Incidental findings: important or not?

Incidental findings on radiological investigations are a vexing problem for all clinicians, and especially sarcoma specialists. The correct interpretation of incidental findings is critical in planning patient care, because they may influence decisions regarding prognosis, as well as surgical and medical intervention. Clarification of the true identity and relevance of an indeterminate lesion will help with clinical decision making, will maximize concern in worrisome lesions, and will minimize unnecessary additional testing and invasive procedures. In this study from **Iowa City, Iowa (USA)**, the authors evaluated 149 patients with bone or soft-tissue sarcomas who had undergone a staging CT scan as part of their treatment, and in which at least one abnormal finding was observed.[1] In total, 33% of patients presented with indeterminate lung nodules, 10% with indeterminate liver lesions, 3% with indeterminate bone lesions, and 38% with enlarged lymph nodes. Overall, 15/49 of patients with indeterminate lung nodules, 1/15 with liver nodules, 0/4 with bone lesions, 4/13 with lymph nodes between 1 and 2 cm in size, and 2/44 with lymph nodes below 1 cm went on to have clear metastatic spread on subsequent follow-up. A primary tumour size greater than 14 cm in its greatest dimension was more suggestive of indeterminate nodules representing true metastatic disease, compared with smaller primary tumours in both lung and lymph nodes. The authors concluded that although it is extremely common for abnormal findings and incidental nodules to be present at the time of a staging CT scan in patients with sarcoma, the majority of these findings do not represent true metastatic disease. Furthermore, they did not find any indeterminate lesions that progressed to clear metastatic disease in low or intermediate-grade tumours. While these patients will be kept under regular follow-up by the treating team, it would seem reasonable to presume that those patients with low and intermediate-grade tumours are unlikely to have the incidental finding of a metastatic deposit if the appearances are indeterminate on CT scanning.

The biopsy tract and tumour seeding

There are several methods of carrying out a biopsy of a suspicious lesion, all of which have their benefits and drawbacks. Needle biopsy is a commonly used technique, and traditional teaching has been to subsequently excise the needle tract during definitive surgery due to the risk of tumour cell seeding. This study from **Istanbul (Turkey)** has sought to definitively confirm this long-held theory, which has in recent times has been questioned.[2] The authors conducted a prospective evaluation of 55 cases of osteosarcomas that had been investigated with needle biopsy for evidence of tumour cell seeding in the biopsy tract. Cases involving open biopsy procedure were excluded. The authors showed that in 11 cases (20%), microscopic tumour foci were demonstrated within the previous biopsy tract. As a result, these patients showed higher local recurrence rates and worse recurrence-free survival. As mitotic rate, tumour cell pleomorphism, and matrix production in main tumour foci were higher in cases with tumour seeding, the authors suggest that tumours that show seeding may have aggressive biological features. However, they failed to demonstrate any significant relationship between the presence of tumour cells along the biopsy line and metastasis or survival. This is, of course, most likely to do with the small number of cases involved. Either way, the excision of the needle biopsy tract is a good idea in those cases where this technique is used.

Gastrocnemius flap augmentation and active knee extension

Radical resection of a musculoskeletal tumour often leaves patients with significant anatomical defects and, as a consequence, limited function. One such radical procedure is excision of the proximal tibia, following which a rotational gastrocnemius flap can be used to facilitate soft-tissue reconstruction. The excision will often remove the soft-tissue coverage to the extensor mechanism, and the functional recovery of this procedure is an unknown quantity. This group from **St. Louis, Missouri (USA)** have sought to assess the severity of complications and the extent of extensor mechanism after this reconstruction.[3] Their paper, akin to many in such rare conditions, is formed from a single-surgeon case series, reporting 18 patients reconstructed with a gastrocnemius flap over the patellar tendon and cemented endoprosthesis after proximal tibia resection for primary bone sarcoma. Two patients were lost to follow-up or died of disease before the 24-month minimum follow-up interval, and hence were excluded. The median follow-up of the remaining 16 patients was six years; three patients died of disease, and four have not been seen within the last five years. Range of movement (ROM) in patients with successful limb salvage was graded as excellent (flexion of 110° and no lag), good (flexion of 90° to 110° and lag of 10°), fair (one function limited: either flexion < 90° or lag > 10°), or poor (both functions limited: flexion < 90° and lag > 10°). At latest follow-up, three patients had undergone amputation for deep infection. ROM was excellent in nine patients, good in three, fair in one, and poor in none. The authors observed 18 complications during the period of follow-up requiring reoperation in 12 patients, including deep infection (n = 4), patellar tendon avulsion/attenuation (n = 3), and flap necrosis (n = 1). Survivorship free from revision or loss of the gastrocnemius flap was 74% at two, five, and ten years. Survivorship free from reoperation for any cause was 74% at two years, 52% at five years, and 35% at ten years. The authors concluded that although most patients regained functional ROM including active extension, and despite the observed risks, the gastrocnemius flap with split-thickness skin graft should be considered a suitable approach to provide active extension and soft-tissue coverage, given the paucity of good surgical options for the extensor mechanism.

