Osteblastomas of the spine: a comprehensive review

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Osteblastomas are primary bone tumors with an affinity for the spine. They typically involve the posterior elements, although extension through the pedicles into the vertebral body is not uncommon. Histologically, they are usually indistinguishable from osteoid osteomas. However, there are different variants of osteblastomas, with the more aggressive type causing more pronounced bone destruction, soft-tissue infiltration, and epidural extension. A bone scan is the most sensitive radiographic examination used to evaluate osteblastomas. These osseous neoplasms usually present in the 2nd decade of life with dull aching pain, which is difficult to localize. At times, they can present with a painful scoliosis, which usually resolves if the osteblastoma is resected in a timely fashion. Neurological manifestations such as radiculopathy or myelopathy do occur as well, most commonly when there is mass effect on nerve roots or the spinal cord itself. The mainstay of treatment involves surgical intervention. Curettage has been a surgical option, although marginal excision or wide en bloc resection are preferred options. Adjuvant radiotherapy and chemotherapy are generally not undertaken, although some have advocated their use after less aggressive surgical maneuvers or with residual tumor. In this manuscript, the authors have aimed to systematically review the literature and to put forth an extensive, comprehensive overview of this rare osseous tumor.

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OSTEOLASTOMAS are primary bone neoplasms with a predilection for the spine. Histologically, they are generally indistinguishable from their smaller counterparts, osteoid osteomas.^{11,70} Osteblastomas are generally greater than 2 cm in diameter, whereas osteoid osteomas are 1.5 cm or less.¹¹ Osteblastomas tend to predominate in the pediatric population during the 2nd decade of life.¹¹ They were first described by Lichtenstein in the 1950s as “osteogenic fibromas of bone.”⁵³ In the following decade, numerous accounts of this primary bone tumor were being reported throughout the literature.^{8,13,20,22,27,35,52,59,62,84,96}

Osteblastomas represent 1% of all bone tumors, and close to 40% are localized to the spine.^{3,11,101} They encompass 10% of all osseous spinal neoplasms.^{42,56} Osteblastomas in the spine are typically found in the posterior elements, predominating in the pedicle and lamina.¹¹ An osteblastoma masquerading as a posterior articular synovial cyst has been reported in the literature.⁹²

Two types of osteblastomas have been described in the

literature; conventional osteblastomas and aggressive osteblastomas.¹⁰¹ Differences exist between these 2 subtypes. Preoperative alkaline phosphatase levels have been shown to be significantly higher in the more aggressive variant. Radiographically, aggressive osteblastomas have a greater tendency to display lytic features than their conventional counterpart. Aggressive osteblastomas more often display paravertebral and epidural extension, and they also are on average approximately 1.5 cm larger than conventional osteblastomas. Surgical blood loss appears to be significantly higher in the more aggressive variant as well.¹⁰¹

Methodology

We performed a PubMed/PubMed Central and MEDLINE search using a combination of the terms “osteoblastoma,” “spine,” and “spinal column” in an effort to coalesce a wide variety of detailed information on spinal osteblastomas. We were specifically interested in de-

ABBREVIATIONS VA = vertebral artery.

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scribing the epidemiological patterns of the disease, the variety of radiographic locations and clinical presentations, histopathological variants, and up-to-date information on management strategies including both surgical interventions and adjuvant therapies. Our search using the above-mentioned terms yielded 585 manuscripts with publication dates ranging from 1954 to 2016. We limited our reference inclusion to 103 manuscripts specifically pertaining to osteoblastomas of the spinal column.

Epidemiology

Osteoblastomas of the spine typically affect the pediatric population, predominately children 10–15 years of age.¹¹ Lucas and colleagues reported on 306 cases of osteoblastomas, with the majority localizing to the spine. They described an average age of 20.4 years at presentation, with an age range of 6 months to 75 years.⁵⁶ Approximately 80% of patients present by 30 years of age.^{42,65} The male/female ratio for spinal osteoblastomas is 2.5:1.⁶⁵ In 1 series comparing conventional osteoblastomas with aggressive osteoblastomas, it was found that the mean duration of symptoms overall was approximately 16.2 months in patients with conventional osteoblastomas, whereas patients with the more aggressive variant tended to present almost 1 year earlier.¹⁰¹

