

ROUNDUP³⁶⁰

Oncology

Spinal osteosarcoma: all hope is not lost

■ Researchers in **Stuttgart (Germany)** have shed some light on the prognosis facing patients with the rarely presenting high-grade osteosarcomas of the mobile spine. The osteosarcoma study group were able to collate the results of 20 patients presenting since 1977 with high-grade osteosarcoma of the mobile spine. Patients in this series were a median age of 29 with tumours most commonly seen in the lumbar and thoracic spine. The majority of patients presented prior to metastasis (85%, n = 17/20), and although this is a retrospective case series so standardised treatment protocols were not designed as part of the study, all patients were treated in a broadly similar manner with surgery and chemotherapy. In addition, 65% of patients also underwent radiotherapy. Of the 20 patients in the series, 60% achieved complete remission, and recurrence occurred in 40% (25% local, 10% local and metastatic and 5% metastatic). Of the eight patients suffering recurrence, six died and two survived. Over the subsequent course of the study a further three patients developed local or distant recurrence and subsequently died. The five-year overall (60%) and event-free (43%) survivals were comparable to those of the more widely reported appendicular osteosarcomas.¹ The study team identified young age (under 40), non-metastatic disease at presentation and complete remission

as significant predictors for overall survival. We would tend to agree with the authors that with an aggressive initial treatment strategy this difficult tumour can be treated with acceptable survival rates.

Intralesional curettage for low-grade chondrosarcoma?

■ Like most things in life, bone tumours are a continuum and defining what is meant by low-grade chondrosarcoma and how best to treat it is fraught with difficulty. Researchers in **Florence (Italy)** aimed to establish some evidence on which to base clinical criteria to support surgical and oncological decision making, with particular reference to the suitability of patients for intralesional curettage. The researchers designed a retrospective case series (Level IV evidence) from their single-centre series. All patients with a diagnosis of low-grade chondrosarcoma were included with the study goal of assessing the oncological outcome of these patients. The primary outcome measure was recurrence rates and the researchers also reported secondary outcomes of complications and metastasis. The researchers identified 85 consecutive patients who all underwent a notes review. The majority were female and a broad spectrum of ages was seen (20 to 76 years). The lesions were located predominantly in the femur (35 cases), humerus (33 cases) and tibia (15 cases), with just two cases in the fibula. The vast majority (75%) were treated with intralesional curettage while a minority were treated

with wide resection (21 patients). There was a significant selection bias in this sample as those patients treated with wide resection all had aggressive radiological appearances. The authors were able to report an average of just over 5.5 years of follow-up (24 to 206 months) and they noted no differences in the incidence of recurrence between the two groups; nor did they find any cases of distant metastasis. They did, however, note (as would be expected) a higher complication rate associated with the more radical surgery. The authors conclude that “low-grade chondrosarcoma of the appendicular skeleton without aggressive radiological patterns can be treated with intralesional surgery with good oncological outcome and very low rates of postsurgical complications.”² While the authors do make a compelling argument, it did occur to our boffins here at 360 to question whether, given the highly impressive results presented here for curettage of low-grade chondrosarcoma, the tumours are actually chondrosarcomas or just atypical enchondromas. Given the lack of aggressive radiological changes and the huge difficulty pathologists and radiologists have in agreeing when is a low-grade cartilage tumour a chondrosarcoma there is a very plausible alternative, namely that these patients represent two distinctly different tumours.

MRI might have the answer

■ Sometimes the preparation of 360 is uncanny, with one paper

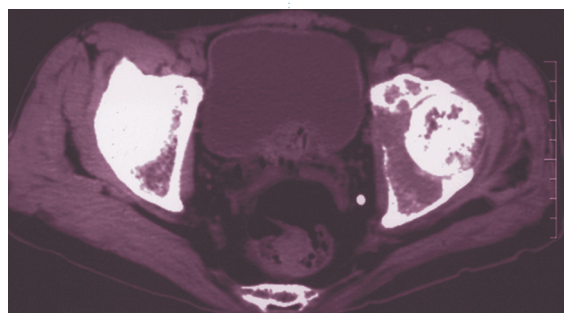
posing a question and another answering it published within the same month. This is the second of such a pairing of papers. Having highlighted the difficulties faced in discriminating between chondrosarcomas and enchondromas, researchers in **Daejeon (South Korea)** may have solved the problem. Noting that the two are notoriously difficult to distinguish between, they designed a diagnostic study to evaluate the potential role for MRI in discriminating between low-grade chondrosarcoma and enchondroma. The researchers identified a series of 34 patients (18 with chondrosarcoma and 16 with enchondromas) who had confirmed histological diagnoses. They then reviewed their medical records and MRIs retrospectively to assess the diagnostic value of a huge range of signs. The researchers identified a number of key features of the lesions' location (central or eccentric; epiphysis, metaphysis, or diaphysis), margin, contour, mineralised matrix, endosteal scalloping, cortical expansion, cortical destruction, soft-tissue mass formation, and periosteal reaction. In addition, they noted the patterns of signal intensity and contrast enhancement (unilobular or multilobular), the presence of a soft-tissue mass, adjacent abnormal bone marrow and soft-tissue signal were also reviewed. Relatively simple statistics were performed using a chi-square test to test strength of associations. The researchers identified a higher incidence of MRI findings which were predominantly seen as