Prognostic factors for survival in Ewing's sarcoma: a systematic review

Ewing's sarcoma is the second most common bone malignancy found in children, with a five-year survival of up to 80% for patients presenting with localized disease reported in the contemporary literature. Reaching a reliable prognosis early in the course of the disease is a challenge; however, the likely prognosis is central to devising treatment strategies and helping the patient make decisions about their care. The authors of this systematic review from **Leiden (The Netherlands)** provide an overview of prognostic factors for survival in Ewing's sarcoma, in order to help guide development of a prognosis prediction model.[4] The team conducted a literature search using the PubMed, Embase, Web of Science, Academic Search Premier, and Cochrane databases to identify all potentially relevant papers. Studies were included in the review if they considered more than 100 patients, had a follow-up of at least two years, recruited patients after 1975, used overall survival and event-free survival as outcomes, and included multivariate analysis. In total, 21 eligible full-text articles were identified for inclusion, and each was reviewed by two independent reviewers. From this extensive review, the authors identified 14 relevant prognostic factors that were widely reported and associated with survival. These include metastasis at diagnosis, large tumours (volume ⩾ 200 ml or largest diameter ⩾ 8 cm), primary tumours located in the axial skeleton (especially pelvic), and a histological response of less than 100%.

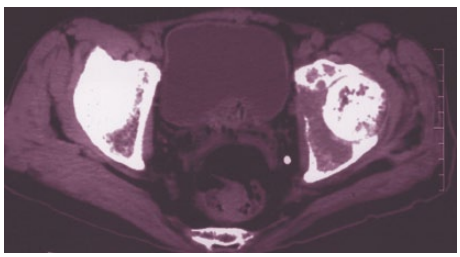
The authors propose that these factors should be included as risk factors in the development of prediction models for Ewing's sarcoma.

Metastatic disease at presentation in Ewing's sarcoma X-ref

The Ewing family of tumours (EFT) represents a significant pathological burden in children and adolescents. Approximately one in four patients with a new diagnosis of Ewing's sarcoma have radiologically detectable metastases on presentation, and as a result these patients face a poorer five-year survival than those without. Despite our experience with the disease, we are insufficiently familiar with the risk factors for metastatic disease being evident at presentation, and what this means in practice for the patient. In this study from **Lebanon, New Hampshire (USA)**, the authors seek to address this gap in knowledge.[5] The authors consulted the Surveillance, Epidemiology, and End Results Program (SEER) registry, examining cases recorded as part of the SEER programme between 2004 and 2012, and identified 870 cases of EFT. Using univariate analyses and multivariate regression, the team then explored the relationships between the demographic and clinical factors, and any discernible metastatic disease at presentation. The authors showed that advanced age, axial tumour location, and increasing tumour size were associated with increased odds of detectable metastatic disease upon presentation with EFT. They comment that although these factors cannot be modified, they work to inform patients about their care and potential outcomes in this condition. While understanding the natural history of diseases like Ewing's sarcoma may not improve survival or individual patient care, it does help inform prognosis and provide much-needed information for patients, relatives, and carers.

