ROUNDUP360

Oncology

✕ *For other Roundups in this issue that cross-reference with Oncology see: Foot & Ankle Roundup 5*

Just what is that suspicious lesion?

■ Suspicious bone lesions are not that uncommon, and usually precipitate an orthopaedic-oncology or, at the very least, an orthopaedic referral. In patients with a known primary tumour, the question is often: does this represent metastatic spread? Radiologists in **New York (USA)** asked the deceptively simple question: what are the chances that a solitary bone lesion in a patient with a known primary tumour represents a metastasis? The authors devised a retrospective study designed to establish the aetiology of solitary bony lesions in the population of patients with bony malignancy. Their study population consisted of 482 consecutive patients (254 women and 228 men) with only a single known primary malignancy. All of these patients presented with an isolated solitary bone lesion and subsequently underwent biopsy. The results were reviewed on a retrospective basis with lesions being classified as benign, metastasis of the known primary, secondary primary malignancy, or indeterminate. The investigators found that in around one in five patients (103 of 482), bone biopsy results suggested a benign pathology in contrast to two thirds of patients with metastatic disease of the known malignancy. In a very small proportion of cases (n = 15) a second primary malignancy was thought to be responsible. Biopsy was diagnostic in over 90% of cases. The population of patients with secondary unrelated malignancies included sarcomas (osteosarcoma n = 4, soft-tissue sarcoma n = 2) with incidence of other blood and solid organ malignancies including lymphoma, plasma cell, lung cancer, thyroid cancer, renal cancer and chondrosarcoma.[1] All in all, while straightforward, this paper is useful formaking a decision with patients. Secondary malignancies causing bone lesions are rare at just 3%. The majority of these cases represent secondary metastatic disease (66%) or benign disease (21%).

Limb salvage in pelvic sarcomas

■ Pelvic sarcoma is perhaps one of the most challenging diagnoses to treat. While limb salvage is commonplace in the majority of limb sarcomas, the jury is still very much out in pelvic sarcomas with proponents for both salvage and amputation. The rarity of primary pelvic sarcoma has made providing evidence on which to base decision making difficult. Researchers in **Mumbai (India)** have attempted to plug the gap, so to speak, and designed a retrospective case series of 106 cases of non-metastatic pelvic sarcoma. The research team aimed to investigate limb salvage with respect to morbidity, oncologic results and functional outcome. They included an unselected series of 106 serial patients recruited over an eight-year period. The population consisted of a variety of diagnoses including chondrosarcoma (n = 65), Ewing's sarcoma (n = 25), osteogenic sarcoma (n = 10), synovial sarcoma (n = 3) with a single case each of malignant fibrous histiocytoma, high grade sarcoma and epithelioid hemangiothelioma. In 103 patients, limb sparing resection was undertaken with the aim of surgical cure. Three patients were excluded from follow-up as they erroneously underwent intra-lesional surgery and a single case was abandoned intra-operatively due to on-table cardiac complications. Primary resection involved the acetabulum in 63% (n = 64/102) of cases. Reconstruction was undertaken in those and in a further two patients with various modalities dependent on the exact configuration of the remaining pelvis. Complete excision was achieved in over 80% of cases (n = 82/102), and 90% of patients were available for follow-up at a mean of 55 months (24 to 122). However, around half of patients suffered from a complication of some variety with a five-year survival of 67%. Functional results were impressive in both groups, although superior in those where the acetabulum had been spared (Musculoskeletal Tumour Society Scores of 22 and 27, respectively).[2] Though complex and challenging, limb sparing surgery in non-metastatic malignant tumours is oncologically safe and has better functional outcomes than after amputation surgery. Limb salvage surgery for pelvic sarcoma remains a real surgical challenge with high rates of major complications and local recurrence arising in 25%. If it is successful, function is considerably better than amputation.

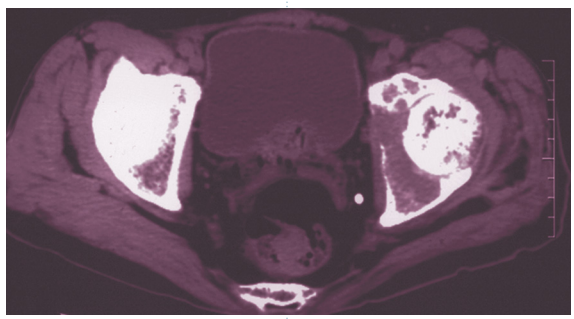
Does infection affect oncological survival?

