Paediatric Oncology: Educational Supervision Guide for subspecialty training

RCPCH ONCOLOGY CSAC
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Paediatric Onc

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This document outlines the Educational Supervision Guide for Paediatric Sub-Specialty: Oncology to be used by PGDiTs and Supervisors.

This is Version 1.0. As the document is updated, version numbers will be changed and content changes noted in the table below.

Version number	Date issued	Summary of changes
1	**12/3/2025**	**Document created and published**

The following guide has been produced by the Paediatric Oncology College Specialty Advisory Committee (CSAC) to help support Paediatric Oncology Sub-specialty Educational Supervisors and Trainees, and guide training centres responsible for the trainees.

General guidance will be followed by sub-specialty advice, where this differs between sub-specialities.

Any questions for items within this guide should be addressed to the CSAC rep who can be contacted via the Paediatric Oncology sub-specialty CSAC web page.

Content

Introduction

This guide has been produced by the Paediatric Oncology CSAC to help support educational supervisors and trainees. It is designed specifically to apply to trainees within the sub-speciality training process, although elements will be relevant for those on SPIN training modules or general paediatric trainees with an interest in paediatric oncology.

The Children's Cancer and Leukaemia Group (CCLG) and the Paediatric Oncology Trainees Group (POTG) are the national groups through which trainees are expected to acquire further training opportunities.

Paediatric Oncology sub–specialty application process

Paediatric Oncology trainees are selected by the College Specialty Advisory Committee (CSAC) panel through a nationally competitive application process after Core Paediatrics training (usually apply the year preceding move to specialty training, at the start of ST4). Successful sub-specialty trainees may not have had significant prior paediatric oncology experience, but will have demonstrated insight, dedication and enthusiasm for the speciality as well as sufficient knowledge, ability and independent achievement to complete training successfully.

Academic trainees may be directly appointed via a university and apply for GRID equivalence via national selection (as described above) once in post.

Sub-specialty training is capability based, and programmes are typically two to three years full-time equivalent. Requests for prospective approval of up to one year of full-time equivalent training can be made to CSAC prior to application to sub-specialty. No retrospective approvals are possible. Relevant PhDs can be counted towards training with prospective approval for up to one year of training. The CSAC will also consider some time in relevant specialties in GRID approved centres. Sign off for capability progression and ultimately CCT needs to be agreed with the trainee's School of Paediatrics as well as with the Oncology CSAC.

Trainee and Educational Supervisor roles

Our trainees are encouraged by CSAC to be adaptive and innovative in their training opportunities in discussion with their local teams to achieve their curriculum capabilities, as well as seeking support early if gaps arise or are foreseen.

The role of the Educational Supervisor (ES) is to nurture and support Paediatric Oncology trainees to explore and develop the specific areas of interest within their chosen sub-speciality, whilst ensuring they are equipped with appropriate access to resources and experiences to progress through all the allied curriculum areas to a high standard and work competently as a consultant in Paediatric Oncology. The ideal model is one of longitudinal supervision, in which trainees are allocated one ES to oversee their entire sub-speciality training programme.

Less than Full Time (LTFT) trainees

Sub-specialty trainees may be LTFT and can switch to this working pattern at any stage of training following discussion with the Deanery. Trainees are now able to switch to LTFT working without providing a reason for their choice (further information on the RCPCH LTFT web pages). In general, progression through training will be pro-rata (e.g. LTFT at 60% = progression at 60%) unless separate capability-based progression arrangements have been agreed and achieved.

Please provide early information regarding weekly activities to allow selection of working days where possible. LTFT trainees working fixed days may inadvertently miss out on training opportunities such as intrathecal lists or MDT meetings. The supervisor and trainee should consider this at the initial induction meeting to allow time to address any obvious training gaps.

Return to Work

There are lots of good resources to support you on your return to work after a period of absence, including: RCPCH website.

Please take up the opportunity for 'Keep in Touch' days during any parental leave or extended time out of clinical practice. For further information see: Trainee toolkit – by trainees, for trainees and download the guide[1].

You should be allocated an educational supervisor prior to your return who can help you ease your way back. You need to meet with them 12-16 weeks prior to returning to work to allow for rota planning. HEE provides funding to support supervised return to practice where necessary, and your Trust should have a supported return to training (SuppoRRT) champion who can signpost you to this. Funding varies according to deanery. Further information can be found on the NHSE website.

Academic posts

From August 2020, nationally recruited (NIHR) Clinical Lectureships (CLs) are considered "in addition" to the training posts. These Academic Trainees are funded by the NIHR and are awarded "GRID Equivalence" at the end of their training programmes.

[1] Note: the guide is a word version will need to be saved in your local drive to view.

Out of Programme (OOP) opportunities

Trainees may take up opportunities outside their official training programme. This may include periods in research, management or education.

OOPs cannot be requested to start at the beginning of sub-specialty training. If this is required, a deferment should be requested at the time of the initial sub-specialty application. Any OOPs should commence at least six months after commencement of sub-specialty training. Please note there is a possibility that the original sub-specialty training post may not be available after an OOP, and this must be considered on application.

Most OOPs cannot be requested in the final 12 months of training prior to Certificate of Completion of Training (CCT). Up to date information on the variety of OOPs available and when/how to apply is available in the GOLD guide.

Discussion with the School of Paediatrics and local Training Programmes Director (TPD) is important when considering OOP opportunities, so that the correct OOP local policies are followed as these vary across deaneries. If a trainee/supervisor feels a future OOP has the potential to be eligible for time to count towards training, they should **contact the CSAC** to discuss suitability and the process of approval **prospectively**. The CSAC will provide comment on the suitability for time to be counted from a Paediatric Oncology perspective. General paediatric capabilities also need to be considered, and therefore advice should be sought from the relevant TPD, if resolution cannot be sourced by the trainee and their supervisor

Academic trainees cannot undertake OOP. Any additional training needs to be incorporated into their research time or discussed with CSAC and the local deanery.

Out of Programme Experience (OOPE) – You go to work somewhere in a related specialty, but this is **not** counted towards your training, but will enrich your clinical experience, so that you may experience different working practices or gain specific experience in an area of practice.

Out of Programme Training (OOPT) – An accredited training centre affiliated to the college and will count towards your training. The GMC must prospectively approve clinical training out of programme if it is to be used towards a CCT or Portfolio Pathway (formerly known as CESR) award (GMC | Out of Programme (OOP)). This could include overseas posts or posts in the UK that are not already part of a GMC approved programme in the same specialty. Further approval from the GMC is not required if the OOPT is already part of a GMC approved programme in the same specialty.

Out of Programme Research (OOPR) –Trainees should be encouraged and facilitated to undertake research where they have an interest and aptitude for doing so. Time taken out

for research purposes is for a higher degree (i.e. a PhD, MD or Master's degree) and will not normally exceed three years. OOPR exceeding three years will need the specific prospective approval of the Postgraduate Dean. Trainees in their final year of training will not be granted OOPR.

Out of Programme Career Break (OOPC) – for any experience or life event where you need time out: family illness, volunteer work, learning Japanese in an intensive training centre in the wilds of the north island etc. You cannot earn as a doctor during this period – i.e. you cannot work as a paid doctor but can be a volunteer. The loophole is that you are allowed to locum.

Out of Programme Pause (OOPP) - this is to allow trainees to continue working clinically but without the need for any of the requirements of training (except a form R at ARCP for revalidation). The OOPP has to be patient-facing and within the NHS. The key difference with OOPP is that is allows trainees to step out of formal for a period of time – currently up to one year - and have any competencies gained whilst out of training assessed upon their return. This may allow trainees to minimise the impact on the time out of programme has on their CCT date.

OOPs are in six-month blocks and are up to one year for OOPP, two years for OOPC, T and E, three years for R. You can mix and match six months OOPC and E, for example if you want to travel. However, less than six months will not generally be considered.

Your Placements/Rotations

The Deanery will usually provide you with your expected rotations for sub-specialty training, at your appointment.

Each post should consist of **no less than 70% of your weekday daytime work spent in the subspecialty (i.e. Approximately 65 days in each six-month rotation for a full-time trainee)**. If this is not the case, speak to your supervisor, and if you are still running into difficulties contact CSAC (trainee representative or training advisor).

How to calculate if your allocated rota slot has adequate sub-specialty time provision, calculation based on your working hours over a six month (20 week) working period:

1. Exclude any annual leave, study leave days, zero/off days.
2. Total all your sub-specialty hours (i.e. normal working days spent in sub-specialty). If you work a long day, with PAIID all day, and then evening ward cover i.e. = 9hr PAIID, 4hrs general [A].
3. Total all your working hours (include in and out of hours worked i.e. night 12.5-hour, long day 13-hour, normal working day 8 hour) [B].

4. [A]/[B] should be at least 0.7 i.e. 70% of working hours/training time should be spent in sub-specialty (increase from 66% to 70% from 2019 onwards).