Dedifferentiated chondrosarcoma of the pelvis: bad news

Dedifferentiated chondrosarcomas (CS) are a high-grade variant of CS that, with current available treatments, have a dismal five-year survival. Chondrosarcomas are generally resistant to chemotherapy and conventional radiotherapy; as such, surgical excision remains the mainstay of treatment. In this study from **Birmingham (UK),** the authors sought to determine the prognosis of patients with dedifferentiated CS, the influence of wide or narrow margins on surgical resection, and the role of adjuvant therapy in affecting patient outcomes.[6] A total of 31 cases of dedifferentiated CS arising from the pelvis were included in this retrospective review. The disease presented at an advanced stage in 13 patients (41.9%), with 18 patients (58.1%) undergoing surgery with curative intent. Overall survival at 12 months was 15.4% for patients treated with palliative intent, and 50% for those treated with attempted curative surgery. In the surgical group, there were higher rates of disease-free survival in patients who underwent hindquarter amputation (HQA) and those who received wide surgical margins. Time to recurrent disease was always less than 24 months. No HQA for recurrent disease resulted in disease-free survival. The authors found no benefit for chemotherapy or radiotherapy used in a palliative setting. No patient who received adjuvant therapy for palliative or recurrent disease had disease control. The authors suggest that wide margins are more achievable with HQA, which translates into improved local control and survival, and hence recommend that the primary operation to consider in those with dedifferentiated CS should be a HQA with wide margins to offer patients the best chance of cure.



Giant cell tumours of bone with pathological fracture and recurrence

Giant cell tumours of bone (GCTB) are benign aggressive tumours that typically affect the long bones of patients aged between 30 and 50 years. Due to the indolent nature of the giant cell tumour, they can present in a variety of ways, and it is not uncommon for them to present with a pathological fracture. Given the nature of the lesion, widely available treatment options include radiotherapy, bisphosphonates, or excision; however, recurrence is reported to occur in up to 25% of cases. In this investigation from **Birmingham (UK)**, the authors use the known outcomes of a series of patients with long bone GCTBs to identify the prognostic factors for local disease recurrence when a GCTB presents with a fracture.[7] A total of 107 patients presenting with fractures through giant cell tumours of bone were studied retrospectively. The initial surgical treatment was curettage with or without adjuvants in 55 patients, resection *en bloc* with or without reconstruction in 45 patients, and neoadjuvant denosumab, followed by resection (n = 3) or curettage (n = 4). The group identified that surgery more than six weeks after the fracture did not affect the risk of recurrence in any of the groups and hence delaying the surgical treatment appeared to be safe, as neither local recurrence nor complications are increased regardless of the type of intervention performed. In Campanacci stage 3 tumours not treated with denosumab, resection *en bloc* had lower local recurrences (13%) compared with curettage (39%). In tumours classified as Campanacci stage 2, intralesional curettage and resections *en bloc* had similar recurrence rates. All patients treated with denosumab followed by intralesional curettage developed local recurrence. The authors conclude that in patients with pathological fractures through GCTBs not treated with denosumab, *en bloc* resection offers overall lower risks of local recurrence in tumours classified as Campanacci stage 3. Curettage or resections show a similar risk of local recurrence for tumours classified as Campanacci stage 2.

Chondrosarcoma transformation

Hereditary multiple exostoses is an autosomal dominant condition characterized by multiple osteochondromas throughout the skeleton. Caused by defects in the EXT family of tumour suppressor genes, the condition is thought to come with a 5% to 10% risk of transformation to chondrosarcoma. Several studies have concluded that screening exostoses may be effective in detecting malignant transformation and hence may positively influence treatment. However, the evidence for screening is slim and the precise lifetime risks of transformation are not terribly well defined. In this study from **Beijing (China)**, the authors carried out a systematic review of the literature in order to identify the rate of malignant transformation and, therefore, the likely cost-effectiveness of a screening programme.[8] The authors identified 18 papers representing 852 chondrosarcomas, and found that the reported incidence of malignant transformation was 4%, predominantly between the ages of 20 and 40 years, with the slim majority affecting the pelvis and proximal femur. They found that plain screening of radiographs showed a cost-per-life-year gain of £19 013 compared with £53 392 for MRI screening. They also noted that for each generation screened by radiographs, 0.65 cancers were caused, and that the psychological harm of false positives was negligible. Based on this admittedly somewhat sparse evidence, screening for chondrosarcoma transformation is cost-effective. The authors conclude by stating that MRI screening of patients may be of value, particularly if focused imaging sequences are used. This is a little-studied subject, and although these authors might not have the answer, they have at least started the debate.