■ Although on the face of it counterintuitive, there is an accumulating body of research to suggest that post-operative infection may actually confer a survival benefit in patients with a diagnosis of osteosarcoma, highlighted initially by researchers in **Birmingham (UK)**.[3] Researchers in another **Birmingham (USA)** set out to establish if this (as yet unexplained) survival benefit may also be seen in patients suffering infection after soft-tissue sarcoma resection. They aimed to investigate the effects of infection on metastasis, recurrence and overall survival. Using a retrospective comparative case series (Level III evidence), the study group identified a series of 396 patients treated surgically for a soft-tissue sarcoma over an eight-year period. A thorough notes review was conducted and demographic, oncological and outcome data were collected. The authors identified a 13.6% infection rate (n = 54) and conducted a comparison between the two groups. On the face of it there were no discernible differences between the groups in terms of demographic factors (age at diagnosis, gender, smoking history and diabetes), tumour characteristics (size, location, depth, grade, margin status, stage, and histologic subtype) or treatment factors (chemotherapy

or radiotherapy). The authors performed hazards ratio calculations and constructed a competing risks model which yielded no differences in survival, local recurrence or metastasis between patients with or without a post-operative infection. The authors were able to demonstrate that an increase in tumour size was the only independent risk factor for metastasis or death. They were unable to find any benefit to post-operative infection in any of their studied outcome measures.[4] Given the contrasts to the previous study demonstrating that patients with osteosarcoma and a post-operative infection of their prosthesis had better survival than those without, this raises some interesting questions. Is the difference in the response to infection related to the differences in host response to the site of infection (prosthesis *versus* soft tissue) or maybe the response of osteosarcoma to the host auto-immune system varies to that of soft-tissue sarcomas?

Cancer patient pathways: the future of patient care?

■ 'Pathway' is a buzz word in all branches of medicine at the moment. The use of rapid referral and structured care pathways would seem as apt to cancer patients as the other areas of orthopaedics (such as hip fracture and trauma) to which care pathways have been applied. Despite implementation of cancer care pathways, there are conflicting reports of their use in the literature. An adverse effect of the referral guidelines is reported from the UK, in the form of a large number of benign tumours being redirected for diagnosis at the specialist centres, thereby overburdening the capacity and possibly delaying the diagnosis and treatment. Researchers in **Aarhus (Denmark)** have taken a fresh look at the usefulness of these pathways. The authors describe a 'natural experiment' by comparing the quality of cancer care using a range of outcome measures both before and after implementation of a nationally agreed cancer care pathway (CPP). The national CPP was implemented at the start of 1999 for sarcomas in Denmark, and their retrospective comparative case series (Level III evidence) describes the care of patients during a two-year window either side of this date. The researchers conducted a case note review for their cohort of over 1000 patients with a diagnosis of sarcoma at the Aarhus Sarcoma Centre. Outcomes recorded for all 1126 patients included milestones, time intervals, diagnostic imaging and tumour size at referral. Their interesting paper shows a statistically significant reduction in median number of days between referral and first appointment for all patients. For those patients with an eventual diagnosis of bone sarcoma, the median time was significantly reduced from 11 to five days between review and treatment. This effect was much more marked in soft-tissue sarcomas where the reduction was from 28 to 18 days. As one might expect, the researchers also found a reduction in median tumour size for soft-tissue sarcomas from 70 mm to 49 mm. The surgeons suggest this may be possibly part of the Hawthorne effect (a secondary effect seen as part of increased awareness).[5] It is interesting to us here at *360* that these data are discordant to what similar studies in the UK have reported. While the authors here found no differences in the proportion of sarcomas diagnosed before or after the implementation of the CPPs, they did find a marked improvement in outcomes. This may represent a difference in the regulation and scale of the healthcare systems between the two countries. Denmark has a small population and the implementation of a well organised hub and spoke model of health care is long standing. This is not so well established in the UK and may to some extent explain the observed differences between pathway effects; certainly food for thought here.



