Staging and treatment of osteoblastoma in the mobile spine: a review of 51 cases

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Abstract

Purpose To define the role of Enneking staging system and of the consequent different treatment options on the outcome of osteoblastoma (OBL) of the spine.

Methods A retrospective review of 51 patients with OBL of the mobile spine conducted to compare the outcomes among the different types of treatments at long term follow-up (25–229 months, av.90). These 51 patients were previously staged according to Enneking staging system and treatment selected accordingly. 10 stage two (st.2) OBLs were treated with intralesional excision and 41 stage three (st.3) OBLs were treated either by intralesional excision or en bloc resection. The intralesional excision group was divided considering the use or not of radiation therapy after surgery. The recurrence rate was compared among these groups and also considering previous open

surgery (“non intact” vs. “intact”). The statistical significance was defined using the Fisher Exact test.

Results No local recurrence occurred in the st.2 patients treated by intralesional excision. Considering the st.3 patients, 2 local recurrences out of 13 patients occurred in the en bloc resection (15.4 %) group. All occurred in “non intact” cases (67 %). In the intralesional group, 5 local recurrences out of 27 patients occurred (18 %) being none in the group that received radiation therapy after surgery. Two occurred in the “intact” (7 %) and three in the “non intact” group (75 %). Considering all patients, the difference between the recurrence rate between “intact” and “non intact” groups was statistically significant ($p < 0.002$).

Conclusions Intralesional excision proved to be effective in st.2 lesions and en bloc resection in st.3. Radiotherapy seems to be an effective adjuvant treatment when en bloc resection is not feasible or requires unacceptable functional sacrifices. The first treatment significantly affects the prognosis as previously treated patients have worse prognosis.

Keywords Osteoblastoma · Treatment · Enneking staging system · Prognosis

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Introduction

Osteoblastoma (OBL) is a rare and benign osteoid-producing primary bone tumor [1–4] that occur mainly in the long bones [5]. Spine location is observed in 36 % of these tumors and the vast majority arises from the posterior elements [5–7].

Since the first descriptions of this condition, the issue of distinguishing from osteoid osteoma is pre-eminent [1, 2, 8, 9]

and it is commonly accepted the main difference is the size being called OBL the lesion bigger than two cm [9].

The other major issues are its broad spectrum of clinical behavior, the local aggressiveness and its capacity of malignant transformation ranging from 12 to 25 % [10]. Therefore, while some OBL must be differentiated from osteoid osteoma, on the opposite it can occur that some OBL must be differentiated from osteogenic sarcoma.

Clinical and imaging details are well known, while treatment options are a matter of discussion in close relationship with the different biological behavior being the heart of the matter how to recognize the level of aggressiveness of the lesion. The decision making process must consider the role of surgery and of adjuvant treatments in order to balance the morbidity of the treatment with the risk of recurrence, potentially associated with progression to malignancy.

At the beginning of the activity of the senior surgeon (SB), a review of 30 cases of surgically treated OBL of the mobile spine was performed [11] where, the Enneking staging system [12] was retrospectively applied. Local recurrence occurred in 4 out of 30 patients (13.3 %), seven percent rate of local recurrence was found in stage two (st.2) (1 patient out of 14) while for stage three(st.3), it was as high as 19 % (3 out of 16).

All the patients were treated with intralesional excision of the lesion. All local recurrences occurred before 2 years from the treatment. To improve these results, surgical techniques were developed selective arterial embolization (SAE) was introduced and a more careful treatment strategy was developed based on the Enneking system prospectively applied to all cases. The relationship between the treatment and the outcome is in this article analyzed in the series of 51 consecutive cases diagnosed and treated by the same team of surgeons and pathologists since 1984 and followed at long term All the cases were submitted to the same diagnostic work-up and the Enneking staging system was the guide to decide the treatment. The purposes of the study are to validate the role of the Enneking staging system as a prognostic tool and to focus on the role of different surgeries and radiotherapy on the long term outcome in a homogenous clinical series.

Materials and methods

Seventy-seven patients received the diagnosis of OBL and were treated in our institution in the period from 1959 to 2010. There were 50 males and 27 females (ratio male to female: 1.85). The ages at the diagnosis varied from 7 to 60 years (average of 23 years of age).