For LTFT trainees, this is calculated pro-rata (i.e. for annual leave). If you are calculating before allocation of annual/study leave subtract the relevant number of days, you are entitled to multiplied by the number of hours in your standard working day shift (i.e. 9 hours for a 08:30 to 17:30 shift).

Sub-specialty trainees, including academic trainees, are required to look after acutely unwell children (i.e. on calls) to gain paediatric competencies, but there is no requirement for day-to-day general paediatric duties. Make the most of your on-call opportunities to sign-off paediatric capabilities.

The role of the College Specialty Advisory Group (CSAC)

The Oncology CSAC comprises the Chair, two Training Advisors, Assessment Advisor, Quality Advisor and Trainee representative. CSAC roles are responsible to the RCPCH and the overall remit of the CSAC is to ensure high quality training within the sub-specialty.

Trainees will usually contact the CSAC when they develop an interest in oncology training and can seek advice about the application process.

The CSAC has responsibility for: -

Sub-specialty interviews

- Trainees apply to sub-speciality training via a national competitive programme co-ordinated by the RCPCH. Successful candidates have insight into the specialty (but not necessarily significant clinical experience), with a commitment to oncology, excellent communication skills, and understanding of research, teaching and quality improvement. The CSAC are responsible for shortlisting candidates for interview, the interview processes itself and providing useful feedback to unsuccessful candidates.

SPIN (special interest module) applications

- Trainees may wish to undertake SPIN training. This programme provides structured training to prepare them to be primarily district general consultant paediatricians with a special interest in paediatric oncology. SPIN training in oncology does not replace sub-specialty training for a trainee who wishes to work as a tertiary oncology consultant.

Career Progression Interviews (CSAC Review)

- Sub-specialty trainees are required to have an annual review with the CSAC to review their sub-specialty training. This is in addition to, and informs, the annual ARCP review for paediatric training, which is undertaken by the Schools of Paediatrics
- The CSAC ePortfolio review includes review of the trainees' e-portfolio, supervisor reports, supervised learning events and reflective entries. Following this, a CSAC progression form is completed and uploaded to the ePortfolio.
- In addition to this, paediatric oncology trainees also complete one CSAC Career Progression Interview per WTE year of training. This involves critical appraisal of a research paper and discussion of a clinical case. In paediatric oncology, interviews are usually held prior to the annual ARCP to facilitate completion of the mandatory CSAC progression form. The arrangement is expected to be trainee-led, and paediatric oncology trainees should contact the CSAC to request an interview at the required time point.
- Further details about the CSAC Career Progression Interviews are located in Appendix 1.

ARCPS

- The ARCP is a Deanery process, managed by the local School of Paediatrics. The CSAC progressions form, and ES trainers report is part of the evidence and inform the ARCP panel.
- Individual interim meetings between trainees and the CSAC can and will be arranged if concerns about training or career progression are raised by trainee or supervisor.

Signing off for CCT

- The CSAC is guided largely by ES reports and therefore depend on the ES' thorough review of the trainee's ePortfolio. Where applicable concerns must be raised as early as possible, and information provided of any measures you/the trainee's department have made to facilitate progress.

Supporting Educational Supervisors

- Educational Supervisors are encouraged to attend the RCPCH Effective Educational Supervision course.
- Paediatric Oncology is fortunate in having a wide group of motivated educational and clinical supervisors. The CSAC are always happy to be contacted by an ES for advice on the supervision of any Paediatric Oncology trainee, or to provide general information specific to sub-specialty training if needed.

- The CSAC will arrange an annual sub–specialty ES online meeting where all sub–specialty supervisors will be invited to attend for an update.
- If you are experiencing difficulties in satisfactorily completing your ES roles in relation to support provided by your Trust (e.g. inadequate protected SPA time for trainee supervision) please contact the CSAC as soon as possible to access support to allow you to fulfil your role.

Supporting Trainees

- The CSAC will support trainees to proactively interact with their local training teams to maximise access and for the protection of paediatric oncology training activities. The CSAC also undertake an annual trainee survey for feedback on training and training centres to ensure trainees are well supported to successfully complete their sub-specialty or academic training.
- While the majority of sub-specialty trainees progress through their training without issues, there may be occasions where trainees find themselves in difficulty and are struggling to progress. This is usually identified by and managed by the trainee and supervisor. The CSAC can, however, support both the trainee and supervisor, and provide specific advice related to training. Early contact is advised in these situations.

Feedback

- We aim to seek regular (annual) feedback from our trainees regarding the training process, experience and training centres. This will be summarised in our annual update, where potential support, new initiatives and solutions can be discussed.
- Trainees are also asked to provide feedback on their training placement at the annual career progression interview. Occasionally, a concern may be raised by a trainee. If a trainee raises concern with their training, the CSAC will liaise with the ES and local deanery as appropriate to address the issue.

Key Documents

Firstly, do become familiar with the Progress+ curriculum (introduced in August 2023) structure, RISR ePortfolio (formerly known as Kaizen) navigation and training requirements (the earlier, the better) available at the weblinks below:

- RCPCH Progress+ Curriculum and Syllabi
- RCPCH Progress+ Oncology sub-specialty syllabus (2023).pdf

The Gold guide is all about your training and is incredibly useful:

- Gold Guide - 10th Edition - Conference of Postgraduate Medical Deans (copmed.org.uk)

Certificate of Completion of training:

The College pages on the CCT process are that there are non-negotiable deadlines for this process, so it is worth being organised and doing as much of it in advance as possible. If you submit after 365 days and have to submit via the Portfolio Pathway route, UK trainees are unable to be awarded anything but general paediatrics so a UK Portfolio Pathway will not have PAIID recognition attached.

- Certificate of Completion of Training (CCT) | RCPCH

For queries regarding Progress+ curriculum and syllabi, please contact:
qualityandtrainingprojects@rcpch.ac.uk

For queries regarding Progress+ ePortfolio, please contact:
training.services@rcpch.ac.uk

The role of the Supervisor

Sub-specialty trainees will have an Educational Supervisor and a Clinical Supervisor. They may or may not be the same person. The Educational Supervisor will ideally oversee their education and progress over the entire training programme. The Clinical Supervisor is the person responsible for the trainee whilst in an individual clinical placement.

Educational and Clinical Supervisors for sub-speciality trainees should be substantive paediatric oncology consultants who have received training on the supervisor role. Training can be from Trusts, postgraduate deaneries or the RCPCH.

Trainees should know to seek early contact with their supervisor and to arrange their induction meeting as close to the start of their placement as possible.

Induction Meeting

Prior to the induction meeting, trainees should ensure their educational and/or clinical supervisors are linked on RISR and can access their portfolio. Supervisors should familiarise themselves with the trainee's progress to date.

At their induction meeting with the Educational Supervisor, we encourage trainees/supervisors to:

- Review recent Paediatric Oncology progression, end of placement and Deanery ARCP reports.

- Review remaining Paediatric Oncology curriculum requirements to focus short and medium-term goals.
- Review any generic paediatric curriculum items in which the trainee may want to gain additional experience.
- Discuss logistics of how/when trainees can schedule rota time for specific curriculum requirements such as:
    - Specialist clinic attendance/observation
    - National Advisory Panel/MDT attendance
    - Opportunities for SLEs
- Discussing rotation specifics:
    - Study leave & internal opportunities
    - START plans
    - Expected CCT date, any OOP plans
    - Management & Leadership opportunities
- Discuss academic requirements: ensure that there is communication/alignment between academic supervisor and ES.
- LTFT trainees may have concerns about training opportunities on days they do not work. Where possible, this should be discussed at the outset and a plan made accounting for these challenges (for example, supervised learning events focused on specialist clinics etc).

For trainees in their **final 12 months** they should ensure that there is a focus on discussing the following areas:

- Opportunities/Inclusion in consultant meetings, consultant management activities.
- Stepping up roles and opportunities specific to that sub-speciality – where registrar activity can be replaced by 'stepping up' activity.
- Signpost to any regional/national NHS management or governance training for new NHS consultants.
- Where feasible protection of time for CCT/consultant role preparation activity, with degree of reduction in some general registrar activities as capacity allows.
- START assessment outcomes (which may take place anywhere from 12-18 months prior to CCT), detailed review of the START PDP, and opportunities for safeguarding time for any remedial/upskilling activities that may be required to address any outstanding capabilities.
- Career opportunities, consultant post opportunities and applications.
- Opportunities for additional review of portfolio three to six months in advance of final ES review and report.

Information regarding approaching a CCT can be found on the RCPCH website.

Supervisor/supervision requirements

Educational Supervisors:

ES for Paediatric Oncology trainees should have completed their Deanery specific mandated yearly training updates, following their Deanery specific initial training programme to be an ES.

It is recommended that every trainee receives a minimum of one hour a week allocated for one-to-one supervision. This protected time should be incorporated into your job plan as a sub–specialty ES as per NHSE regulations.

