloblastoma literature.
2. To investigate pre-existing single-cell-sequencing (SCS) data from 14 Medulloblastoma tumour samples to identify and analyse Copy number variation (CNV) biomarkers which were not yet identified which were a single chromosomal arm or less in length.
3. To analyse focal and sub-chromosomal changes in SCS data and assess their clonality and to note any known Medulloblastoma driver genes in these areas.
4. To assess non-coding gene drivers in the SCS data in these regions of focal and sub-chromosomal change.
5. To analyse the breakpoint locations (centromeric versus Chr17-11P) of tumours exhibiting the isochromosome 17q biomarkers. To establish if breakpoint location could be used as a potential novel biomarker in Medulloblastoma.

Methods
1. A thorough literature review was undertaken with studies having to meet certain criteria such as cohort size. Biomarkers were recorded according to tumour subgroup and additional information such as survival significance were input into a database.
2. A list of CNVs detected through SCS was cross-referenced against the completed biomarker database. The IGV genome browser was used to assess clonality in these remaining chromosomal aberrations.
3. Each changes presence was confirmed in the IGV browser and in whole-exome sequencing and array data. A reference list of influential genes in Medulloblastoma was collated via a literature review. The locations of these genes were compared to the locus of each focal and sub-chromosomal change.
4. Literature was examined and miRNAs known to be dysregulated in medulloblastoma tumorigenesis were pooled. Firstly, the chromosomal arm location of these miRNAs was compared to the Medulloblastoma biomarker database and those equivalently up/down regulated in the pooled. Secondly, the chromosomal locations of shortlisted miRNAs were reviewed against locations of the focal and sub-chromosomal changes.
5. The DNA-methylation array data from 162 patient samples featuring i17q was acquired, separated into Medulloblastoma subgroups and breakpoint location was analysed in the Conumee package.

Results
1. Three medulloblastoma biomarker databases were created of Medulloblastoma biomarkers currently described in the literature and contained 63 CNV, 23 gene expression change and 59 gene mutation biomarkers.

2. Three established biomarkers which had not yet been characterised in the single-cell clonal evolution study were identified.
3. 42 genes were identified which had been linked with the corresponding subgroup of that patient in the literature. These genes were present in 8 patient samples. Four changes containing driver genes were focal and 15 were sub-chromosomal.
4. 63 mi-RNAs with importance in Medulloblastoma were identified. Three SHH subgroup, one Group 3 and one group 4 mi-RNA were present in the SCD and equated to CNV biomarkers.
5. The following are the proportions of centromeric versus Chr17-11P breakpoints in each subgroup and subtype: (Group 3 (4/37), II(2/15), III(1/13), IV(0/2), V(1/7), Group 4(1/120), V(0/14), VI(0/21), VII(1/9), VIII(0/76).

Conclusion Further information has been gained about biomarkers in the SCD and some promising new candidates for future biomarkers have been identified.
[Marina Danilenko]

GFR MEASUREMENT AND NEPHROTOXIC CHEMOTHERAPY DOSE REDUCTION IN PAEDIATRIC SARCOMA PATIENTS, A THREE CENTRE STUDY
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Aims Ifosfamide and methotrexate are commonly used in the treatment of paediatric sarcoma patients and require careful monitoring of renal function and estimation of glomerular filtration rate (GFR) due to nephotoxic side effects. Using radiolabelled isotopes to measure GFR is common in paediatric patients due to increased accuracy, reliability and the difficulties of urine collection. However, it is an invasive and expensive test with unavoidable radiation exposure. With no current national guideline on GFR monitoring there is significant variation in practice. This study aims to evaluate frequency of GFR monitoring, across three paediatric oncology centres, and the impact it had on chemotherapy dosing. Recommendations will be made to standardise practice, identify risk factors for renal toxicity and consider frequency of radiotope GFR measurement.

Methods A retrospective analysis of all paediatric patients diagnosed with Ewing’s sarcoma, osteosarcoma or rhabdomyosarcoma, requiring ifosfamide or methotrexate chemotherapy, from January 2019 – January 2020 was conducted. Data collected included; age, diagnosis, baseline renal function, underlying renal conditions, renal function monitoring during treatment (via isotopic GFR or other method) and any chemotherapy dose reduction. Data has also been included from a previous audit of GFR use from the Royal Marsden Hospital collected in 2013. Data was collated from patients’ clinical notes and online test portals local to each site.

Results 85 patients were eligible for inclusion with 17 patients excluded for incomplete data. The age ranged from 1 month to 21 years, with an average age of 9 years. 62 patients had formal isotope clearance GFR testing and 6 patients had GFR testing via other methods. The 62 patients who received isotope measurement of GFR had a total of 244 GFR tests with an average of 3.9 GFRs per patient (range 1 – 10). Four