

Histopathological diagnosis and its correlations with anatomoclinical features, surgical approach and postoperative prognosis in sacral tumors

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Abstract

Introduction: Sacral tumors encompass numerous histopathological types. They represent an uncommon pathology and, when diagnosed, they are often in advanced stage of the disease, becoming a therapeutic challenge. The correct treatment of a sacral tumor should be established by a multidisciplinary team that will assess the exact anatomical, imagistic and histopathological characteristic of the tumors thus choosing an optimal surgical approach while taking into consideration the risk of recurrence. **Material and Methods:** We conducted a retrospective analysis of both primitive and metastatic sacral tumors in "Bagdasar-Arseni" Emergency Hospital, Bucharest, Romania, for a period of 10 years, studying demographic data, clinical signs, anatomical and histopathological features as well as surgical approach and postoperative prognosis. **Results:** Sacral tumors were diagnosed with a peak incidence in the age group 60–69 years, being more frequent in women. Primitive sacral tumor was predominant and, in this subgroup, chordoma was the most frequent. Metastatic tumors appeared in older subjects. None of the histopathological types associated a preferred topography of the resection or increased resectability. Posterior surgical approach was chosen in most cases, total resection being a hard goal to accomplish due to the invasion of vascular and nervous structures. Bleeding was the most frequently reported incident, carcinomas recording the highest blood loss amongst primitive tumors. Overall prognosis was clearly favorable for subjects diagnosed with primitive sacral tumors. **Conclusions:** Interpreting imaging data in a clinical context, paying attention to histopathological examination and knowing each histological type characteristics is mandatory in choosing the surgical approach thus obtaining the best postoperative outcome possible.

Keywords: sacrum, tumor, histology, primitive, metastatic.

✉ Introduction

Sacral tumors are rare tumors with an important histological heterogeneity [1]. On large series, sacral tumors have a frequency of one at 40 000–46 000 admissions, in adults [2]. The tumors can arise from bone tissue, cartilaginous tissue, neural tissue, vascular tissues or spinal cord and can be classified as primitive benign or malign lesions, metastatic tumors [3]. Some are proved to be extensions from cancers of nearby structures. Primitive tumors of the sacrum, either benign or malignant, represent 2–4% of total bone neoplasms and between 1–7% of primary spinal tumors [4]. The particular embryological development of the sacrum results in the possibility of development of a great variety of primitive sacral tumors [5]. The most frequent benign sacral tumors are giant cell

tumors (GCTs) [6, 7], aneurysmal bone cyst and osteoblastoma [5]. Amongst malignant sacral tumors, chordomas are most common (40%), followed by lymphoma, multiple myeloma, osteosarcoma, Ewing sarcoma in young patients and chondrosarcoma in elderly patients [7]. Approximately half of sacral tumors are metastatic, originating from pulmonary tumors, sarcomas, breast cancer, prostatic or rectal cancer [8]. Being frequently asymptomatic, these tumors are often late diagnosed (when nerve roots or surrounding structures are involved), their management representing a complex medical challenge [9].

✉ Materials and Methods

A retrospective analysis of the clinical data between January 1st, 2005 and December 31st, 2015 was performed.

We included all patients that suffered a surgical intervention for sacral tumors. A total number of 85 consecutive patients were enrolled in the study. A complete evaluation included the demographic data, the symptoms, the histopathological features of each resected tumor, the tumors topography and anatomical features, surgical approach, intraoperative aspects as well as biological status and postoperative prognosis and their correlation with the histopathological type. For analyzing the obtained data, we used Microsoft Excel "Analyse it".

Results

Clinical profile

The studied group was first of all divided in two subgroups, depending on the tumor origin. Thus, almost two-thirds of the patients had primitive tumors of the sacrum, the rest of the cases presenting secondary tumors of malignant proliferations primarily developed in other tissues or organs (Figure 1).

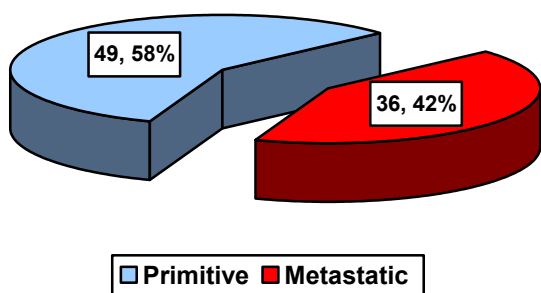


Figure 1 – Classification of sacral tumors.