Any training centre approved by the Paediatric Oncology CSAC should provide the above supervision structure, but fixed sit-down sessions may not always be needed. Additional training and supervision may be achieved through discussion and support at MDTs, 15 min reviews at the end of a ward round, telephone catchups at the end of a clinic, review of clinic letters before posting, support in preparing for a clinic, joint triaging of referrals etc., and via remote activity.

Area Specific Recommendations

Tertiary oncology centres vary widely in size and specialisation, particularly given the national move towards centralisation of key services. While some centres may be able to provide trainees with adequate exposure to all key clinical areas of paediatric oncology, haematology, clinical oncology and bone marrow transplant, others may have devolved these services across networks. Paediatric oncology trainees appointed to these centres are required to spend up to 6 months working in a second centre to facilitate training and acquisition of competencies across all key areas of the curriculum. This should be planned for and discussed early in subspecialty training.

Other innovative ways of gaining exposure to areas such as clinical oncology, such as visiting other centres, linking into MDTs or clinics, or following a patient journey, should also be considered.

Annual Review of Competency Progression

The CSAC will need completed Clinical and ES reports a minimum of two weeks prior to the ARCP process to allow the CSAC enough time for reviewing progression via the CSAC progression form on the RCPCH ePortfolio. For trainees taking time out for research, the Out of Programme Research/Academic Supervision form on ePortfolio should also be completed prior to the ARCP. Preparing for your ARCP guidance can be found on the RCPCH website.

Supervised Learning Events, Workplace based assessments and curriculum tagging

There are no minimum numbers of SLEs. Trainees and supervisors should aim for quality not quantity. A useful SLE will stretch the trainee, act as a stimulus and mechanism for reflection, uncover learning needs and provide an opportunity for the trainee to receive developmental feedback. Ideally, SLEs should be completed by different consultants and other senior members of the multidisciplinary team. Mid-point and end of post reviews should allow the trainee and supervisor to review the appropriateness of tagged items and completion of required competencies.

Please review the appropriateness of tagged items and completion of the competencies during your mid-point and end of placement review with the trainee. Each SLE or ePortfolio item can only be tagged to one (max two) curriculum item. Multiple tagging will not improve the quality of their portfolio.

Examples of all SLEs can be found within the Progress+ Curriculum.

Curriculum Capabilities

At the start of their rotation, please clarify with the trainee how parts of their Paediatric Oncology rota can be protected for achieving curriculum capabilities gaining exposure in the other sub-specialist areas – e.g. clinical oncology, TYA oncology, neuro-oncology, palliative, late -effects etc. It is important for these arrangements to be flexible, considering the trainees' speciality exposure, well-being and work-life balance.

For all trainees
Cancellation of one-week blocks of registrar activity at least twice per rotation to allow trainees to organise: clinic observation/clinical oncology/TYA oncology/adult oncology/palliative care in those slots. Cancellation of clinics well in advance for mandatory and essential training specified events.

Trainees are required to demonstrate evidence of understanding and experience of laboratory tests and investigations found in the trainee's guide to CCT in Paediatric Oncology.

Link to curriculum: - https://www.rcpch.ac.uk/sites/default/files/2023-07/progressplus-oncology-syllabus-2023.pdf

Long Cases

The Paediatric Oncology CSAC requires trainees to prepare four "Long cases" per year full-time equivalent training to facilitate and evidence learning and development of complex clinical decision-making skills. The long cases should demonstrate applied learning and ideally focus on an aspect of the case where things didn't go as one may normally anticipate. This documentation will be reviewed and discussed at the annual Career Progression Interview. Long cases may be completed as word documents and uploaded to the CSAC Progression Form. It is important to ensure anonymisation of any potentially patient identifiable information.

Examples of how to format a long case may be found in Appendix 3 at the end of this document.

Courses and Conferences

Trainees will be required to attend local paediatric training days as advised by their local School of Paediatrics. They should ensure mandatory requirements are met, including life support and leadership and management training.

In addition, trainees may request study leave for oncology-specific courses and conferences.

Study Leave

Trainees are NOT required to request study leave for: sub-specialist experience, observing in specialist clinics or any other items listed within the curriculum requirements for Paediatric Oncology competencies. These activities should be arranged within the trainee's Paediatric Oncology rota.

Although not mandatory we recommend trainees are supported to attend the following:-

Core Courses and Meetings • Children's Cancer and Leukaemia Group (CCLG) Annual Meeting • Paediatric Oncology Trainee Group (POTG) Meetings • Paediatric Oncology Education and Training (POET) Education Sessions • POTG GRID Teaching Sessions • Advanced Paediatric Oncology Course (APOC), Edinburgh (biannual) • CCLG Education Days Special Interest Courses and Meetings • Society of International Paediatric Oncology (SIOP) Europe Course for Young Oncologists • International Society of Paediatric Neuro-Oncology (ISPNO) Meeting • Junior Investigators Course • European Paediatric Soft Tissue Sarcoma Study Group (EpSSG)

- Experimental Cancer Medicine Centre (ECMC)

Other useful resources include: -

- CCLG Website (protocols etc)
- Cure4Kids Website

These training days and learning points should be recorded using development logs in the RCPCH ePortfolio. The CSAC encourage reflections based on all learning events.

Optimising the learning experience in Paediatric Oncology

ES and CS can help to maximise the achievement of their trainee potential through:

1. Facilitating ease of access to experiences and resources required for their training. Optimising learning opportunities, creating a good learning environment and being creative in learning experiences.
2. Supporting the development of their interest areas where capacity allows.
3. Highlighting areas where targeted upskilling may be required and supporting personal development in these areas.
4. Overseeing sustained achievement of generic paediatric capabilities.
5. Capitalising on peer observation and feedback also including that of other health professionals and colleagues.
6. Ensuring adequate meetings with trainees to check progress and develop educational reports for CSAC reviews and ARCPs.

Research, audit and quality improvement

Trainees will be expected to undertake good clinical practice (GCP) training and keep this up to date in order to support the team in recruiting patients to national and international clinical trials and assist in data collection as part of their consultant work.

Supervisors will ensure trainees are aware of open research studies in their department and support them in participating.

Trainees will be encouraged to participate to national surveillance research, local and national audits and quality improvement projects.

Feedback

The Paediatric Oncology CSAC is committed to supporting educational and clinical supervision and Paediatric Oncology training centres to support trainees to continue to

complete their Paediatric Oncology training to an exceptional level as services continue to adapt in this time.

Therefore, if you have any suggestions, issues or think of anything you feel the CSAC can support you, other ESs, training centres or trainees with, do please reach out to any of the CSAC team.

Appendix 1: -

The Paediatric Oncology CSAC Career Progression Interview

Sub-specialty trainees are required to have an annual CSAC ePortfolio review to guide their sub-specialty training, following which a CSAC progression form is completed. This is in addition to, and informs, the annual ARCP review for paediatric training. The CSAC ePortfolio review includes review of the trainees' e-portfolio, supervisor reports, supervised learning events and reflective entries. For paediatric oncology, ePortfolio reviews are held prior to the annual ARCP.

In addition to this each trainee should have one CSAC career progression interview per year of full-time equivalent clinical training, including one prior to the final ARCP at which the CCT will be awarded. These interviews are held over Teams and are trainee led, and it is the responsibility of the trainee to contact the CSAC to request an interview at the appropriate time points. Interviews are held three times each year to correspond to the different time points at which ARCPs take place nationally.

The aim of the Paediatric Oncology CSAC Career Progression Interview is to assure the trainee, their ES and the CSAC that subspecialty training is progressing appropriately, and that the trainee is on track to attain the competencies required to work successfully as a paediatric oncology consultant. It is hoped that any issues identified may be addressed in a timely fashion, and that trainees may be supported to access opportunities to explore particular areas of interest or professional development.

The structure of the interview is as follows: -

- Critical appraisal of a research paper (30 minutes preparation followed by 10-minute discussion)
- Clinical case discussion (10 minutes)
- Career development interview and ePortfolio review (20 minutes)

Prior to the interview, members of the CSAC review panel review the trainee's ePortfolio paying particular attention to ES reports, the MSF, PDPs, reflections and sub-specialty curriculum coverage.

Paediatric Oncology subspecialty trainees are expected to collate some additional evidence on 'their ePortfolio to support their learning, which should be completed as word documents and uploaded to the CSAC Progression Form.

This should include: -

- Long cases (4 per year WTE)
- Career reflection, including summary of achievements and aspirations

Examples of how to structure this documentation may be found in the appendix. The emphasis should be on learning points, and the aim of this is to encourage reflective practice and consideration of complex decision making within paediatric oncology.

Appendix 2: -

Additional Information for Paediatric Oncology Sub-specialty Trainees

Welcome to Paediatric Oncology Sub-specialty training. We have compiled some information below which may be helpful in guiding you over the next few years.

