Orthopaedics & Traumatology: Surgery & Research 109 (2023) 103086

Contents lists available at ScienceDirect

Orthopaedics & Traumatology: Surgery & Research

journal homepage: www.elsevier.com

Original article

Is magnetic resonance imaging reliable for assessing osteosarcoma of the knee joint in children?

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ARTICLE INFO

Article history:
Received 6 May 2020
Accepted 24 September 2020

Keywords:
Pediatric osteosarcoma
Knee
Extension into the joint space
Extra-articular resection
MRI

ABSTRACT

Introduction: The study of tumor extension in knee osteosarcomas is an essential diagnostic tool that helps determine the surgical approach. Magnetic resonance imaging (MRI) is the key component in this decision-making process, but the interpretation of signals can be difficult because peritumoral edema and inflammation may be mistaken for the tumor.
Hypothesis: There is a discrepancy between MRI and histopathology findings in the assessment of joint involvement in pediatric osteosarcomas of the knee.
Materials and methods: All children who underwent an extra-articular resection for an osteosarcoma of the knee between 2007 and 2016 were included. This was indicated if there was at least one of the following MRI signs: presence of articular effusion, involvement of either the peripheral capsuloligamentous structures, central pivot or patella, or lesion abutting the articular cartilage.
Results: Nine patients were operated on with a mean age of 13 ± 2.7 years. There were at least two of the described signs, mainly the involvement of the peripheral capsuloligamentous structures (78%) and central pivot (56%). The histopathology confirmed that the resection margins were healthy in all cases, but the indication for extra-articular resection could have been avoided in 89% of them.
Discussion: MRI is the current gold standard for assessing tumor extension, but the signs contraindicating the transarticular approach remain poorly defined. Joint effusion detected by clinical or radiological assessment is the least reliable one. It seems that the tumor's proximity to the articular cartilage, as long as there is no loss of continuity in the latter, or its extension into the central pivot should no longer be considered as relevant signs. The involvement of the peripheral capsuloligamentous structure remains an indication criterion because oncologic resection is otherwise impossible, and the risk of false-negative histopathologic diagnoses is higher. Other MRI sequences could better assess the true extension into the joint space.
Level of evidence: IV, retrospective study.

1. Introduction

Osteosarcoma is the most common primary malignant bone tumor in children and adolescents (3 to 5% of childhood cancers), with 50% of cases around the knee [1,2]. The spread into the joint space is slowed in children by the natural barrier formed by the growth plate [3,4]. The study of tumor extension into the joint is an essential diagnostic tool that helps determine the oncologic resection technique (trans- or extra-articular) [5,6]. Extra-articular resections are technically more difficult and continue to be associated with high rates of complications and unpredictable functional outcomes [5–9]. The signs determining whether the joint should be removed in a single piece remain unclear in the literature and are based on a set of clinical and radiological evidence [2,5,6]. The analysis of preoperative magnetic resonance imaging (MRI) during multidisciplinary team meetings is currently the key component in the decision-making process [2,4,10,11]. Joint infection is found in nearly one in four adult cases, but it is less common in children and is associated with a later onset [3,4]. The interpretation of MRI signals is, however, often complicated by peritumoral edema

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https://doi.org/10.1016/j.otsr.2021.103086

and inflammation, which are often mistaken for the tumor [10–13]. Therefore, the purpose of our study was to analyze the correlation between MRI and histopathology assessments of joint involvement on a series of operated pediatric osteosarcomas of the knee, the hypothesis being that there is a discrepancy between MRI and histopathology findings.

2. Materials and methods

2.1. Population

Once approved by the local ethics committee, this retrospective single center study included all consecutive patients who underwent an extra-articular resection for knee osteosarcoma with suspected joint involvement between 2007 and 2016. The surgical decision was taken during a multidisciplinary medical and surgical team meeting. All patients were receiving preoperative neoadjuvant chemotherapy that was continued postoperatively.

2.2. Indication

MR images of the entire femur or tibia, performed before the diagnostic biopsy, were analyzed and reviewed by two experienced radiologists. The MRI protocol included T1- and T2-weighted sequences, with and without fat suppression, with and without injection of gadolinium, and dynamic sequences [10,13]. The T1-weighted sequences were performed to measure the bony margins and epiphyseal extension of the tumor, and search for skip metastases. The fat-suppressed T2-weighted sequences were used to analyze soft tissue extension and peritumoral edema to assess the relationship with neurovascular bundles and joint involvement. The fat-suppressed T1-weighted sequences, after the injection of gadolinium, were used to identify areas of necrosis to help guide the biopsy, and the 3D T1-weighted dynamic sequences were used to identify the peritumoral edema. Extra-articular resection was indicated if there was at least one of the following signs of intraarticular extension on the prechemotherapy MRI and if it was unanimously identified: joint effusion, involvement of the peripheral capsuloligamentous structures, central pivot or patella, or lesion abutting the articular cartilage (Fig. 1). The abnormalities were still present on the post-chemotherapy MR images. No joint aspiration was performed.