Gender distribution

Two-thirds of the patients were women, and the proportion has been preserved in both primitive and metastatic tumors (Figure 2).

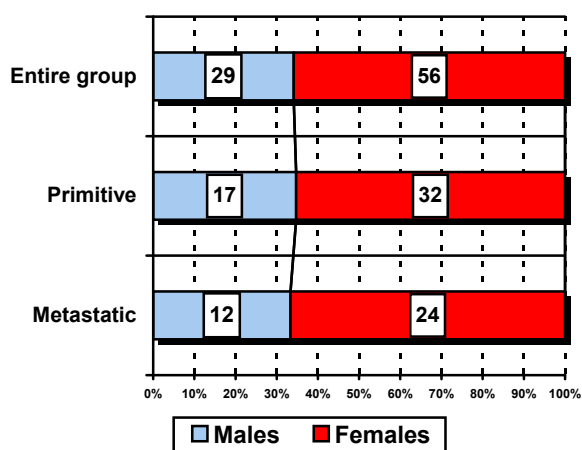


Figure 2 – Gender distribution.

Age distribution

Although the general mean age was around 53 years (with the youngest patient having 20 years and the oldest patient having 80 years), there was a clear difference between the patients with primitive tumors and those

with metastases concerning the age. Thus, whereas the former had a mean age of around 47 years within a wide range (between 20 and 78 years), the latter were usually elderly people, with a mean age of 63 years and a narrower range having the lowest limit at 49 years ($p < 0.0001$) (Figure 3).

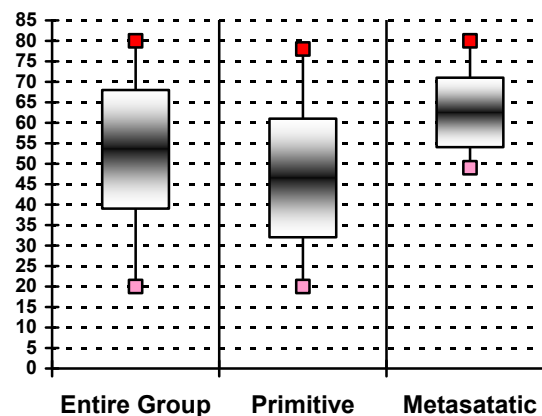


Figure 3 – Mean age in patients with metastatic tumors vs. primitive tumors.

Dominant symptom

The most frequently encountered symptom at the admission in both primitive and metastatic tumors was the pain (84.7% for the entire group and around 90% for the metastatic group), with a wide range of clinical variants: sciatica, low back pain, coccydynia, buttock pain, perianal pain and radicular pain (Figure 4).

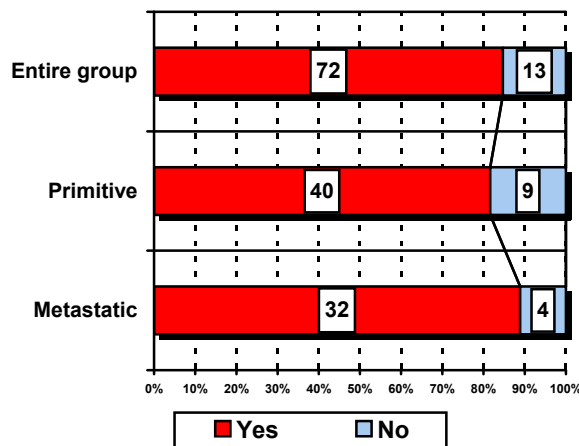


Figure 4 – Presence of pain.

Morphological profile

Tumor site and dimensions

Depending on their extension within the sacrum, tumors had a wide range of dimensions, from localization to only one or two sacral vertebrae until the involvement of the entire bone (Figure 5).

When diagnosed, the majority of patients presented with large tumors, extended to at least two vertebrae. Tumors involving the bone from the first to the fifth sacral vertebrae (all) were encountered in around 18% of cases ($p < 0.02$) more frequently in the metastatic tumors.