First, if you haven't done so already, we would strongly recommend you join the Children's Cancer and Leukaemia Group (CCLG) and the Paediatric Oncology Trainees Group (POTG). The CCLG is an invaluable source of information, training and support for paediatric oncologists, and the POTG is a dedicated trainee's group within the CCLG. To join the CCLG visit cclg.org.uk, to join the POTG email POTG@cclg.org.uk

The POTG organises a yearly trainees' meeting, 3 monthly afternoon virtual teaching that maps to the GRID curriculum, and monthly peer-to-peer evening Paediatric Oncology Education and Teaching sessions (POETs). These are advertised on the CCLG website and through emails directly from the POTG. We would encourage you to volunteer to deliver at least one POET session, with support of a consultant at your centre.

Curriculum

The Progress+ Paediatric Oncology Sub-specialty curriculum can be found on the RCPCH website (https://www.rcpch.ac.uk/resources/paediatric-oncology-sub-specialty). This is a more detailed mapping to the 4 broad learning outcomes within your ePortfolio.

CSAC reviews/Paediatric Oncology CSAC Career Progression Interviews

The CSAC is responsible for assessing your progress throughout subspecialty training. CSAC reviews of the ePortfolio take place annually, prior to each ARCP, following which a CSAC progression form is completed.

In addition to this, the CSAC conduct one Career Progression Interview per year of full-time equivalent training. The aim of the Paediatric Oncology CSAC Career Progression Interview is to assure you, your ES and the CSAC that subspecialty training is progressing appropriately and that you are on track to attain the capabilities required to work successfully as a paediatric oncology consultant. It is hoped that any issues identified may be addressed in a timely fashion, and that the CSAC may support you to access opportunities to explore particular areas of interest or professional development.

As everyone has a different training journey (e.g. with options for career breaks, OOP, Academic and LTFT training), arranging CSAC ePortfolio reviews and interviews is trainee-led. Each trainee is responsible for arranging one CSAC ePortfolio review prior to each ARCP, and one CSAC Career Progression Interview per year of full-time equivalent training. Please contact the CSAC Chair (currently Sara Stoneham – sara.stoneham@nhs.net) to arrange these.

If, for any reason, your CSAC reviews fall out of line with your Deanery's ARCP, we would be happy to complete the CSAC Progression form required by the Deanery following review of your ePortfolio and ES Trainer's report. In these cases, again please contact the CSAC Chair with at least two months' notice to advise us of your requirements.

Information on what to expect from a CSAC Progression Interview can be found in Appendix 1 of this document.

CSAC interviews can feel daunting but please remember the aim is to ensure that each trainee is managing to access appropriate learning and is feeling supported to gain the experience needed to function as a safe and effective paediatric oncology consultant. It can be difficult to know if you're on track to acquiring all the new additional skills and knowledge required, despite your best efforts and all the hard work you put in.

Evidencing your learning

In addition to using the ePortfolio, you may find it helpful to keep a logbook of cases and learning points from each. A few of these cases can then be used for the four "Long cases" that you are required to prepare for the CSAC review (details in Appendix 1). The long cases should demonstrate applied learning and ideally focus on an aspect of the case where

things didn't go as one may normally anticipate. Long cases may be completed as word documents and uploaded to the CSAC Progression Form. Examples of these may be found in Appendix 3 of this document.

We recommend you arrange to meet with your educational supervisor as soon as you can. Your ES will be able to help you understand the interplay between your overall paediatric training and your specialism in paediatric oncology. Training time can go by very fast, so it is best to set realistic goals to enable you to focus your learning to enable you to get the most out of your sub-specialty training.

Mentorship

You may have benefitted from the POTG mentorship scheme prior to attaining your sub-specialty training position, you are still able to gain further mentorship from more senior trainees or consultants. Please also consider becoming a mentor to new prospective sub-specialty trainees with the next call for mentees/mentors, as your help would be invaluable.

We wish you the best of luck and will be there to support you through your sub-specialty training.

Best wishes,

The CSAC Team and the POTG

Appendix 3

Long case examples

Long Case 1: A 16-year-old with delayed diagnosis of BCOR Sarcoma

Case history

A 16-year-old girl presented to her local with a 2–3-week history of left sided lower abdominal painless swelling. She had not told her parents about this as she had been

focussed on preparing for her GCSEs. An MRI on 17th June 2023 demonstrated a large left retroperitoneal mass arising from/involving the left psoas muscle and extending inferiorly into the groin. She was referred to our tertiary oncology centre and underwent an ultrasound guided biopsy of the mass. On 20th June, histology was in keeping with a soft tissue sarcoma arising from the left psoas (non-Ewings, non-rhabdomyosarcoma). She underwent full staging (which confirmed localised disease) as follows:
CT chest – several small subpleural nodules bilaterally, favoured to represent benign intrapulmonary lymph nodes
PET-CT – large moderately FDG avid soft tissue sarcoma centred on the left iliopsoas. No metastatic FDG avid disease but small scattered pulmonary nodules seen.
Bone marrow aspirates/trephines – no malignancy

Whilst molecular testing to further characterise the tumour was awaited, the mass lesion appeared to increase in size. She underwent another MRI, 2 weeks after initial MRI which demonstrated an interval increase in the size of the abdominal mass (40% volume increase). No metastatic disease. MDT discussion took place about potential local vs systemic therapy options. Decision was made to commence chemotherapy as per the EpSSG NRSTS strategy with doxorubicin and ifosfamide.

Diagnostic and Management challenges

Unfortunately, initial biopsy was insufficient for molecular profiling. Given clinical evidence of progression the MDT decision was to proceed with chemotherapy, following the EpSSG 2005 NRSTS strategy, which commenced on 5th July. A repeat biopsy was performed on 10th August. With regards to local therapy, given the size and location of the tumour, it was deemed unamenable to total surgical resection at diagnosis. Even marginal resection would pose a challenge therefore surgery would likely involve debulking only. Radiotherapy was discussed as a definitive therapy and also as a neoadjuvant therapy before or after surgery. Late effects of radiotherapy were discussed – muscle fibrosis, hip joint stiffness, osteopenia and increased risk of pelvic fracture, persistent bladder symptoms, bowel adhesions, infertility, complications in pregnancy and 2nd cancers.
Reassessment after 3 cycles (MRI and PET-CT) demonstrated a partial response to chemotherapy. MDT local therapy decision as to proceed with preoperative radiotherapy and surgical resection, given that highest chance of cure would be achieved through this multimodality strategy (accepting R1 macroscopic resection). She was referred for proton beam radiotherapy to limit long term toxicity to surrounding tissues and received 6 weeks (50.4Gy).
Eventually molecular profiling results were available, reported by Manchester as consistent with BCOR sarcoma (BCR: CCNB3 fusion) on 25th October. She had received 5 cycles of Ifosfamide and Doxorubicin. In view of this, the chemotherapy regimen was amended to 2 weekly VC/IE during concurrent radiotherapy (4 more cycles).

Discussion: Diagnostic uncertainty and BCOR Sarcoma

The first point of discussion with this case is around the diagnostic delay. Lack of molecular characterisation meant that treatment decisions had to made on best available diagnostic information. This was a collaborative approach involving the oncology MDT – radiology, medical and clinical oncology, pathology and surgery. It was deemed a high-grade lesion therefore the optimal local strategy was sought with both radiotherapy and surgery. This uncertainty led to much anxiety for the family. We attempted to support them as best as possible with clear and comprehensive communication, explaining the rationale behind all decisions made. We involved psychology and the family had regular input from our nurse specialist and support worker team.

This patient had a tumour classified as an undifferentiated round cell sarcoma characterised by BCOR::CCNB3 rearrangement. Previously known as Ewing-like sarcoma, these tumours are currently distinguished from Ewing sarcoma in the current WHO classification. The BCOR: CCNB3 gene fusion is defined by molecular assay (transcript identification) or CCNB3 immunohistochemistry. Rare BCOR sarcoma was described in a group of small round cell bone tumours lacking the EWSR1 translocation (4 *BCOR::CCNB3* positive tumours could be identified in an analysis of 594 sarcoma patients).[i] It accounts for 4% of undifferentiated round cell sarcomas. Commonest sites of presentation include bone (mostly long bones), soft tissues and viscera (e.g. kidney). Both CCNB3 and BCOR::CCNB3 as a full fusion transcript play a role in oncogenesis and phenotype.[ii] Treatment strategy is recommended as per Ewings sarcoma with multiagent chemotherapy, surgery +/- radiotherapy.
A retrospective multicentre study from France was conducted which assessed the clinical, radiological and pathological presentation, treatment and outcome of 26 patients with Ewing-like sarcoma harbouring *BCOR-CCNB3* gene fusion transcript. Patients diagnosed between 1994 and 2012 were included and median age was 3 years. 24/26 had localised tumours. Most patient received chemotherapy (15/26 on Ewings protocols). 46% patients received both surgery and radiotherapy. The study concluded that relapses (local and metastatic) were of poor prognosis, and induction chemotherapy and treatment according to an Ewing protocol might influence survival in patients with localised tumours. Five-year overall survival and disease-free survival were 76.5% (95% CI, 58%–95%) and 67.9% (95% CI, 48%–88%).[iii]

This patient received a very much individualised treatment regimen in view of initial diagnostic uncertainty and change in chemotherapy following molecular diagnostic confirmation. It is unclear what effect this will have on overall prognosis given the challenges to adequate local control. The chemosensitivity of BCOR::CCNB3 tumours advocates use of polychemotherapy associated with best local control, hence pursuing both radiotherapy and surgical treatment. Her surgery will be undertaken jointly by the paediatric surgical team and adult retroperitoneal sarcoma surgeon, hence advocating for preoperative radiotherapy in keeping with adult practice. There is a challenge in paediatric

oncology to define the optimal therapeutic strategies in such patients given their rarity, and barriers to conducting clinical trials in such small patient groups.