All patients were surgically treated either by en bloc resection or by intralesional piecemeal excision (curet-

age). All were followed recording recurrence rate, complications and final results. In order to identify diagnostic and prognostic criteria based on the study of a homogeneous series, the study was restricted to the cases fulfilling the following inclusion criteria:

- patients observed after 1984, the senior author leading the surgical team and the diagnostic and staging procedures being prospectively standardized.
- patients that completed a minimum follow-up of 24 months or died before (in our previous study no local recurrence occurred later than 2 years).

Fifty-one patients were selected as they met the inclusion criteria. There were 34 males and 17 females, with a male to female ratio of 1.94. In this group, the age at diagnosis varied from seven to 60-year-old (24.1 years of average). All patients presented with local pain. There were two patients that presented with thoraco-lumbar scoliosis.

All cases had standard radiograms and computed tomography (CT scan) before diagnosis. Starting at the year of 2000, MRI was also performed. The cases were staged according to the Enneking system: st.2 for active lesions and st.3 for benign aggressive lesions [12]. This staging system has recently been submitted to a intra and interobserver reliability study which confirmed its validity [13].

St.2 lesions were defined as mostly combined lytic and osteosclerotic image, with well defined borders. Frequently the lytic area is found surrounding an ossified core, strongly resembling the appearance of an osteoid osteoma. Diameter, by definition, must be superior to two cm. The clinical course is slowly progressive with pain and possible deformity related to muscle spasm. The lesion does not infiltrate the soft tissues as shown in Fig. 1.

St.3 lesions were defined as fully lytic images, eroding the cortex and invading the canal and/or the surrounding soft tissues. The margins are not well defined, confirming the aggressiveness of the tumor. Some spot of pathologic bone can be found inside the lesion. The clinical course is faster with early possible neurologic symptoms (Fig. 2). According to Enneking classification, 10 cases (20 %) were classified as st.2 and 41 cases (80 %) as st.3.

Extension of the lesions were defined by the Weinstein–Boriani–Biagini system (WBB) [14]. The neurological status was graded at the admission and at the last follow-up according to Frankel classification [15]. Before treatment, 48 patients were assigned as type E, two D3 and one as D2. 10 patients were referred with a recurrent or progressive tumor after previous unsuccessful treatment or open biopsy. These will be later on simply defined as “not intact” cases.

Eleven tumors were located in the cervical spine, 17 in the thoracic spine and 23 in the lumbar spine. The most

Fig. 1 St.2 osteoblastoma: CT axial image of C2 showing a lytic area surrounding an ossified core strongly resembling the appearance of an osteoid osteoma. Diameter superior to two cm

Fig. 2 St.3 osteoblastoma: CT axial image of L4 showing a fully lytic image eroding the cortex and invading the surrounding soft tissues. The anterior margin is not well defined confirming the aggressiveness of the tumor

frequent level was L5 (eight cases, 15 %), followed by L4 (seven cases, 13 %), L3 (five cases, 10 %) and T4 (four cases, 8 %). There were no lesions found in T7, T9 and L1. All 51 patients were submitted to surgical treatment. All 10 cases st.2 were treated with intralesional excision. Among the 41 st.3, en bloc resection was performed in 13 patients and intralesional excision in 28.

Five intralesional excisions were followed by radiotherapy. The decision to include radiotherapy in the treatment strategy of st.3 OBL was taken as en bloc resection was considered not feasible or exposing to high morbidity

and residual tumor was expected after intralesional excision. The 13 patients treated by an en bloc resection were located from T2 to L5. 10 were operated by a posterior approach only, while three underwent to a combined anterior and posterior approach. In all the specimens a gross and histological study of the margin was performed, resulting in intralesional margin in three cases, marginal margin in three and wide margin in seven cases. Since 1998, all intralesional excisions received pre-operative embolization (13 out of 38 patients).

As one patient died in first post-operative day, 50 patients were followed ranging from 25 to 229 months (average 90 months). Clinical and radiographic studies were performed each 3 months for the first 2 years, each 6–8 months until 5 years and each year later on. The rate of recurrence was compared according to the staging system and also according to the classification of “intact” (first treatment performed by the authors) and “not intact” (cases referred for local recurrence or after open biopsy performed elsewhere) The statistical significance was defined using the Fisher Exact test.