Dynamic prediction of overall survival for patients with high-grade limb soft-tissue sarcoma X-ref

Prediction models are important in the individualized management of patients with malignancy

because of their impact on treatment selection and consequent outcome. They have become the expected standard of care in many oncology settings and are used to aid complex decisions such as which patients should have adjuvant therapies, and which are likely to do poorly. We are a little behind in orthopaedic oncology in terms of prediction models, perhaps due to the rarity of musculoskeletal tumours. In this study from **Leiden (The Netherlands)**, the authors sought to use dynamic prediction to assess survival times at various points during follow-up in patients with high-grade limb osteosarcoma.[9] A total of 14 centres contributed data to this series, which contained treatment data on 2232 patients diagnosed with high-grade limb soft-tissue sarcoma, all of whom underwent surgery. The outcomes of these patients formed the basis of the dynamic prediction model, which included baseline and time-dependent covariates with the aim of delivering a model that was able to determine likely five-year survivability throughout their follow-up. Alongside this, the team investigated the effect of covariates at different timepoints throughout the follow-up period and adjusted the model accordingly. The model shows that surgical margin and tumour histology demonstrate a varying effect with time on survival, which is most evident immediately after surgery and falls away over time. The development of local or distant metastases during follow-up has a powerful effect on survival, which is taken into account in the model. Overall, the authors conclude that prediction models need to be updated as time passes following treatment, in order to grant an accurate prognosis. The model described here can be used to make better treatment decisions and more accurate prognoses, thus enhancing the ability of patients to make decisions about their care.

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Children's orthopaedics

X-ref ***For other Roundups in this issue that cross-reference with Children's orthopaedics see: Spine Roundup 2; Oncology Roundup 5; Research Roundup 1.***

The gonadal shield and DDH research

The use of gonadal shields is subject to geographical variation, with many centres using gonadal shields routinely in pelvic x-rays for assessing developmental dysplasia of the hip (DDH). There is reasonable evidence that we should be using gonadal shields to protect immature organs. Multiple papers report, however, that these shields are frequently misplaced or cover the intended bony architecture. If further exposure is required to glean the required information, then this is potentially deleterious, and if the shield itself does not cover the gonads, then this is also inappropriate. This paper from **Hong Kong** focuses on this issue from the perspective of loss of data in the clinical research scenario, noting that a loss of over 20% of data in a well-structured prospective study or randomized controlled trial significantly affects the quality of the results.[1] With regard to DDH, the authors argue that the gonadal shields frequently block the anatomy required to assess the congruency of the hip and development of the acetabulum. The authors retrospectively reviewed 138 pelvic radiographs taken for DDH surveillance over a one-year period in a single tertiary paediatric centre. Radiographs were assessed for the ability to determine critical anatomical measurements for DDH. During this time, a written protocol was in force mandating the use of a gonadal shield and guiding its use. Worryingly, gonadal shields were still only used in 42% of cases. In those with gonadal shields, only 26% of x-rays had acceptable protection of the patient's gonads, and 58% of cases had critical bony anatomy obscured. This was worse in female patients, showing gonadal protection in only 21% of girls *versus* 55% of boys. In 97% of female x-rays, the gonadal shield obscured the anatomy. Ironically, all adequately protected female pelves had obscured anatomy. This paper argues that the use of the gonadal shield reduces meaningful data, which is important both clinically and in a research context, where studies using shields would introduce bias at an unacceptable level. Hip dysplasia is more common in female patients, for whom the gonadal shield must be lateral to protect the ovaries. However, this usually leads to the appropriate anatomy being obscured, necessitating repeat radiographs. With this in mind, should we be using gonadal shields in these patients?

Recurrence and infantile tibia vara classification revisited

Infantile tibia vara usually results from medial proximal tibial physis growth asymmetry leading to genu varum, which is distinct from physiological bowing. The condition has classically been described by the Langenskiold classification, but the ability of the classification system to predict the recurrence of deformity following intervention has been widely questioned over recent years. The present study from **Fort Worth, Texas (USA)** tries to iron out the creases in the original work of Langenskiold and suggests a modified classification.[2] The original work suggested that patients with stage I to III pathology could be surgically addressed before the age of eight years and definitively treated with osteotomy. However, more recent work suggests that patients with stage III disease, or even stage II, often suffer recurrence, suggesting a more significant growth disturbance than originally predicted. The authors therefore set out to retrospectively review 22 years of cases at their institute between 1990 and 2012, and designed a modified classification system that they felt would best predict outcome. To form the basis of this classification, 82 cases (115 limbs) were included, all of whom underwent surgical correction and were assessed using the Langenskiold classification. New classification system scores were also recorded, in addition to a number of radiological parameters. The modified system includes a three-stage approach: a type A deformity is a partially lucent medial metaphyseal defect, with or without