[i] Pierron G, Tirode F, Lucchesi C, et al. A new subtype of bone sarcoma defined by BCOR-CCNB3 gene fusion. *Nat Genet*. 2012; **44**(4): 461-466.

[ii] Kösemehmetoğlu K. BCOR::CCNB3 sarcoma. PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/boneBCORCCNB3.html. Accessed January 2nd, 2024.

[iii] Cohen-Gogo et al. Ewing-like sarcomas with BCOR-CCNB3 fusion transcript: A clinical, radiological and pathological retrospective study from the Societe Francaise des Cancers de L'Enfant. Pediatr Blood Cancer. 2014; 61(12); 2191-2198.

Long Case 2: Metastatic Wilms Tumour Complicated by IVC and Right Atrial Tumour Thrombus

Presentation

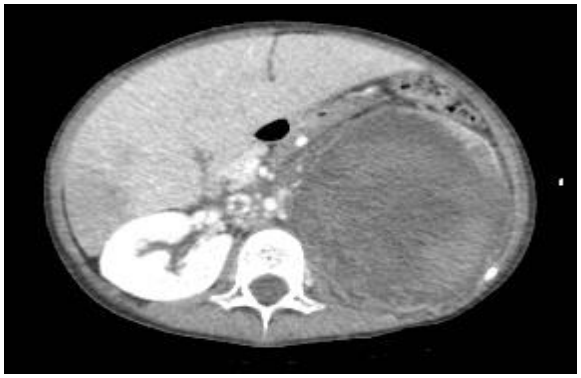
FD presented to her local hospital at 6 years of age with a four-day history of lethargy, reduced appetite and left sided abdominal pain. On examination, she was found to have a large left sided abdominal mass extending 8.5cm below the costal margin that was firm and non-tender, and hepatomegaly (2cm below the costal margin). Systemic examination was otherwise unremarkable.

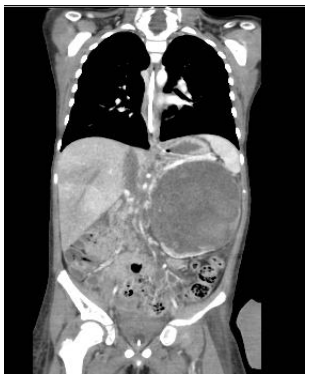
Abdominal ultrasound revealed appearances suggestive of a left renal tumour with extension into the inferior vena cava and right atrium, with risk of AV valve orifice occlusion. The most likely differential diagnosis at this stage was Wilms Tumour (nephroblastoma). She was subsequently transferred to our Primary Treatment Centre for further investigation and definitive management.

Upon arrival, FD developed an oxygen requirement and had a palpable left flank mass. Urgent CT chest, abdomen and pelvis demonstrated a left renal tumour extending into the IVC and filling the right atrium. There was possible para-aortic lymphadenopathy/medial tumour rupture surrounding the aorta. The tumour/thrombus extended into the right renal vein and also into the IVC below the level of the renal veins. Lung metastases were also seen. An echocardiogram revealed extensive tumour thrombus extending into right atrium,

partially obstructing AV valve, indicating the child was at risk of pulmonary embolism and sudden cardiac event.

Fig.1. CT chest, abdomen and pelvis





Diagnosis: Metastatic Wilms Tumour (Stage IV)

Management

FD was treated on the UMBRELLA Protocol SIOP-RTSG 2016, with pre-operative chemotherapy with AVD, followed by surgery, and risk adapted chemotherapy and radiotherapy.

Her parents were counselled appropriately and informed of the significant risk of fatal cardiac decompensation with general anesthetic. In view of this, a peripherally inserted long line (PICC line) was inserted to allow administration of chemotherapy. FD developed significant haematuria and was catheterized for 3 weeks in view of this. She also required supportive nutritional care in view of poor oral intake and vomiting and received 5 weeks of TPN prior to establishment of NG feeds.

Treatment guidelines for metastatic Wilms Tumours (stage IV)

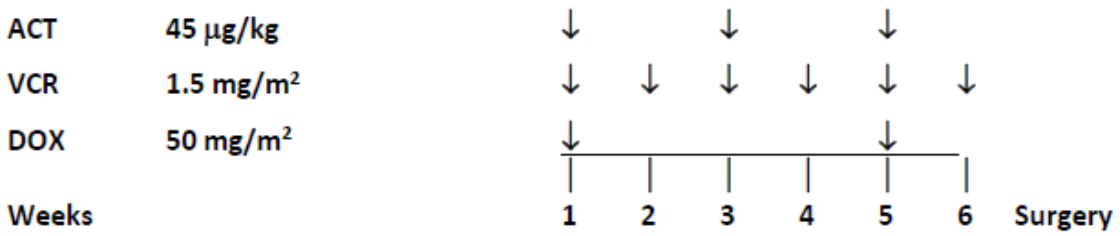
Preoperative AVD

All Stage IV with lung nodules >2 mm

Three drugs (vincristine (VCR), actinomycin D (ACT) and doxorubicin) x 6 weeks

- • Vincristine: 1.5 mg/m2 (max 2 mg) weeks 1, 2, 3, 4, 5, 6
- • Actinomycin D: 45 µg/kg (max 2 mg) weeks 1, 3, 5
- • Doxorubicin: 50 mg/m2 weeks 1, 5

Vincristine and actinomycin D are given by intravenous bolus, doxorubicin as a 4–6-hour infusion



FD developed liver dysfunction with deranged ALT prior to commencement of chemotherapy. As actinomycin can cause veno-occulsive disease (VOD) it was decided to substitute this for Adriamycin until her liver function returned to normal, which it did by week 3. She was treated with an additional two weeks (weeks 7 and 8) of vincristine as it was not possible to time her complex surgery to coincide with completion of week 6 pre-operative chemotherapy.

Surgery

Planned surgical resection of the primary tumour was undertaken on week 9.

Histopathology revealed a large (>500ml) partly encapsulated tumour which was completely necrotic /haemorrhagic (90% necrotic/haemorrhagic) with approximately 10% chemotherapy related regressive changes. Excision appeared to be complete, and there was no viable tumour within the main renal mass. Regressive change was seen in the sinus. Chemotherapy induced change was seen in one hilar lymph node asserting this as a Stage 3 tumour. According to the UMBRELLA protocol, the presence of mature tubules is not considered as evidence of viable tumour. The tumour was therefore determined to be **completely necrotic low risk, stage 3** (UMBRELLA).

The tumour thrombi in the retrohepatic, right atrium and infrarenal all showed complete chemotherapy induced change with only a single mature tubule seen. It was noted that given the tumour was completely necrotic, and there was no previous biopsy, it could not with certainty be confirmed that this was a Wilms tumour, especially in the absence of nephrogenic rests. However, with complete necrosis it was generally accepted that no other tumour would respond so well to Wilms' Tumour preoperative chemotherapy.

DIAGNOSTIC SUMMARY (Left kidney):
- Presumed Wilms tumour (>500ml volume)
- Completely necrotic low risk histology
- Stage 3 due to chemotherapy induced change in hilar lymph nodes
- Chemotherapy induced change in tumour thrombi in retrohepatic, right atrium and infrarenal, no viable tumour
- Total of 1/10 lymph nodes showing chemotherapy induced change

Post-operative treatment

After surgery, the different histological subtypes and local stage of the tumour can be determined. Combined with tumour volume, these prognostic factors dictate post-operative treatment. In this SIOP protocol, tumour volume has been added as a risk stratification factor for a subgroup of Wilms tumours. ***Patients with a tumour volume of > 500 ml after preoperative chemotherapy and non-stromal or non-epithelial intermediate risk histology and local stage II or III are treated more intensively with AVD.*** This decision is based on analyses of patients from SIOP 2001, which demonstrated tumour volume to be a significant risk factor. Patients with a high tumour volume had a significantly poorer outcome if randomized to only AV compared with AVD. For patients with stage I intermediate risk or any stage with epithelial and stromal subtype, large tumour volume (500 ml) after pre-operative chemotherapy did not significantly affect the outcome.