Results

A total number of 7 local recurrences occurred out of the 50 patients followed (14 %) (Tables 1, 2). 2 out of 13 patients treated with en bloc resection and five after 32 intralesional excision. There were no recurrences after intralesional excision combined with radiotherapy (five cases) or in the group of en bloc resection with wide/marginal margins (10 cases). All recurrences occurred in patients classified as st.3, whose global rate of local recurrence amount to 17.5 %. 2 local recurrences were found out of 40 “intact” patients (5 %), while five followed the treatment of 10 “non intact” patients (50 %).

Recurrence after en bloc resection

No recurrence occurred in the 10 patients who had no treatment before (“intact”), including one patient whose resection was defined intralesional the local control was achieved. Conversely, out of the three recurrent cases that came to us for treatment originated from other services (“not intact”), two local recurrences occurred after en bloc resection (67 %) (Fig. 3). Both were successfully treated later on by intralesional excision and radiotherapy (Tables 3, 4).

Recurrence after intralesional excision

The total recurrence rate, considering intralesional excision and intralesional excision plus radiotherapy groups was

Table 1 Stage 2 patients

Treatment	Number of patients	Local recurrence (time of FU, average time)	NED (time of FU, average time)	AWD (time of FU, average time)	Dead (time of FU, average time)
Intralesional excision	10	0	10 (30–229, av. 86 months)	0	0
Total	10	0	10	0	0

F.U Follow-up, *NED* no evidence of disease *AWD* alive with disease, *av* average

Table 2 Stage 3 patients available at follow-up

Treatment	Number of patients	Local recurrence (time of FU, average time)	NED (time of FU, average time)	AWD (time of FU, average time)	Dead (time of FU, average time)
Intralesional excision	22	5 (6–27, av. 13 mos)	22 ^a (25–223, av. 78 mos)	0	0
Intralesional excision + RT	5	0	5 (39–166, av. 70 mos)	0	0
En bloc intralesional	3	2 (13–25 mos)	3 (33, 93, 188 mos)	0	0
En bloc marginal/wide	10	0	10 (87–212, av. 130 mos)	0	0
Total	40	7	40	0	0

One patient submitted to intralesional excision died in the immediate post-op course and therefore is not included

F.U Follow-up, *NED* no evidence of disease, *AWD* alive with disease, *av.* average, *mos* months

^a 1 Spontaneous regression of local recurrence

13 % (5 out of 37). All occurred in the st.3 patients treated exclusively with intralesional excision, with a rate of 23 % (5 out of 22). They occurred 6 to 27 months after treatment, average 13 months. Considering only the intact cases, there were 2 local recurrences out of 28 patients (7 %), and in the not intact group 3 local recurrences occurred out of 4 patients (75 %). In the last group, one patient had been submitted to three and another one to two others surgeries, before the referral to our institution (Tables 3, 4).

The recurrence rate considering the intact and the non intact group was statistically significant ($p < 0.002$) for both intralesional and en bloc resection.

Evolution of recurrent cases

Six recurrent tumors were successfully treated with an intralesional surgery after the recurrence. The latest follow-ups varied from 25 to 188 months (average 80.7 months), with the second intralesional surgery taken place between 6 and 27.3 months (average 12.5 months). All 6 patients had “no evidence of disease” at the final follow-up. In one patient submitted to intralesional excision (Fig. 4a, b) an image consistent with local recurrence was observed (Fig. 4c), associated with night pain and spasm, but the patient always refused further treatment. At the most recent follow-up (54 months) she results fully asymptomatic and the CT scan shows the ossification of the lytic change (Fig. 4d). This can be considered a case of spontaneous regression.

Complications

Six complications occurred (one in st.2 and five in st.3), five after intralesional excision and one after en bloc resection. The most severe complication occurred in 1984: the patient died in the immediate post-operative period due to profuse bleeding. This was a st.3 OBL of C4, submitted to intralesional excision. At that time embolization was not available.