Radiographic Presentation and Location

Osteoblastomas, unlike most other primary osseous tumors, typically arise in the spine.¹¹ Some authors have reported equal frequency of these tumors in the cervical, thoracic, and lumbar spine.⁴² Others have reported the cervical and lumbar spine to be the predominant spinal segments involved, followed by the thoracic region and sacrum.⁷⁶ It has been reported that 17% of spinal osteoblastomas occur in the sacrum.^{16,33,93} Coccygeal osteoblastomas have been reported in the literature as well, although there are few reports of this.⁸¹ Isolated vertebral body involvement is rare and occurs in only 3% of cases.^{24,42,56,65,66,90,98} The one subset of these osseous tumors that are more frequently seen in the vertebral body are those located in

the cervical spine.⁸⁵ Extension from the posterior elements into the vertebral body is quite common, however, and has been reported in approximately one-third of cases.^{55,68}

On plain radiographs, osteoblastomas are typically radiolucent.¹¹ They can have variable features, though. One pattern of representation is similar to osteoid osteomas, with a radiolucent nidus and surrounding sclerotic changes. A CT scan may reveal calcification and mineralization of the nidus. Another pattern, which is the most commonly seen, involves an expansile lesion with a multitude of small calcifications and a prominently sclerotic rim (Fig. 1).

The most aggressive variant displays an expansile pattern, with matrix calcifications, cortical bone destruction, and paravertebral and epidural extension.^{11,70} These more aggressive types of osteoblastomas may radiographically mimic aneurysmal bone cysts, osteosarcomas, or bone metastases.^{70,97}

Technetium-99 bone scanning reveals avid uptake at the site of the lesion.^{11,72} Bone scintigraphy is the most sensitive radiographic scan for osteoblastomas.^{57,69} They display an intermediate to low signal on T1-weighted MRI, whereas T2-weighted MRI depicts an intermediate to high signal.⁷⁶ A variable enhancement pattern has been noted on MRI.^{42,86} The reactive area surrounding the osteoblastoma often enhances on MRI, which may confound the interpreted boundaries of the lesion.¹¹ A “flare phenomenon” has been described in spinal osteoblastomas. These osseous tumors have the potential to cause a diffuse reactive inflammatory response within adjacent vertebrae, surrounding paraspinal soft tissues, and ribs within proximity. This radiographic appearance can be somewhat confusing to the radiographic examiner, who may interpret these tumors as entities such as Ewing’s sarcoma or lymphoma.²¹ Adjacent bone remodeling at the level of the articular facet may present as facet hypertrophy. This may be a secondary inflammatory reaction to the osteoblastoma.⁷⁸

Pathology

Histologically, osteoblastomas display both osteoblas-

FIG. 1. **Left:** Sagittal cervical spine CT scan obtained without contrast showing an expansive lesion with a multitude of small calcifications and a prominently sclerotic rim arising from the posterior vertebral elements of C-3. The final pathology results were consistent with osteoblastoma. **Right:** Coronal cervical spine CT scan obtained without contrast showing the same lesion causing mild stenosis of the spinal canal. The mass extends into the pedicle of C-3; these tumors may extend to the vertebral body through the pedicles.

tic and osteolytic characteristics. They generally are 2 cm or larger in maximal diameter, and only the nidus is taken into consideration when drawing conclusions about their size. The average size of an osteoblastoma is 3–4 cm, and those isolated to the sacrum are often much larger.⁷⁶ They tend to be expansive lesions, and have a central, richly vascular, friable nidus (Fig. 2). The peripheral region of this nidus contains reactive bone, and usually varies from sclerotic to thin. At times, regions of hemorrhage are noted on pathological specimens. Components of aneurysmal bone cysts are reported to be present in approximately 10%–15% of cases of osteoblastomas.^{34,40,60,70,73,93} This finding may confound the final pathology findings. Osteoid osteoma transitioning to an osteoblastoma has been reported in the literature, although this not a common occurrence.^{17,75}

Some osteoblastomas display a rather aggressive growth pattern, differentiating a certain percentage of them from their smaller histological variant, the osteoid osteoma, to which they are often compared. Spinal osteoblastomas have the capability to invade surrounding soft tissues.¹¹ Osteoblastomas that appear more histologically aggressive do not necessarily entail a more virulent clinical course, however.⁵⁶