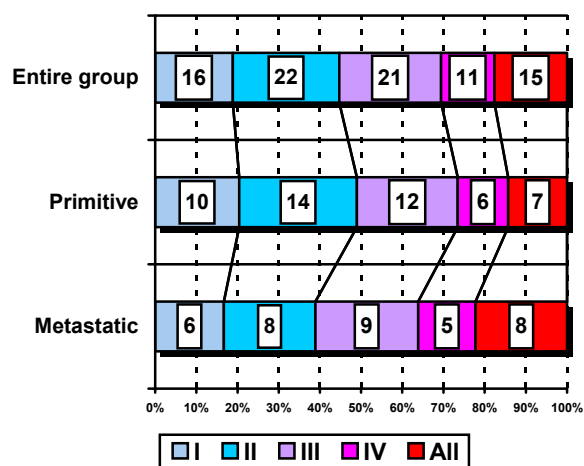


Figure 5 – Tumor extension within the sacrum.

When only one vertebra was involved (I), it was only in the upper part of the sacrum, usually the first (S1) followed by the second (S2) sacral vertebra. When two vertebrae were involved (II), the upper segment of the sacrum was involved, usually the first two sacral vertebrae. The same situation was when three vertebrae were involved, those being usually the first three sacral vertebrae (S1–S3).

There was no preferential localization within the sacrum of primitive tumors compared with metastatic tumors. Only few tumors developed on the ventral side of the sacrum (10.6%).

Tumor extension

Two aspects of tumor extension were assessed: the invasion of spinal nerves roots and the invasion in the nearby structures.

Radicular invasion was in most of the cases bilateral (72.9%; $p < 0.0001$) whether the tumor was primitive or metastatic. When unilateral, primitive tumors specially were prevailing in the right side (Figure 6).

The extension outside the sacral bone was present in almost two-thirds of the cases, involving in two of three cases only one of the neighboring structures (Figure 7).

The most affected tissue structures were those of the pelvic cavity (like rectal wall, blood vessels, uterus in women and prostate in men), either alone or in association with other extensions (38.8% of patients; $p < 0.0001$).

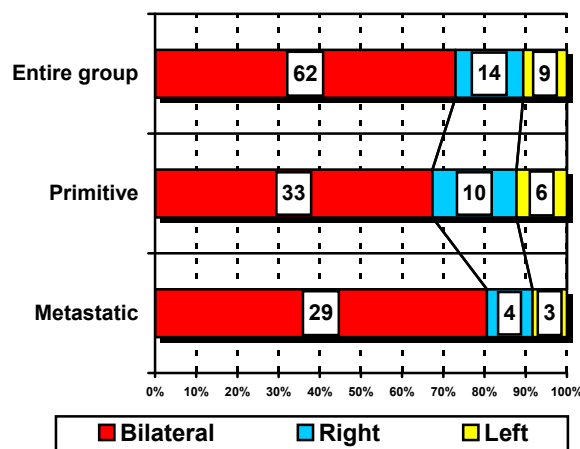


Figure 6 – Radicular involvement.

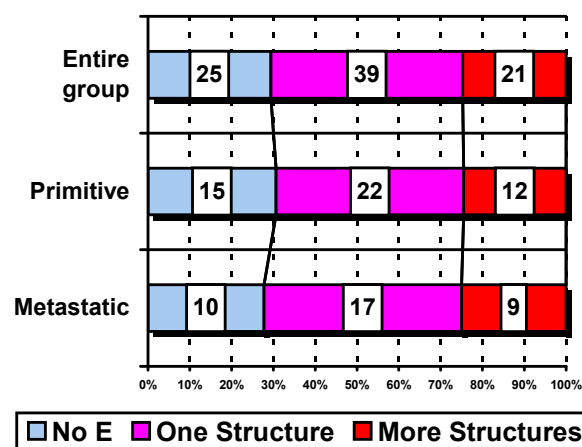


Figure 7 – Local extension.

Other frequently invaded neighboring structures were the lumbar spine, sacral iliac joint and iliac bone, both in primitive and metastatic tumors (Figure 8).