an intermediate signal on T1-weighted images (72% versus 25%) with a typical appearance of multilocular (83% versus 44%) lesions with cortical destruction (33% versus 0%), a soft-tissue mass (28% versus 0%) and peri-lesional abnormal signal (22% versus 0%). The researchers also noted a higher level of involvement of the epiphysis (56% versus 19%) in low-grade enchondromas.³ We applaud the research team for a relatively simple study which appears to have shed some light on the differential appearances on MRI. While all of the findings noted by the research team are previously known to be associated with malignant lesions, the differential incidence between these two histologically similar lesions has not previously been shown. Perhaps the take home message for us with these two papers is that intralesional curettage is likely to be safe if MRI findings are consistent with an enchondroma.

Isolated limb perfusion is a salvage option

■ With the ever-shrinking boundary of the 'unresectable' tumour, surgical oncologists have consistently pushed back the limit as to what is and what is not an unresectable tumour. One option available in these cases is to use isolated limb perfusion to increase the maximal local dose of chemotherapy permissible, and thereby more effectively shrink the tumour. While this may have the benefit of effective tumour shrinkage, it runs the risk of potential toxicity. With only a few reports in the literature, surgeons in **Birmingham (UK)** have performed a systematic review to establish the benefit or otherwise of this technique. The study team performed a thorough literature search for all reports of the isolated limb perfusion (ILP) technique reporting outcomes in patients over the age of 12 since 1980. The study team selected primary endpoints of tumour response and limb salvage rates, but also went on to report secondary endpoints of

complications and recurrence rates. 18 studies were identified reporting the outcomes of 1030 patients treated with ILP utilising most commonly a TNF-alpha and melphalan regime. The cumulative analysis demonstrated a response rate of 22% for complete response (n = 216/964) and an overall response rate of 72% (n = 660/911). There were significant differences in follow-up times, with median follow-ups ranging between 11 and 125 months, giving some difficulties in interpretation of the long-term results. The overall limb salvage rate was, however, 81% in patients who otherwise would have suffered an amputation. While the primary outcomes were impressive,



the collective authors also reported high rates of recurrence (27% local and 40% metastatic). The picture was similarly bleak with regards to complications, with 4% suffering locoregional recurrence and 1.2% suffering early amputations due to complications.⁴ This systematic review highlights the potential of ILP as a treatment modality to facilitate limb salvage. However, there is currently insufficient data to estimate the effects on overall survival and with significant recurrence rates one has to wonder if there is a significant compromise in long-term survivorship with this method of treatment.

Worryingly high infection rates in patients with endoprostheses

■ In the second systematic review worth inclusion in **360** this month researchers in **Hamilton (Canada)** have quantified what we all fear, the high rates of deep infection in

endoprosthesis. With small numbers of implantations in any one centre and the difficulties associated with quantifying the relatively small event rate of infection accurately, the research team constructed a systematic review with the aim of not only quantifying the risk of deep infection but characterising the typical causative organism. They also aimed to establish what current practice is with regards to antibiotic prophylaxis, and, if at all possible, establish what effect prophylaxis regime has on the risk of subsequent infection. The authors conducted a thorough review of 21 years of orthopaedic literature including all English language articles reporting

infection rates in patients treated with endoprosthetic replacements for tumours of the lower limb. The review team were able to identify 48 studies reporting on just over 4800 patients. Using pooled analysis (with weighting for study design) the team identified a 10% post-operative deep infection rate (95% CI 8% to 11%), and the most common organisms were Gram Positive cocci. More refined analysis suggested that the use of an extended prophylaxis regime cuts the post-operative infection rate from an adjusted 13% to 8%.⁵ The most marked finding of this review is the high post-operative infection rate. This is, however, hardly surprising given the extended nature of these operations, and the poorer immunological status of many of the patients following chemotherapy. The use of extended prophylaxis does seem sensible. Given these findings, we do wonder if it is high time a

tumour arthroplasty register was set up to start to answer some of these seemingly simple questions such as, what antibiotic is best?