Some authors have made clear distinctions between 2 subtypes of osteoblastomas; aggressive and conventional. Overall recurrence rates for osteoblastomas after intervention has been reported to be 10%.^{56,87} Long-term follow-up is indicated because recurrences as long as 9 years after resection have been reported.⁴¹ Relapse rates as high as 50% have been reported in the literature for the more aggressive variants.^{56,87} When recurrences do occur, they typically are seen 5–10 years after an initial attempted excision.⁹⁴ Although rare, inadequate excision of osteoid osteomas has been reported to result in recurrence as osteoblastomas in the same anatomical location.⁶ Aggressive osteoblastomas tend to be an intermediate histopathological grade between an indolent osteoblastoma and osteosarcoma.⁸⁷ From a pathological perspective, the main differences between aggressive and conventional osteoblastomas lie within the ability of the aggressive variant to invade cortical bone, as well as the larger epithelioid osteoblasts relative to the conventional counterpart.¹⁰¹ Ag-

gressive osteoblastomas tend to be more immature and to show increased synthesis of alkaline phosphatase.³⁷ Other histopathological features of aggressive osteoblastomas include prominence of nucleoli, larger and more irregular trabeculae, eosinophilic cytoplasm, and a tendency to exhibit osteoclast-like cells more frequently. Mild cellular pleomorphism as well as mitoses are occasionally seen in the more aggressive variant.¹⁰¹ Preoperative alkaline phosphatase may be a screening tool to aid in differentiating aggressive from conventional osteoblastomas. Irrespective of the pathological aggressiveness, large osteoblastomas situated in precarious locations such as the craniovertebral junction and those that extend into the spinal canal often are the most worrisome to encounter for both patients and neurosurgeons.^{56,87}

Osteoblastomas and osteosarcomas have overlapping radiographic and clinical features. Wan and colleagues revealed that nuclear beta-catenin staining strongly suggested osteoblastoma, while staining in the cytoplasmic/membranous structures was more consistent with osteosarcoma.⁹⁷ On rare occasions, an osteoblastoma can degenerate to an osteosarcoma and metastasize.^{59,70}

Fine-needle aspiration may be used for preoperative diagnosis.⁹⁵ This diagnostic modality can be used for osteoblastomas as well as other osseous tumors of the spine. When epidural extension is causing neurological deficits, this fine-needle aspiration allows for an expeditious diagnosis.⁹⁵

Clinical Presentation

Whereas osteoid osteomas often present clinically with nocturnal local pain relieved by salicylates, their more aggressive counterpart, the osteoblastoma, tends to be associated with less pain and a less robust response to medications such as nonsteroidal antiinflammatory drugs and aspirin.⁶⁵ When pain is a presenting complaint, it tends to be dull and difficult to localize.^{33,46} Midthoracic back pain in an adolescent that is persistent and refractory to conservative measures should not be quickly dismissed as inflammatory or postural in nature. Thoracic osteoblastomas may be an unusual source of this symptomatology,

FIG. 2. **Left:** Photomicrograph of an osteoblastoma specimen consisting of outer dense sclerotic bone trabeculae that merge into a thin lacelike osteoid matrix with loose connective tissue, prominent vessels, and prominent osteoblastic rimming. H & E, original magnification $\times 100$. **Right:** Higher-power photomicrograph of the central aspect of the lesion showing lace-like osteoid matrix admixed with giant cells and fibrovascular stroma. Noteworthy is the distinct absence of cellular anaplasia. H & E, original magnification $\times 200$.

especially when progressive thoracic myelopathic features ensue.^{38,48} Neurological deficits such as paraparesis and paraplegia occur in almost one-third of cases.^{7,11,76} Radicular symptoms may also occur in as many as 50% of patients.¹¹ Thoracic osteoblastomas may present with an intercostal neuralgia.⁵⁰ True neurological symptoms attributed to osteoblastomas are primarily a direct effect of their invasive nature and larger size.⁴² They have a propensity to extend into the epidural space.¹¹

Specific neurological signs and symptoms may be present based on the anatomical location of the osteoblastoma. Oropharyngeal pain coupled with neck discomfort and lower cranial nerve palsies may be the presenting clinical scenario for an individual with a craniovertebral junction osteoblastoma.⁸⁷ New-onset torticollis may be the presenting complaint in a child harboring a cervical osteoblastoma.^{4,74,80} Painful torticollis or scoliosis in a child should raise the index of suspicion for the possibility of harboring an osteoblastoma.⁶³ Other location-specific presentations include thoracic myelopathy or lumbosacral radiculopathy.^{38,48} A palpable paravertebral mass may be present on physical examination.⁸² Sacral osteoblastomas have been shown to present with abdominal manifestations.⁹¹