		Tumour volume after preoperative chemotherapy	**Stage I**	**Stage II**	**Stage III**
Low Risk (only CN)		All	No further treatment	AV2	AV2
Intermediate Risk		≤ 500 ml	AV1	AV2	AV2 + RT
Intermediate Risk*		> 500 ml	AV1	AVD	AVD + RT
High Risk	**BT**	All	AVD	HR-1	HR-1 + RT
	DA	All	AVD	HR-1 + flank RT	HR-1 + RT

*Table 15.2.1: Overview of postoperative treatment. (*with the exception of stromal and epithelial type, they are always treated independent of tumour size: AV1 in stage I and AV2 in stage II and III); CN: completely necrotic; A= actinomycin D, V= vincristine, D =doxorubicin (cumulative dose 250 mg/m²), HR = high risk histology; BT: blastemal type; DA: diffuse anaplasia; RT: radiotherapy; Note that for Stage 1 tumours with low risk histology, no postoperative chemotherapy is given. All tumours in this category should be send for urgent pathological central review (< 2 weeks for result))*

It was difficult to stage FD in accordance with the table above. It could be argued that she had Stage III low risk disease in view of the complete necrosis in the tumour and should therefore only receive AV2 postoperatively. It must be remembered, however, that this child had received additional preoperative chemotherapy which may have increased the percentage of necrosis in the tumour. If she had conversely had Stage 3 Intermediate Risk disease, with a tumour volume after preoperative chemotherapy of >500 ml, she would be recommended to receive AVD and whole abdominal RT, with lung radiotherapy in view of her persistent unresectable pulmonary metastases.

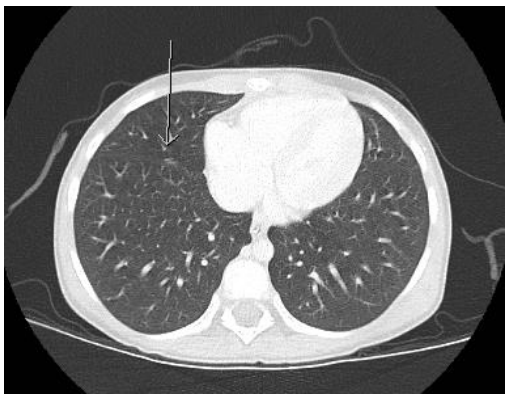
Ongoing management of an unusual case

As discussed above, due to the problems with FD's high risk for surgery, surgery took place after 8-9 weeks and she received extra chemotherapy. She was also noted to have a 4mm pulmonary metastasis. Her tumor showed 100% necrosis, but the additional pre-operative chemotherapy which could potentially affect her post-operative staging. Her consultant and her parents were concerned about the late effects of whole abdominal radiotherapy and discussions were initiated about whether this could be omitted in view of the excellent chemotherapeutic response demonstrated by the tumor. In view of the challenging decision-making, it was decided to discuss the case in the local MDT with a view to taking it further to national panel for advice on radiotherapy.

An MDT decision was made that FD should be discussed by the renal panel, and that she should continue her current regime of chemotherapy with formally reassessment after ten weeks of post-operative treatment (AVD as per the UMBRELLA protocol). A decision regarding the lung metastasis would be made at the end of treatment if it was still present and in accordance with any management plan agreed by the renal panel. Resection of the metastasis could be considered, as could pulmonary irradiation plus abdominal/flank radiotherapy following discussion with the National Panel.

Reassessment imaging following 10 weeks of AVD

Fig 2. CT chest



Chest CT with contrast was performed to reassess the pulmonary metastatic disease at 10 weeks post nephrectomy. Any node >3 mm would need consideration for resection.

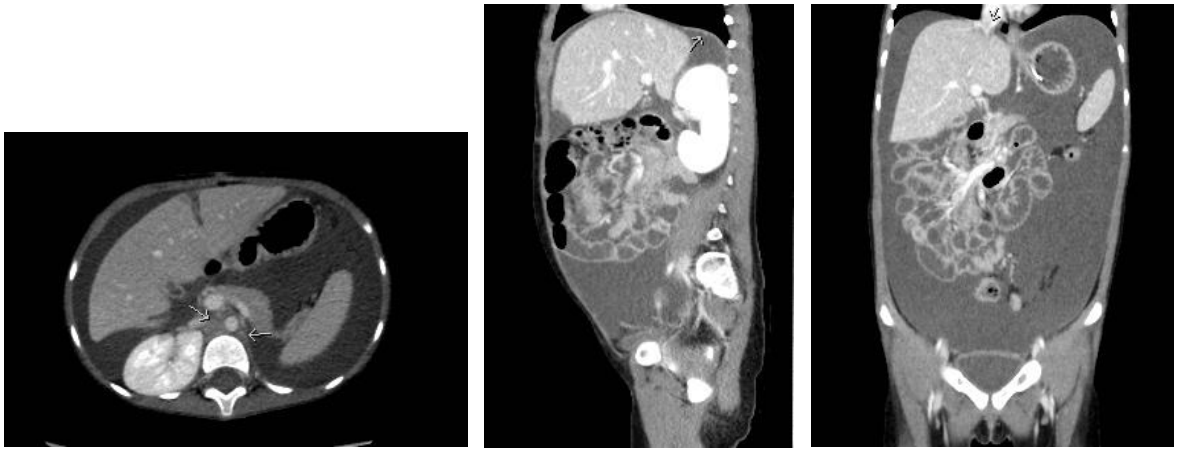
Within the right middle lobe abutting the oblique fissure the previously reported largest nodule was again noted. The size of the nodule measured approximately 5 mm (previously 5 mm), but as appearances were slightly blurred due to the respiratory artefact an accurate size could not be reported. The lungs and pleural

effusions were otherwise clear with no new focal lesions seen. Moderate ascites was noted within the imaged upper abdomen.

Development of ascites

Following 5 weeks of treatment with AVD, FD developed clinically apparent ascites. Differential diagnoses included malignant ascites or VOD. She was not clinically jaundiced and FBC and LFTs were unremarkable. CT imaging was carried out urgently to assess the ascites.

Fig.3. CT abdomen and pelvis



A large volume of ascites was seen in the abdomen and pelvis. There was mild thickening and enhancement of the peritoneum within the pelvis and adjacent to the left hemidiaphragm. The liver was normal in appearance, and the portal and main hepatic veins were patent. There was normal homogeneous enhancement of the liver parenchyma, with no masses identified, and the caudate lobe was normal in appearance. There was no evidence of tumor recurrence in the left renal bed, and no new masses were seen. There was some soft tissue thickening seen around the abdominal aorta, but no discrete significant lymphadenopathy.

In summary, the aetiology of ascites was unclear. Injury to the lymphatic system was a possibility. Although peritoneal disease was thought unlikely so soon surgery, it was felt this should be excluded and ascitic tap performed.

Chylous ascites

Ascitic tap revealed no evidence of malignancy, confirming a diagnosis of chylous ascites. An abdominal drain was inserted and TPN commenced. Following 3 weeks of supportive care, ultrasound showed evidence of improvement. An MCT diet was

commenced for 6 weeks, following which the ascites clinically resolved, and a normal diet was recommenced uneventfully.

Reassessment imaging following 10 weeks of AVD

FD underwent further imaging following 10 weeks of AVD to assess disease response and resolution of ascites. CT showed no new metastases in the lungs. The pulmonary metastasis previously seen, which had measured 6.6mm at the start of treatment, had reduced to 4mm. The UMBRELLA protocol determined that if pulmonary metastases had resolved by week 10 of chemotherapy, whole lung radiotherapy would not be indicated.

This case was unusual in that FD did not receive the normal chemotherapy regimen, and that although histology suggested low-risk disease, her clinical course was not typical of that of a low-risk patient. In view of this, it was decided to seek further advice from the national panel regarding the indication for whole lung radiotherapy.

The decision at the NRAP MDT was that FD should not receive whole lung radiotherapy given the small volume of disease in the lung which had almost resolved. It was also recommended to omit abdominal radiotherapy in view of the complete necrosis demonstrated by the tumor. Her parents were happy with this decision and were made aware that it could be an option if needed in the future. She is currently well.

Learning points

- The management of cases following an unusual clinical course through incorporating necessary adaptations to established treatment protocols (e.g. substituting Adriamycin for actinomycin given the increased risk of VOD in the presence of hepatic dysfunction)
- The UMBRELLA protocol, and the use of prognostic factors for determining post-operative chemotherapy and radiotherapy
- Indications for lung radiotherapy in the context of pulmonary metastases
- The importance for discussion of unusual cases at national MDT, particularly when there has been significant deviation from the original treatment protocol

CSAC Case 3: Extramedullary spinal Ewing sarcoma with catastrophic spinal injury

Introduction

Emergency presentation is frequent in extramedullary tumours and acute surgery is often necessary. Spinal Ewing sarcomas are often diagnosed in an emergency, in the face of severe clinical deterioration. There is a key role for surgery in obtaining biopsy and protecting the spinal cord by reasonable decompression. Here I describe a challenging case of extramedullary soft tissue Ewing Sarcoma – the initial presentation and complex multidisciplinary management.