Kyphotic deformity followed the intralesional excision of two OBL arising in the posterior elements of C6 (st.2) and T4 (st.3). Both cases, respectively ageing 6 and 9 years did not receive fusion after the excision. Posterior instrumentation and fusion was further performed to restore the correct alignment and the stability of the spine. They were both asymptomatic at the last follow-up. A third patient with an OBL in T1 and aging 14 years, also developed a kyphotic deformity after a hardware failure and was re-operated 23 months after the first surgery to treat the local recurrence and the deformity. At last follow-up the patient was asymptomatic and without any evidence of disease.

One local infection was successfully treated with debridement, surgical flap and antibiotics in a patient with a st.3 OBL treated by en bloc resection. An asymptomatic screw breakage was identified 69 months after en bloc resection of a L4 OBL. No treatment was performed and the patient is still asymptomatic after 212 months without evidence of the disease. As a whole, eight secondary operations were needed, five to treat local recurrences, two

Fig. 3 **a** CT axial image showing a local recurrence of a st.3 osteoblastoma in T12 after intralesional excision. **b** Immediate post-operative CT axial image after en bloc resection and anterior

reconstruction with a carbon fiber cage. **c** MRI axial image showing a local recurrence 25 months after en bloc resection

for surgical complications and one for both problems at the same time.

Role of radiotherapy

Conventional radiotherapy (40–44 Gy) was delivered as adjuvant in two “intact” and three “not intact” cases after intralesional excision. Radiotherapy was most frequently used as treatment of recurrence: two patients recurrent after en bloc resections were treated with intralesional excision

and radiotherapy. All patients were found without evidence of disease at last follow-up (41–166 months).

Neurological status

Three patients had sign of cord compression classified as D2 and D3 (two cases). At the final follow-up they had a complete neurological recovery. Conversely a motor impairment due to L5 nerve root compression in another case remained unchanged.

Table 3 Final follow-ups in “intact” cases (first treatment performed by the authors)

Treatment	Number of patients	Local recurrence (time of FU, average time)	NED (time of FU, average time)	AWD (time of FU, average time)	Dead (time of FU, average time)
Intralesional excision	28	2 (16 and 6 months)	28 (25–229, av. 83 months)	0	0
Intralesional excision + RT	2	0	2 (41 and 167 months)	0	0
En bloc intralesional	1	0	1 (94 months)	0	0
En bloc wide/marginal	9	0	9 (36.2–212, av. 124 months)	0	0
Total	40	2	40	0	0

FU Follow-up, NED no evidence of disease, AWD alive with disease, av. average

Table 4 Final follow-ups in “not intact” cases (OBL recurrent after treatment performed elsewhere)

Treatment	Number of patients	Local recurrence (time of FU, average time)	NED (time of FU, average time)	AWD (time of FU, average time)	Dead (time of FU, average time)
Intralesional excision	4	3 (6–27, av. 14 months)	4 ^a (25–229, av. 97 months)	0	0
Intralesional excision + RT	3	0	3 (39–56, av. 48 months)	0	0
En bloc intralesional	2	2 (10 and 26 months)	2 (105 and 32 months)	0	0
En bloc wide/marginal	1	0	1 (156 months)	0	0
Total	10	5	10	0	0

FU Follow-up, NED no evidence of disease, AWD alive with disease, av. average

^a 1 spontaneous regression of local recurrence

Discussion

The target of this paper is to give an answer to the questions:

- which is the role of the Enneking staging system to decide the treatment and to assess the prognosis?
- which is the best treatment of the different stages of OBLs of the spine?
- what is the role of radiation therapy?

Harrop et al. [16] in a recent systematic review, found 211 papers on OBL, only 17 pertinent to the same questions addressed in the present paper. According to these studies, the “aggressive” OBL variant (Enneking st.3) is associated to a local recurrence rate superior to 50 % after intralesional excision while the “less aggressive” OBLs (Enneking st.2) are credited of a recurrence rate between 10 and 15 %. On these limited bases (a very low quality literature) intralesional resection can be strongly recommended for “active” OBL (Enneking st.2), while en bloc resection, when anatomically feasible, is strongly recommended for “aggressive” OBL (Enneking st.3).