Association With Scoliosis

Scoliosis is a common presentation of spinal osteoblastomas, most notably in males.^{1,58,76} The deformity may present as a painful scoliosis that rapidly progresses.^{31,58} Osteoblastomas of the rib have been associated with progressive scoliosis as well.^{2,23,26,30,36,49,100} Aggressive variants of osteoblastomas have a greater tendency to be associated with a scoliotic curve.¹⁰¹ The convex side of the scoliotic curve is often contralateral to the lesional side of the spinal column.⁶⁶ The curvature is thought to arise as a reaction to pain.^{11,66} This phenomenon is most commonly seen with thoracic and lumbar osteoblastomas.^{42,65,83} Most patients tend to have an improvement or complete resolution of their deformity after the appropriate surgical intervention.¹⁰¹ A delay in treatment may result in a progressive structural curve.⁷⁹

Treatment

Treatment options for osteoblastomas can be considered based on the oncological grading of the tumor.^{11,28,29} This approach to treatment may in fact reduce the recurrence rate.¹⁰ The vast majority of patients have a significant reduction in their pain postoperatively.¹⁰¹ Most experts agree that radical resection of the osteoblastoma yields the best overall outcome.^{3,10,12,14,43,53,54,67,71,103} Total excision of an osteoblastoma has been shown to have a more favorable outcome than subtotal excision (curettage) combined with radiation therapy. It has also been shown that total excision reduces relapse rates.¹⁰¹ Some authors believe that total en bloc resection is a good option when possible. A complete spondylectomy may be warranted in cases with posterior element, pedicular, and vertebral body involvement. In cases in which a substantial amount of the facet joint or pars interarticularis is disrupted, instrumented stabilization and fusion is warranted to ensure long-term stability and to prevent a progressive deformity.¹⁸

Osteoblastomas of the cervical spine may lie close to the foramen transversarium, or even encompass the vertebral artery (VA) itself (Fig. 3).⁸⁸ This poses the potential for significant morbidity if the VA is violated during the course of resection.³² In such cases in which the tumor is abutting a critical structure such as the VA, it may be a wise decision to perform an intralesional excision, as opposed to the ideally used marginal resection, so as to avoid unnecessary morbidity.⁶⁴ An alternative option is to cautiously mobilize the VA if possible, prior to excision of the osteoblastoma.⁵¹ Utilization of advanced technologies such as intraoperative navigation and/or CT scanning may assist in a safer resection of the osteoblastoma.^{77,88}

Osteoblastomas are known to be vascular tumors. Pre-operative embolization has been reported in the literature to significantly reduce intraoperative blood loss.²⁵ Meticulous dissection, ensuring that one stays outside the tumor borders, and progressive coagulation are all generally sufficient for limiting intraoperative blood loss.¹⁸ Neurosurgeons should be prepared to carefully peel tumor off the dura when resecting epidural extensions of osteoblastomas.⁸⁰

Adjuvant Therapy

Radiation therapy for spinal osteoblastomas is a controversial topic among experts. It has been reported that radiotherapy may in fact have an association with late sarcomatous change, and that it is a potentially ineffective therapeutic modality.^{41,61} Others have suggested its adjuvant use after intralesional curettage of Stage 3 osteoblastomas that may be not be surgically amenable to en bloc resection.¹¹ Radiotherapy and chemotherapy, either together or individually, have been used for patients with unresectable lesions or in cases of recurrent disease.⁵ Recurrence-free survival of up to 25 years after adjuvant radiotherapy has been reported in the literature.^{16,87} The optimal dose for radiation has been reported to be a fractionated dose of 50 Gy, giving 2 Gy for 5 days per week, over the course of 5

FIG. 3. Axial cervical spine CT scan obtained without contrast showing the same lesion causing mild stenosis of the spinal canal. The mass extends into the pedicle of C-3; these tumors may extend to the vertebral body through the pedicles. Note the close relationship of the mass with the right VA canal.

weeks.⁸⁷ Radiation therapy usually causes either arrest of the tumor's growth, or partial reduction in its size. Longitudinally, radiotherapy causes ossification of the tumor. It is rare that radiation can be successfully used as monotherapy. Radiofrequency ablation has been described as a potentially viable treatment option for spinal osteoblastomas as well, although this has not been widely used universally.⁹⁹