Case history and management

A 3-year-old girl presented to her local hospital following a 1-week history of being generally unwell then acute flaccid paralysis. She was taken for MRI and had a cardiac arrest in the scanner. She was resuscitated and ventilated. The MRI showed an extensive C2-T4 extradural haemorrhagic tumour with foraminal extension, and she was transferred under the Neurosurgical team for C3-T5 laminectomy and tumour debulking the same day. There was residual disease at C3-T1 neural foramina. The histology was positive for CD99 positive, INI1 retained small round blue cell tumour. Molecular testing detected a EWSR1::FLI1 fusion consistent with a diagnosis of Ewing sarcoma. She underwent full staging including bone marrow aspirate and trephines, bone scan, whole body MRI and CT chest with no evidence of metastatic disease.

Following her acute presentation she remained ventilator dependant and tetraplegic. There were conversations led by the PICU team around the implications of her high spinal cord injury on quality of life and questions raised around whether treating her cancer was in her best interests. Parents were counselled around the fact that she was unlikely to make a neurological recovery despite cancer treatment however with localised disease, she could be treated with curative intent. Parents were very clear that if she were able to communicate and express her needs, they wished to pursue treatment. There were discussions around possible tracheostomy, but the oncology team had mixed opinion on delaying treatment further. Therefore she started chemotherapy as per the EuroEwings 2012 Arm B strategy, with intensive VDC/IE chemotherapy. She was having frequent bradycardias with some requiring CPR, felt similar to neurogenic shock and a pacemaker was considered, but it was felt further surgeries were not appropriate. Additionally, having a pacemaker would complicate oncological

surveillance as she would not be able to access MRI. Over a few weeks these episodes settled, however she developed intermittent episodes of bradycardia, possibly related to autonomic dysreflexia.
Her first cycle of chemotherapy was complicated by systemic fungal infection, neurosurgical wound breakdown and mucositis; however she recovered and continues on chemotherapy in PICU. She remains ventilated, now via tracheostomy, and has an indwelling catheter. She is under the joint care of several teams - PICU, oncology, neurosurgery, urology, and neurorehabilitation team including physiotherapy, play specialists, and dietetics. She has several comorbidities which make her more susceptible to side effects of chemotherapy, mainly her neurological sequalae, respiratory sequalae and vascular instability. She will likely need some radiotherapy after her systemic chemotherapy.

Discussion

There are a few aspects of this case that I wish to reflect on: 1) optimising local therapy in the case of residual disease, 2) the role of high dose chemotherapy and stem cell rescue, and 3) the ethical challenges posed in managing this patient.

It is well understood that local treatment (surgery and/or radiotherapy) is an essential part of curative therapy. Most patients will already have micro-metastatic disease at time of diagnosis. Prior to the 1970s, outcomes were poor when treatments were targeted at only the primary disease site. This was dramatically improved by the introduction of multi-agent chemotherapy. A multimodal approach according to the EuroEwings strategy is now our standard of care, using pre-operative induction chemotherapy, followed by definitive local therapy, and postoperative adjuvant therapy. Rationale for this includes: early treatment of micrometastases, facilitation of subsequent local therapy due to tumour shrinkage and decreased vascularity, and evaluation of tumour response to induction chemotherapy.

Radiosensitivity of Ewing sarcoma was first recognised in 1921 by James Ewing, and plays a major role in local therapy, however it is not the local treatment of first choice. Primary surgery is preferable to irradiation given the survival advantage incurred, and indicated for lesions in expendable bones, pathological fractures, distal extremity sites, bulky primary tumours and in patients with poor response to initial chemotherapy. Pre-operative radiotherapy may be indicated for situations such as tumour progression during chemotherapy, in emergencies such as spinal

cord compression or when incomplete surgery is anticipated. Postoperative radiotherapy is indicated in this clinical case, in view of incomplete surgical resection, or in cases where there are positive surgical margins or poor histological response to induction chemotherapy. Doses vary between 45 and 55.8 Gy. A retrospective analysis of the effect of different radiotherapy doses on event free and overall survival in Ewing sarcoma patients (Ewing 2008 database) found that definitive radiotherapy with higher doses >59Gy were associated with better EFS.[iii] Non radical margins were an independent risk factor for worse prognosis in the combined surgery and radiotherapy group. However, given the retrospective nature of the analysis, there were selection biases for dose indications found, and therefore future studies should assess radiotherapy dose in a randomised setting. A systematic review of primary intradural extramedullary Ewing sarcoma cases concluded that whilst surgery is the mainstay of treatment, tumour recurrence is a significant concern due to the adhesive nature of the disease precluding complete resection, and therefore adjuvant radiotherapy should be considered to improve overall outcome.[iii]

The role of high dose therapy with autologous haematopoietic stem cell rescue (HDCT ASCT) in certain risk groups is controversial and was investigated in the EuroEwings trial. The rationale is that HDCT will overcome prior chemotherapy resistance of tumour cells. Randomization between busulfan and melphalan (BuMel) or standard chemotherapy (vincristine, dactinomycin, and ifosfamide [VAI], seven courses) was offered to patients if they were younger than 50 years of age with poor histologic response (≥ 10% viable cells) after receiving vincristine, ifosfamide, doxorubicin, and etoposide (six courses); or had a tumour volume at diagnosis ≥ 200 mL if unresected, or initially resected, or resected after radiotherapy. In an intent-to-treat analysis, the risk of event was significantly decreased by BuMel compared with VAI: 3 and 8-year EFS were, respectively, 69.0% versus 56.7%, and 60.7% versus 47.1%. Overall survival (OS) also favoured BuMel. The results suggested that a subgroup of patients with high-risk localised disease would benefit from BuMel and autologous stem cell rescue, however these results were confined to patients who received this therapy after vincristine, ifosfamide, doxorubicin, and etoposide induction. Thus the relative benefit of HDCT ASCT is still controversial. This treatment is associated with severe toxicity and adverse effects, including mucositis, metabolic problems, and long-lasting bone marrow aplasia, with the risk of life-threatening veno-occlusive disease, bleeding and infection. Hence it was not considered as an appropriate option in our case, in view of the lack of evidence for its use following VDC/IE chemotherapy, and our patients'

numerous comorbidities which would put her at significant risk from this treatment.

This case posed ethical challenges in initial management as there were conflicting views across the multidisciplinary teams as to what was in the patients' 'best interests'. She has been left tetraplegic and ventilator dependant due to the spinal cord injury inflicted by her tumour. In spite of this and a poor neurological outcome, once histology confirmed the diagnosis and staging was complete, it was felt that oncologically, her disease could be treated with curative intent. Parents were very clear that as she is able to communicate and express her needs, they wish to pursue treatment as they feel they can provide her a good quality of life. In order to facilitate her treatment, she continues to reside in the paediatric intensive care department and in need of maximal supportive care. Given the number of professionals involved in her care, there is a real need for comprehensive communication and joined up working to ensure her needs are adequately met and teams are working towards the same goals and understanding of her clinical condition and tolerance of treatment. In such a case, I find the following RCPCH document very useful: "Making decisions to limit treatment in life-limiting and life-threatening conditions in children: a framework for practice".[iii]

It highlights the importance of considering:

- The likely quality of future life for the child with and without treatment.
- The intolerability of treatment or outcome.
- The relevant clinical considerations.
- The pain or suffering caused by the treatment.
- The pleasure a child may derive from its current life including the child's awareness.

Long Case 4: Primary refractory Acute Myeloid Leukaemia

Case history

A 10-year-old boy presented with a 5–6-week history of feeling unwell with intermittent fevers, night sweats, lethargy and weight loss. He had attended the GP several times and received a course of amoxicillin for otitis media and penicillin V for tonsillitis. Throat swab grew streptococcus. In view of ongoing fevers, he had blood tests which showed pancytopenia and blood film demonstrated myeloid blasts. Peripheral flow cytometry showed 65% blasts, CD117+, CD33 weak+, CD34 weak+, CD13 weak+, CD19 neg, MPO neg. Bone marrow aspirate demonstrated 45% myeloid blasts which were CD117+, DR+, CD34+, MPO – consistent with acute myeloid leukaemia (AML). CNS1 status. FISH showed no evidence of CBFB, KMT2A

(MLL) or RUNX1::RUNX1T1 rearrangement. An additional copy of KMT2A was observed of unclear significance. Thus consistent with intermediate risk cytogenetics. He was treated as per the Myechild01 protocol with mitoxantrone, cytarabine and one dose of gemtuzumab ozogamicin. Unfortunately end of cycle 1 reassessment showed 90% blasts on bone marrow aspirate by morphology consistent with primary refractory disease and he was allocated to the high-risk arm of Myechild and received a course of FLA-Ida (fludarabine, cytarabine, idarubicin with cardioxane). His treatment course has been complicated by systemic fungal infection, poor nutritional status and psychosocial challenges. End of FLA-IDA reassessment demonstrated residual disease of 15-30% by flow/morphology therefore refractory disease following two standard escalated induction courses. He was discussed at the local and National leukaemia and HSCT MDT with the recommendation to proceed with venetoclax-azacitadine in attempt to control disease as a bridge a T-cell replete cord transplant.