2.3. Surgical technique and histopathology

The extra-articular resection was performed via a wide medial parapatellar approach removing the biopsy area en bloc, and the knee extensor mechanism was reconstructed with a medial gastrocnemius flap sutured to the rectus femoris muscle and the prosthesis (Fig. 2), regardless of tumor location (tibia or femur) [7,14]. Whenever possible, a thin portion of the patella was maintained by cutting the latter in the frontal plane (four cases) without opening up the joint. All reconstructions were performed using custom-made cemented megaprostheses (Stanmore Implants, United Kingdom) with six modular (METS) and three growth-friendly expandable magnetic prostheses. The surgical specimens were sent to the histopathology department for freezing with no frozen section analysis. The resection margins were verified with tumor mapping of the surgical specimen taking samples from potentially affected areas.

Fig. 1. MRI images illustrating joint involvement: joint effusion and synovitis (a: axial T2 – weighted TSE and b: sagittal T2 – weighted FatSat), involvement of the peripheral capsule – ligamentous structures (c: sagittal T1 – weighted FatSat and d: coronal T2 – weighted FatSat), involvement of the posterior cruciate ligament (e: axial T1 – weighted FatSat and Gd) and lesion abutting the articular cartilage (f: sagittal and coronal T2 – weighted FatSat).

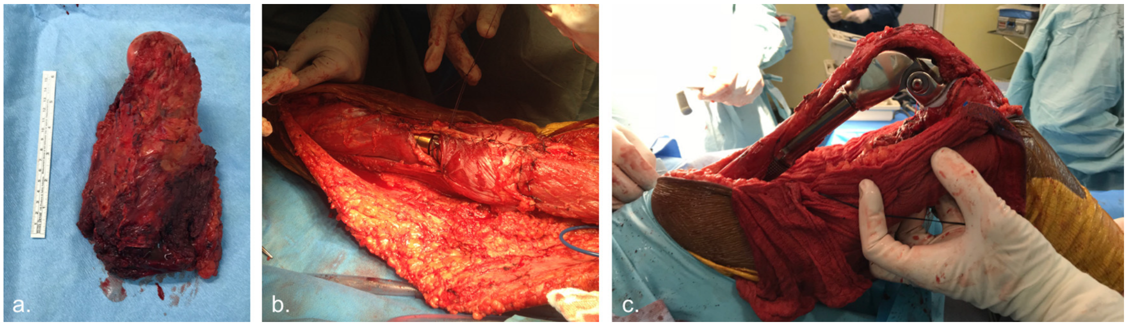

Fig. 2. Intraoperative views showing the resection specimen of a proximal tibial osteosarcoma (a), reconstruction of the extensor mechanism (b) and tensioning of the extensor mechanism with intraoperative 90° knee flexion (c).

Table 1
Clinical and MRI characteristics of the study.

Case	Sex	Age	Bone	Lesion size (mm) LA × SA	Fluid wave test	MRI signs of tumor extension into the joint space			
						Joint effusion	Capsuloligamentous abnormality	Juxtaposition to the articular cartilage	Central pivot involvement
1	F	7	Femur	61 × 39		+	+		
2	M	13	Tibia	67 × 14	+	+	+	+	+
3	F	10	Femur	74 × 40		+	+		
4	F	10	Femur	103 × 14	+	+	+		+
5	F	15	Tibia	71 × 27		+		+	+
6	F	16	Femur	140 × 34	+	+	+		
6	F	14	Tibia	96 × 14			+	+	
8	F	12	Femur	163 × 75	+	+	+		+
9	M	13	Tibia	101 × 69				+	+

LA: long axis diameter; SA: short axis diameter.

2.4. Functional assessment

Functional results were assessed using the Musculoskeletal Tumor Society (MSTS) score [15]. All complications during follow-up were reported.

2.5. Statistical analysis

The statistical analysis was performed with SPSS statistics software version 23.0 (SPSS Inc., Armonk, NY, USA). Given the sample, only numbers and means (± standard deviation) were calculated.