The analysis of the series here reported further confirms these points. First of all, the application of the Enneking staging system allows understanding the range of clinical and imaging patterns and the different behavior of OBL. Second, this staging system seem an excellent guide to select the appropriate treatment. st.2 OBL has a biological

behavior more similar to osteoid osteoma, and can be successfully and less aggressively treated by intralesional excision. The possibility of spontaneous regression as occurred in one of our recurrent cases and already reported by Collignon et al. [17] can also be considered.

For the treatment of st.3 OBL, a more aggressive strategy should be chosen. Resection attempting wide margins en bloc should be the first option of treatment. The risks of those more demanding procedures are justified weighting the higher risk of recurrence and progression to malignancy.

When anatomic constraints or tumor volume prevent from performing en bloc resection with appropriate margins, or when the patient refuse the higher morbidity or the possible loss of function connected with en bloc resection, radiation therapy can be an option, which in this series resulted constantly effective. Our series add further elements in favor of radiation as a valuable adjuvant, in recurrent lesions or incompletely resected aggressive OBLs (Enneking st.3).

However, in the literature [4, 10, 18–24] the role of radiation therapy in recurrent lesions or lesions that are incompletely resected is controversial, with the majority of cases illustrating no advantage [8]. Marsh et al. [10] in a review of 197 OBL cases conclude that “radiotherapy does not alter the course of the disease and appears to be contraindicated”. Tonai et al. [25] followed a series of incomplete excised OBL treated with re-excision and noted

Fig. 4 **a** Axial CT of a st.3 osteoblastoma of L5. **b** Axial CT image of the immediate post-operative after intralesional excision and posterior fixation. **c** Local recurrence after 6 months. **d** Spontaneous regression after 4 years of the first surgery

no recurrence at 2 years and proposed this as the optimal treatment strategy rather than radiation therapy.

Harrop after the systematic review on the topic concluded that only a weak recommendation can be done for the role of radiation for incompletely resected or recurrent OBLs [16]. Finally, it is remarkable the figure coming from the comparison between cases already treated (“not intact”) and cases treated in the same institution since the beginning (“intact”). The incidence of recurrence among “not intact” patients was significantly higher compared to “intact” cases: 2 local recurrences out of 40 “intact” patients compared to 5 local recurrences out of 10 “not intact” patients. After intralesional excision the recurrence

rate was 75 % in “not intact” and 7.5 % in “intact”. The rate of recurrence was even higher after en bloc resection (67 % vs. 0).

No local recurrences occurred when radiotherapy was added to surgery. This figure enhances the role of radiotherapy when en bloc resection is not feasible, particularly in huge tumors located in difficult surgical areas and in recurrent or inappropriately removed tumors?

Notwithstanding the series here discussed represents one of the largest series collected in a single Institution, the small absolute numbers do not allow any statistical significance, however, these data are offered as a possible base for future multicentric prospective studies able to

provide evidence to the most important question: is the combination of intralesional, less invasive surgery and radiation therapy effective in st.3 OBL as the more morbid en bloc resection is?

Conclusion

Osteoblastoma can occur with different clinical and radiographic patterns, related to different clinical behavior. Progression of malignancy is possible and even lung metastases are reported. On the other hand, even regression of the disease is reported in this series and in the literature. These observations endanger diagnostic and treatment problems.

This study was conceived with the purpose to understand the role of the Enneking staging system to identify the aggressiveness of the tumor and therefore to select the appropriate treatment. Starting 1984 all the cases of OBL were staged and treated accordingly.

Recurrence rate after intralesional excision results 10 times higher in patients previously submitted to open biopsy or in recurrent cases. Even en bloc resection is scarcely effective in “non intact” patients. The rate of recurrence is 67 % while no local recurrence followed the en bloc resection performed in st.3 OBL who had no previous treatment. The difference of local recurrence considering “intact” and “not intact” patients was statistically important ($p < 0.002$). Therefore it is possible to conclude that the first treatment significantly affects the prognosis.

Intralesional excision proved effective in st.2 lesions and en bloc resection in st.3. Intentional margin violation or intralesional surgery can be combined with radiation therapy when wide margin en bloc resection is not feasible or when it is associated to unacceptable morbidity or functional sacrifices.

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Conflict of interest None.

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