Radiological arthritis with cement augmentation in GCT

■ Subarticular giant cell tumours (GCTs) can be treated in a number of ways, but one of the mainstays of treatment has always been intralesional excision, which can then be augmented with either bone cement or graft to provide structural support to the subchondral bone. Opinion is divided as to the benefits or otherwise of this kind of augmentation. One of the specific concerns clinicians have is the effect that cement may have in subarticular GCTs upon the incidence of OA later in life. Theoretically, the highly exothermic setting of the cement may result in thermal necrosis to the cartilage with temperatures reaching up to 60°C. Researchers in **Leiden (the Netherlands)** set out to determine if this is indeed a problem. In their retrospective single-centre study of patients with subchondral GCTs, they were able to include 53 patients over two decades. The median age at final follow-up was 42 years and follow-up was with radiographs to detect osteoarthritic changes. The study team defined osteoarthritis with the Kellgren and Lawrence grading system as grade 3 or 4. They then investigated predictors of outcome including age, gender, tumour, cartilage proximity, subchondral bone involvement, bone-grafting, intra-articular fracture and multiple curettage procedures. Aside from predictors for osteoarthritis, the investigators also took the opportunity to assess outcomes of quality of life (SF-36) and functional measures (Musculoskeletal Tumour Society (MSTS) score, and Knee injury and Osteoarthritis Outcome Score (KOOS)). This long-term cohort study achieved a follow-up of just over seven years. Age, gender, subchondral bone-grafting, intra-articular fracture, multiple curettage procedures, and complications did not affect progression to KL3-4. Patients with KL3-4 reported lower scores on the KOOS symptom subscale (58 *versus* 82; p = 0.01), but their scores on the other KOOS subscales, the MSTS score (21 *versus* 24), and the SF-36 (76 *versus* 81) were similar to those for the patients with KL0, 1, or 2 (KL0-2).[6] In this study, 17% of patients with giant cell tumour around the knee had radiological findings of osteoarthritis after treatment with curettage and PMMA. Predictors for poorer outcomes included a large amount of subchondral bone involvement (hazard ratio 9.0 with > 70% involvement), and proximity < 3 mm to the articular cartilage (hazard ratio 4.2) increased the risk for radiological changes of osteoarthritis, a finding that on the face of it is slightly worrying. Perhaps more importantly, the radiological changes associated with osteoarthritis didn't impact on the function and quality of life scores. The authors concluded that despite some more aggressive osteoarthritic changes in patients with large amounts of subchondral PMMA, this treatment remains safe for primary and recurrent giant cell tumours, even in large tumours close to the joint.

Post-chemotherapy increase in tumour volume as a predictor of poor prognosis

■ Post-chemotherapy increase

in tumour volume could never be thought of as good news. While widely regarded as a poor prognostic indicator, there is little data to support threshold values for tumour size increase; in other words, how much of an increase is a bad prognosticator? A study team in **Seoul (South Korea)** set about designing a study to answer this question. They created a retrospective cohort study including an impressive 567 patients, all of whom were treated for stage IIB osteosarcoma. Knowing the eventual outcome, the investigators used the receiver-operating characteristic (ROC) curve analysis to establish what the most sensitive threshold for tumour volume increase was for the prediction of subsequent oncological failure (metastasis or local recurrence). Across over 550 patients they established that a volume increase of around 15% predicted subsequent oncological events well (sensitivity 64.7%, specificity of 81.5%). On careful re-analysis, this cutoff value appears appropriate for all tumours included in this series bar humeral tumours.[7] This simple study has a straightforward message and could serve as an easily assessable parameter for risk-adapted therapy.

REFERENCES

1. **Raphael B, Hwang S, Lefkowitz RA, et al.** Biopsy of suspicious bone lesions in patients with a single known malignancy: prevalence of a second malignancy. *AJR Am J Roentgenol* 2013;201:1309-1314.
2. **Puri A, Pruthi M, Gulia A.** Outcomes after limb sparing resection in primary malignant pelvic tumors. *Eur J Surg Oncol* 2013;(Epub ahead of print) PMID: 24239184.
3. **Jeys LM, Grimer RJ, Carter SR, Tillman RM, Abudu A.** Post operative infection and increased survival in osteosarcoma patients: are they associated? *Ann Surg Oncol* 2007;14:2887-2895.
4. **Behnke NK, Alamanda VK, Song Y, et al.** Does postoperative infection after soft tissue sarcoma resection affect oncologic outcomes? *J Surg Oncol* 2013;(Epub ahead of print) PMID: 24284805.
5. **Dyrop HB, Safwat A, Vedsted P, et al.** Cancer Patient Pathways shortens waiting times and accelerates the diagnostic process of suspected sarcoma patients in Denmark. *Health Policy* 2013;113:110-117.
6. **van der Heijden L, van de Sande MA, Heineken AC, et al.** Mid-term outcome after curettage with polymethylmethacrylate for giant cell tumor around the knee: higher risk of radiographic osteoarthritis? *J Bone Joint Surg [Am]* 2013;95-A:e159-e159.
7. **Jeon DG, Kong CB, Cho WH, et al.** Examination of the cutoff value of postchemotherapy increase in tumor volume as a predictor of subsequent oncologic events in stage IIB osteosarcoma. *J Surg Oncol* 2013;(Epub ahead of print) PMID: 24243222 .