3. Results

3.1. Patients and surgery

Over a nine-year period, nine patients (seven girls and two boys) with high-grade osteoblastic osteosarcoma underwent extra-articular resections performed by two experienced senior surgeons, at a mean age of 13 ± 2.7 years. None of the patients initially showed any limited range of motion and the fluid wave test was positive in four cases. MRI and clinical characteristics of the tumors are summarized in Table 1. All children had at least two of the previously described MRI signs, with no patella invasion observed. The most frequent were joint effusion and involvement of the peripheral capsuloligamentous structures (seven cases each), followed by the involvement of the central pivot ($n = 5$), and finally contact with the articular cartilage ($n = 4$). There was no correlation between the clinical presentation of joint effusion (positive fluid wave test) and imaging study (positive predictive value 57%, $p = 0.3$). The mean time between the diagnostic biopsy and the surgery was 4 ± 0.7 months. Tumor resection was performed on average 3.6 ± 1.6 weeks after the chemotherapy was stopped. No neurovascular complications or intraarticular fractures were reported during the procedures.

3.2. Correlation between MRI and histopathology

The histopathology confirmed healthy bone resection margins in all cases with a mean distance between the tumor and the margins of 4.6 ± 0.8 cm (mean necrosis rate of 58 ± 12.6%, of which five were poor responders), but joint invasion was confirmed in only one case (patient No. 2, true positive on MRI, Table 1). This was the only patient who had four of the five MRI signs for joint invasion. In this case, the histopathology reported a poor response to chemotherapy (necrosis < 5%), an infiltration at the base of both the cruciate ligaments and the medial collateral ligament, and the tumor was located less than one centimeter from the articular cartilage. Intraarticular infection was suspected in case No. 3 due to a poorly performed biopsy, but the analysis of the surgical specimen came back negative (Fig. 3). The indication for extra-articular resection could therefore have been avoided in eight out of the nine cases (false-positive results on MRI).

3.3. Local surgical complications and functional outcomes

The mean follow-up was at 4.4 ± 1.5 years, with a total of seven local complications, but no local recurrence of the disease. Two common peroneal nerve palsies were noted during the immediate postoperative period, with a full recovery at eight months for one case and partial recovery for the other. Five patients also presented complications that required surgical revision (Table 2). Three patients presented skin necrosis at 12 ± 2 weeks postoperatively. There were five cases of late-onset infection, in particular the three patients with initial skin necrosis (mean time to onset 6.7 months) and their treatment consisted of a lavage and surgical

Fig. 3. Resection specimen (a) and MRI images of the distal femur of a 10-year-old girl with a coronal section showing the transphyseal approach and involvement of the lateral capsuloligamentous structures (b: T1 – weighted FatSat) and two axial sections showing joint effusion and the involvement of the posterior capsular structures (c: T1 – and T2 – weighted FatSat).

Table 2
Complications and functional outcomes.

Case	Complications					Lung metastases	MSTS score	Oncological status at follow-up	
	Common peroneal nerve palsy	Late-onset infection	Skin necrosis	Aseptic loosening	Treatment				
1						+	17	Remission	
2		Group B streptococcus			Removal and reimplantation of prosthesis	+	22	Remission	
3		CoNS	+		Lateral and medial gastrocnemius flap	+	18	Distance recurrence (pelvis)	Death
4		MRSA	+		VAC + thin skin graft		18	Remission	
5	+			+			18	Distance recurrence (talus)	
6						+	22	Spinal metastases	Death
7		MSSA	+		Lateral gastrocnemius flap	+	8	Death	
8	+					+	12	Death	
9		CoNS			Removal – arthrodesis		16	Remission	

CoNS: coagulase-negative *Staphylococcus*; MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-sensitive *Staphylococcus aureus*; VAC: vacuum-assisted closure or negative wound pressure therapy.

debridement with no replacement of the prosthesis. The other two cases of late-onset infection required prosthesis removal and reimplantation 27 months postoperatively, and knee arthrodesis 13.7 months after the initial procedure, respectively. The five patients with late-onset infection were also given a long-term antibiotic therapy for three months (15 days intravenously). One case of aseptic loosening was also observed at 3.5 years postoperatively, with no functional complaint to date. On a functional level, the mean MSTS score at follow-up was 16.8 ± 1.4, i.e. 56% of the normal function. Mean flexion was 82 ± 11° and a flexion contracture (between 10 and 30°) was noted in four of the cases. During the last examination, all patients had an extensor lag with a mean value of 31 ± 6°, and the use of a walking aid was reported in all cases.

4. Discussion

The natural barrier provided by the growth plate makes the possibility of joint invasion less likely in children [4,7]. MR imaging is the current gold standard for studying tumor extension, but assessment and reliability of signs remain difficult in pediatric osteosarcomas of the knee. The results of our study found a discrepancy with the histopathology and emphasized the need for improving preoperative analysis [2,11].