How bad is endoprosthetic infection?

■ Having established that endoprosthetic infection rates are upwards of 10%, the next question that naturally occurs to us here at **360** is: so what? While infection can be disastrous, to truly understand the size of a not insignificant problem it is important to understand what the long-term sequelae and functional difficulties posed by the problem are – is limb function actually compromised? A study team in **Tokyo (Japan)** has come to the rescue and attempted to answer this very question. Using a retrospective comparative cohort series (Level III evidence) the team collated data on 125 patients who had malignant bone and soft-tissue tumours of the knee treated with endoprosthesis. The cohort consisted of 125 patients (57 with infection) and functional outcomes were assessed using the musculoskeletal tumour society score (MTS). The research team identified an association between both infection and extra-capsular resection with eventual amputation. However, the picture was more complex with regards to the functional outcomes. There were no differences in some subscales (pain, support, walking and gait) between the two groups, while there was a difference in the functional activities subscale associated with deep infection (as well as age, duration of operation, and extra-capsular resection). The mean functional scores were significantly poorer in the infection group (64.3%) than the control group (72%). Despite this clinically significant change, we do wonder here at **360** if this is really a clinically relevant difference.⁶

Operatively treated metastatic disease

■ Surgeons from **Lappeenranta (Finland)** report one of the

most useful papers we have seen this month. While the use of the scoring systems in oncology and metastatic disease is commonplace (e.g. Mirel's score for predicting risk of pathological fracture), there are no accurate prognostic scores to help inform decision making in these patients. The authors note that with increasing numbers of patients living with metastatic disease due to better prognosis in almost every cancer diagnosis, there are more and more patients living with the complications of metastatic diseases including fracture, pain and metabolic disturbance. Despite this marked growth in patients and survival, there is little high quality research examining survival and disease-free survival in patients undergoing surgery for metastatic disease. The study team used data from the Scandinavian Skeletal Metastasis registry, to obtain data on 1107 patients with 1195 skeletal metastases, including patients treated over a ten-year period at eight teaching hospitals in Scandinavia. Patients with 'typical' bone metastatic disease (breast, prostate, renal, lung and myeloma) accounted for nearly 80% of the patients with an overall survival of just over a third at one year follow-up. The complication rates were seen to vary with type of surgery and use of pre-operative

radiation therapy. Complication rates were higher in patients with impending fracture than those who had fractured, and overall survival was found to be affected mostly by primary diagnosis and the presence of visceral metastasis.⁷ The study team used the wealth of data they were able to collate to develop a straightforward prognostic scoring system for these patients. The score they propose is simple, useful and reliable at predicting survival among metastatic patients. The scoring system aids in predicting the prognosis when selecting the surgical method, allowing intervention where necessary to provide benefit without unnecessary complications in those with very poor prognoses.

Cementoplasty gives immediate pain relief

■ The beady eyes of the 360 editorial board alighted on a second interesting paper on metastatic bone disease this issue. In a relatively small but interesting series, a team of interventional radiologists in **Tuen Mun (Hong Kong)** report on the efficacy of cementoplasty for painful refractory metastasis. Practiced widely in the spine, cementoplasty has been shown to demonstrate some analgesic benefit in some large randomised controlled trials,⁸ In their four-year study the investigators were able to

perform the procedure on just 12 patients (13 lesions), although sadly two were excluded due to rapid disease progression. The patients presented with a range of primary diagnoses, and metastatic lesions were treated in the axial skeleton only, with the majority in the pelvis and the remainder in the spine and scapula. In just over 30% of cases the cementoplasty was combined with radiofrequency ablation. The authors report a statistically significant fall in pain scores (from 5 to 2) within a week of surgery.⁹ While we certainly welcome this study, we can't help but think that this must be a highly selective case series. Just one patient every four months has undergone this treatment for a wide variety of diagnoses, and in such a small heterogeneous patient and treatment population it is almost impossible to draw any meaningful conclusions from this type of study. An interesting concept and with any luck another group will pick up the baton and produce a slightly more scientifically rigorous report.

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