Discussion

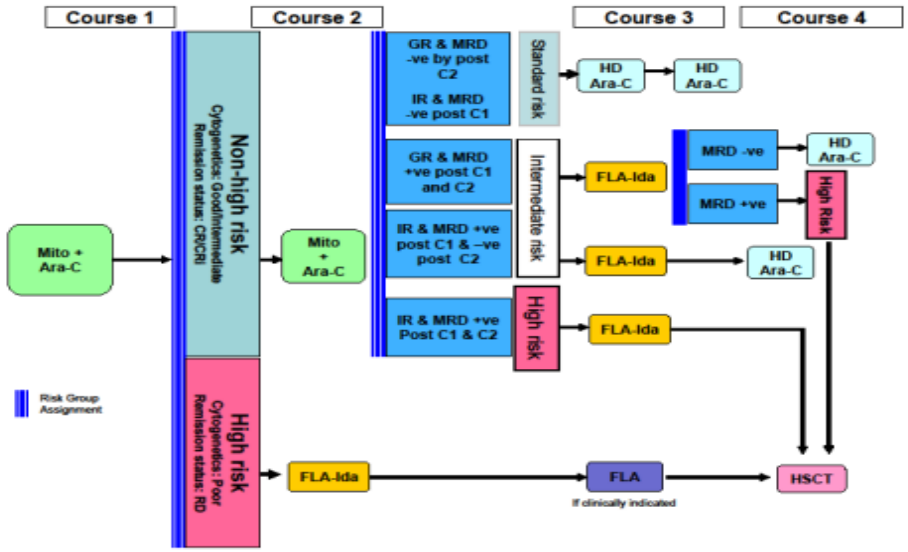
I wanted to use this case as an opportunity to reflect on the therapeutic strategy in AML and current evidence for treatments in the refractory/relapse setting including bone marrow transplant.

Primary treatment and the Myechild01 study

The Myechild01 study is now closed to recruitment but was an international randomised phase III clinical trial in children with AML. The trial aimed to test strategies in both induction and consolidation for value in improving survival without significant increase in toxicity, with 4 randomisations and incorporating an embedded dose finding study of gemtuzumab ozogamicin in combination with induction chemotherapy. Gemtuzumab ozogamicin is an anti-CD33 antibody linked to the anti-tumour antibiotic calicheamicin. After internalisation and intracellular release, gemtuzumab ozogamicin delivery is targeted to CD33–expressing leukaemia cells. More than 80% of cases of AML express CD33. Cardiac myocytes do not express CD33 therefore gemtuzumab ozogamicin may enable treatment intensification without increasing cardiotoxicity. The study investigated the maximum number of doses (up to 3) of gemtuzumab ozogamicin which can safely be combined with the intensive induction chemotherapy

There was an initial randomisation comparing 2 induction regimens (mitoxantrone and cytarabine vs liposomal daunorubicin and cytarabine) for efficacy and toxicity however this closed early due to manufacturing issues with liposomal daunorubicin. The 3rd randomisation compared the current standard UK and French consolidation of high dose cytarabine (HD Ara-C) with fludarabine and cytarabine (FLA) in patients with good and intermediate risk cytogenetics who become MRD negative early in treatment. FLA is an effective non-anthracycline

containing regimen used in relapsed AML which might be considered more treatment-resistant, therefore may have greater efficacy than HD AraC as consolidation in children with newly diagnosed AML. The 4th randomisation compared standard myeloablative transplant conditioning (busulphan/cyclophosphamide) against a reduced intensity conditioning (fludarabine/busulfan) in an effort to maintain outcomes with reduced toxicity/transplant related mortality. The results of Myechild01 study are awaited however the current standard of care schema is shown below.



Treatment is risk based according to cytogenetic/molecular characteristics at presentation and response to treatment assessed by morphology and by flow minimal residual disease (MRD) or molecular transcript levels after each course. Between 10-15% of children will either not have a marker, or not have a marker of sufficient sensitivity, for flow monitoring. These patients should be monitored by a molecular marker, if an informative molecular marker is present. Patients with neither a flow nor a molecular marker should have their treatment assigned by cytogenetic/molecular genetic risk group. The MRD discriminatory level for flow monitoring will be 0.1% and for molecular monitoring a transcript level reduction of 3 logs. Definition of 'CR' by flow, molecular or FISH is a level <5%.

Refractory disease management

Targeted agents

Despite improvements in survival rates for children with de novo AML, relapse still occurs in more than 30% of patients. Despite numerous clinical studies, outcomes for relapsed/refractory AML have been consistently disappointing with 5-year

overall survival rates of 35 ± 2%. Poor prognostic factors in this case include lack of first remission and poor response to reinduction therapy.

Allogeneic haematopoietic cell transplantation (HCT) at the time of second complete remission remains the only reliable option with curative potential. However, recent approval of several new agents has transformed treatment paradigms that had been in place for almost half a century in AML.[iii] Given the biological complexity and differences in frontline treatments, there are therapies approved for only subgroups of R/R AML. Therapeutic approaches, including allogeneic HCT, triggered by the presence of MRD, have recently evolved to prevent overt haematologic relapse. Salvage therapy with chemotherapy or targeted therapy is often administered before HCT to reduce the leukaemic burden.

Gilteritinib, a tyrosine kinase (FLT3) inhibitor, is approved by the Food and Drug Administration and European Medicines Agency for patients with relapsed *FLT3* mutated AML, whereas targeted therapy for relapsed *IDH1/2* mutated AML has only FDA approval.

Another treatment option, as used in this case is azacitidine and venetoclax (AZA/VEN) though patients who are R/R after AZA/VEN have a dismal outcome. We await the result of this patient's bone marrow reassessment following initiation of this therapy. Venetoclax is a highly selective BCL-2 inhibitor promoting apoptosis in BCL-2 dependent cells. Venetoclax combined with azacitidine has demonstrated efficacy in older/unfit adults with AML, become an effective therapeutic option.[iii] Venetoclax has shown promising efficacy and safety in paediatric patients with relapsed AML in the early phase setting.[iii] A randomised phase III study in the US is currently evaluating if the randomized addition of venetoclax to a chemotherapy backbone (fludarabine/cytarabine/gemtuzumab ozogamicin [GO]) improves survival of children/adolescents/young adults with AML in 1st relapse who are unable to receive additional anthracyclines, or in 2nd relapse (NCT05183035). Azacitidine is an epigenetic therapy with DNA methyltransferase inhibitor which has been used to reduce chemotherapy resistance with promising results in refractory AML.

Ongoing developments include menin inhibitors, a targeted therapy for patients with mutated *NPM1* or *KMT2A* rearrangements, antibodies targeting the macrophage immune checkpoint CD47, and triple combinations involving AZA/VEN. The latter cause significant myelosuppressive effects, which make it challenging to find the right schedule and dose.[iii]

CAR-T

Despite encouraging preclinical activity of chimeric antigen receptor T cells (CART) for AML, establishing safety and efficacy remains a challenge compared with ALL. AML CAR-T approaches are limited by on-target/off-tumour haematopoietic toxicity, disease heterogeneity, decreased CAR-T persistence, and aggressive disease progression while product is being manufactured. A first-in-human, phase I paediatric trial investigating the safety and activity of CD33- directed CART is actively accruing at multiple sites (NCT03971799, NCT05105152). Additional targets for CART therapies are being explored to address the limitations of targeting CD33. These include and C-type lectin-like receptor 1 (CLL-1, also known as CLEC12A) high protein expression on AML blasts (NCT04219163). Preclinical data on FLT3-directed CART are promising, with clinical trial development underway. CAR-T for AML remains a significant unmet need, and future innovative approaches such as multiantigen targeting and cells with enhanced persistence are being pursued.[iii]

Cord blood transplant

The current plan for this patient is to proceed to T cell replete cord blood transplant (TRCB) if MRD negative or in the setting of MRD detectable disease, if he is clinically well enough. Cord blood (CB) allows T-cell replete CB transplant (TRCB), enabling enhanced graft-versus-leukaemia.

A retrospective study collected data from 367 patients who had undergone TRCB or other cell source SCT for paediatric AML/MDS in the UK and Ireland between 2014-2021. Patients in the TCRB cohort had higher rates of poor prognostic features including MRD positive at transplant, refractory disease and 2nd relapse after previous transplant. Despite these factors, event-free survival was 64% in the TRCB cohort, 50% in MRD positive patients and 79% in MRD negative patients. These exciting results indicate that CB transplant without serotherapy may be the optimal transplant option for children with myeloid malignancy, giving a chance of cure where previously there was none, even for patients with MRD detectable disease. Compared with other cell sources, TRCB transplant resulted in improved disease-free survival and relapse risk in paediatric AML/MDS with less chronic GvHD and particularly improves GvHD-free, relapse-free survival.[iii]