4.1. Extra-articular resection: complications and functional outcomes

This procedure requires extensive bone resections and several improvements have been described on how to preserve or reconstruct the knee extensor mechanism, a key component of successful functional prognosis [7,14,16,17]. Although it is associated with a satisfactory oncological outcome (healthy margins and no local recurrence in the series), it is still technically more difficult than transarticular resection, particularly during periarticular dissection of the neurovascular bundles [5,7,8,14,16]. High complication rates have been reported in the literature (overall rates between 40 and 80%), with mainly skin necrosis (30% to 35%), prosthetic joint infections (20% to 60%) and mechanical complications (10% to 50%) [5–9,11,18]. Functional outcomes were also poorer, with MSTS scores ranging between 56% and 76% [5–9,18].

4.2. Correlation between imaging and histopathology

The lack of correlation between MRI and histopathologic assessments has already been noted in the literature, with no histopathologic diagnosis of joint involvement in 22 to 72% of cases [2,4,5,7,18]. Furthermore, Quan et al. described how the presence of peritumoral edema and inflammation can make interpreting MRI scans difficult [11]. Our pediatric study strongly corroborated these data as joint involvement was only confirmed in one case. In the Chelli Bouaziz et al. series, extra-articular resections were also performed "excessively" in 40% of cases [2]. The criteria used in their study were not identical to ours, but it is the only study that assesses the reliability of MRI signs in knee sarcomas. Their population was more heterogeneous and some of their transarticular resections were not cancerous [2]. The other component poorly defined in the literature is the optimal timing of the reference MRI [10,11]. The usual protocol involves at least one pre-chemotherapy and one post-chemotherapy scan performed a few weeks prior to surgery [10]. In this study, only the first MRI was assessed because the decision regarding the surgical approach, and consequently the custom-made prosthesis to order, require a delay of several weeks that is incompatible with the short period between the end of the chemotherapy and surgery. However, a retrospective analysis of the various studies revealed that all the signs identified on the initial MRI remained present or questionable on the last scan.

4.3. When to choose extra-articular resection?

The signs contraindicating the transarticular approach remain to date poorly defined [5,7–9]. Joint effusion detected by clinical or radiological assessment is the least reliable one, especially when isolated [2,6,10]. The most evocative clinical arguments are the existence of an intracapsular pathologic fracture, a limited range of motion and/or knee flexion contracture, and finally an iatrogenic transmission during the diagnostic biopsy (patient No. 3) [5–7,18]. However, they only manifest themselves at a later date and are absent at the beginning of the disease progression. Therefore, MRI modality continues to play a key role, and sequence analysis is fairly well standardized to determine bone resection margins [10–12]. Joint involvement is more complicated to ascertain because of peritumoral edema and inflammation, and 3D T1-weighted dynamic sequences could potentially better differentiate lesions [10–12]. The commonly accepted MRI signs are a breach in the articular cartilage, especially the region of the intercondylar notch, and the involvement of the patella, but none of these were present in the series [2,6,11,18]. The most debated signs are the involvement of the central pivot and the peripheral capsuloligamentous structures, and widespread lesions that abut the articular cartilage [2,6,16]. Tumor extension into the central pivot does not seem to be a true contraindication to transarticular resection, since ligaments can be oncologically resected using the "pseudo" extra-articular technique which preserves the extensor mechanism, as described by Zwolak et al. [2,6,16]. In our cohort, four of the five patients with suspicious pivot images had no histopathologic confirmation of involvement. It seems that the tumor's proximity to the articular cartilage, as long as there is no loss of continuity in the latter, should no longer be considered as a relevant sign [3,4,7]. However, the suspicion of an involvement of the capsuloligamentous system via the collateral ligaments or the posterior capsule, seems to be an indication criterion, since oncologic resection is otherwise not feasible, and the risk of false-negative histopathologic diagnoses is higher in this anatomically more extensive region.

4.4. Study limitations

Our study had a limited number of patients, but this condition is rare and has an uncertain prognosis. Nonetheless, our exclusively pediatric series had the advantage of being consecutive and homogeneous, with all cases being reviewed by the same radiologists and all procedures performed by the same surgeons. However, the inter- and intraobserver reproducibility of the five MRI signs was not evaluated and will need to be further studied in the future.

5. Conclusion

The results of this study show that the indications for extra-articular resection based on the search for five signs on the initial MRI were not confirmed by the histopathologic assessment of the surgical specimen. Further research is needed to better assess the presence of tumor extension into the joint space, in particular the use of dynamic sequences. However, this complicated procedure remains satisfactory from an oncological standpoint, and caution, even excessive, cannot be criticized in the management of pediatric tumors.

Disclosure of interest

The authors declare that they have no competing interest.

Funding

None.

Contributions

All authors contributed actively to the study.

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