Methotrexate has been used as a chemotherapeutic agent within the same context as radiotherapy's use as an adjuvant treatment to surgical intervention. Others have also reported the use of polytherapy with doxorubicin, cisplatin, and methotrexate. Polytherapy has been shown to yield progression-free survival up to 33 months.^{5,15,87} Bufotalin has been investigated for its potential induction of apoptosis in osteoblastoma cells. Zhu and colleagues have demonstrated in an animal model that endoplasmic reticulum stress activation contributes to bufotalin-induced osteoblastoma cell death. This agent holds potential as an antiosteoblastoma agent in the future, once further investigations are undertaken.¹⁰² Bisphosphonate therapy has been used as a nonoperative management option for symptomatic osseous tumors such as osteoblastomas.¹⁹

Surgery

Varying surgical treatment options exist for spinal osteoblastomas.⁴⁵ Complete resection has been reported to be curative, although despite an acceptable extent of resection, recurrence rates are approximately 10%. Intralesional curettage and marginal en bloc resection are the mainstays of surgical options. Larger lesions often require a more extensive resection, which may in turn destabilize the spine, necessitating spinal stabilization (Fig. 4). Large osteoblastomas may require a 2-stage approach. Haghnegahdar and Sedighi described a large upper cervical osteoblastoma that was first approached with a posterior subtotal resection and subsequent instrumented stabilization.

This was later followed by a total resection of the remaining lesion via an approach using the natural corridor between the sternocleidomastoid muscle and the carotid sheath. An expandable cage was used for anterior column support.³⁹

The Enneking system for benign osseous tumors has been used for staging osteoblastomas.⁴⁴ The radiographic appearance of the tumor margins is the basis of this classification scheme. The 3 stages are defined as latent, active, and aggressive. In 2012, Boriani et al. described a more detailed staging system specifically for spinal osteoblastomas, which used the Enneking classification system as a foundation.⁹ Boriani et al. described Stage 2 osteoblastomas as displaying a combination of lytic and sclerotic changes, with well-defined borders. These osteoblastomas resemble osteoid osteomas, with the lytic region on the periphery of an ossified core. Stage 2 osteoblastomas do not invade the surrounding soft tissues. Stage 3 lesions are entirely osteolytic. They erode the cortical bone margins, can enter the spinal canal, and infiltrate soft tissues. The stage of the tumor plays a significant role in the surgical decision-making process. Complete marginal resection should be undertaken for Enneking Stage 1 and 2 lesions. Stage 3 lesions generally require a more extensive resection to ensure that any soft-tissue involvement is excised.^{18,47,77} Preoperative embolization of feeding vessels may be necessitated for hypervascular osteoblastomas (Fig. 5). An intraoperative bone scan can be used to ensure that total excision of the lesion has taken place.⁸⁹

Conclusions

Osteoblastomas are primary osseous neoplasms with a predilection for the spine. They can present in an insidious fashion predominantly with pain-related issues, or they may cause significant mass effect on the spinal cord leading to paralysis. Aggressive radical resection is the preferred treatment for these osseous tumors, because they do have the potential to cause local destruction, as

FIG. 4. Left: Postoperative sagittal CT scan of the cervical spine obtained without contrast. The lesion was resected and fixation of C2–3 performed. Intralesional curettage and marginal en bloc resection are the mainstay of surgical options. Extensive resection will frequently destabilize the spine, requiring spinal stabilization. Right: Postoperative axial CT scan of the cervical spine obtained without contrast. The lesion was resected and fixation of C2–3 was performed; postoperative changes related to intralesional curettage and marginal en bloc resection can be seen.

FIG. 5. Angiography study of the right VA demonstrating the significant arterial blood supply to the lesion. Preoperative embolization aids in the resection of these tumors.

well as degenerate to a more malignant tumor such as an osteosarcoma. In addition, early treatment of osteoblastomas generally leads to resolution of pain-related issues and associated scoliotic curvatures.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Conception and design: Galgano, Goulart. Acquisition of data: Galgano, Goulart, Iwenofu. Analysis and interpretation of data: Galgano, Goulart. Drafting the article: Galgano, Goulart. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Galgano. Administrative/technical/material support: Galgano, Goulart, Iwenofu. Study supervision: Chin, Mendel.

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