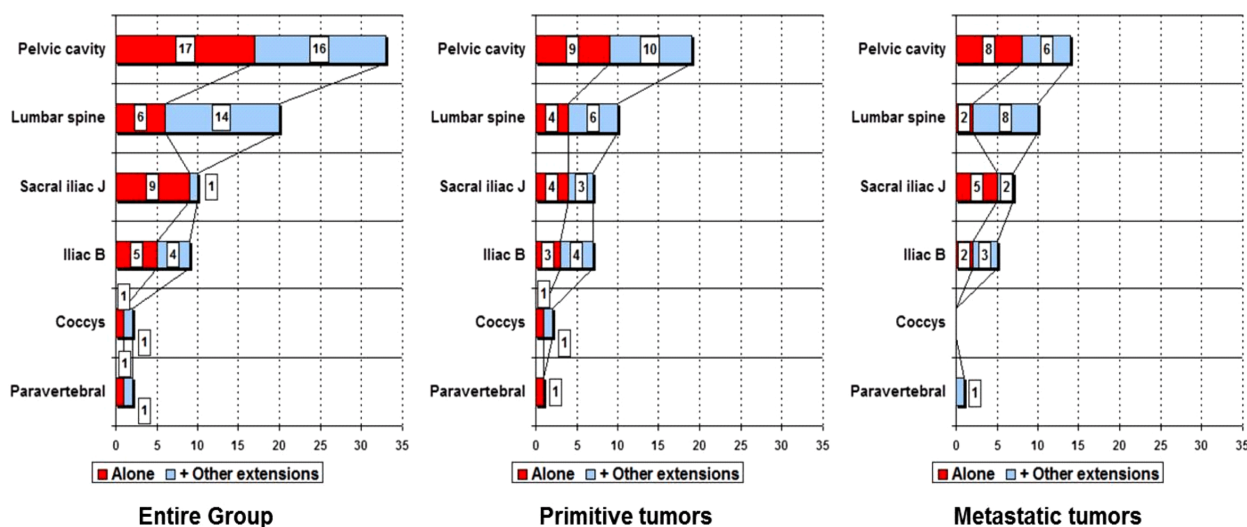


Figure 8 – Sites of local extension of sacral tumors.

Histopathological type

The majority of investigated tumor formations located at the sacral level were malignant neoplasms. However, 10% of them were non-neoplastic proliferations represented by cystic formations and hamartomas (Figure 9).

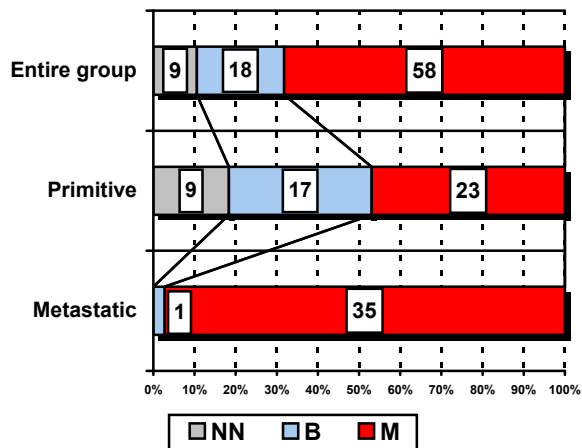


Figure 9 – Tumor histogenesis.

Primitive tumor formations included besides malignant neoplasia an important percentage of benign neoplasia and all non-neoplastic conditions whereas metastatic tumors were with only one exception malignant proliferations.

Primitive tumors

Histopathological examination of the resected specimen showed a high variety of histopathological entities amongst primary sacral tumors (Table 1).

Table 1 – Primary sacral tumors

Primary sacral tumor	No. of cases	%
Chordoma (Ch)	11	22.6
Schwannoma (Sch)	8	16.3
Ewing's sarcoma (Ew)	6	12.3
Tarlov cyst (Tc)	4	8.2
Neurofibroma (Nf)	3	6.1
Epidermoid cyst (Epc)	2	4.1
Hamartoma (H)	2	4.1
Plasmacytoma (P)	2	4.1
Rhabdomyosarcoma (R)	2	4.1
Giant cell tumor (Gct) (Osteoclastoma)	2	4.1
Endodermal cyst (Enc)	1	2.0
Myxopapillary ependymoma (Me)	1	2.0
Fibrolipoma (F)	1	2.0
Primitive neuroectodermal tumor (PNET)	1	2.0
Teratoma (T)	1	2.0
Non-Hodgkin's lymphoma (NHL)	1	2.0
Osteoblastoma (O)	1	2.0

The most frequent primitive sacral tumor in our subjects was **chordoma** (Figure 10, a and b), with more than one fifth of the cases ($p < 0.0001$).

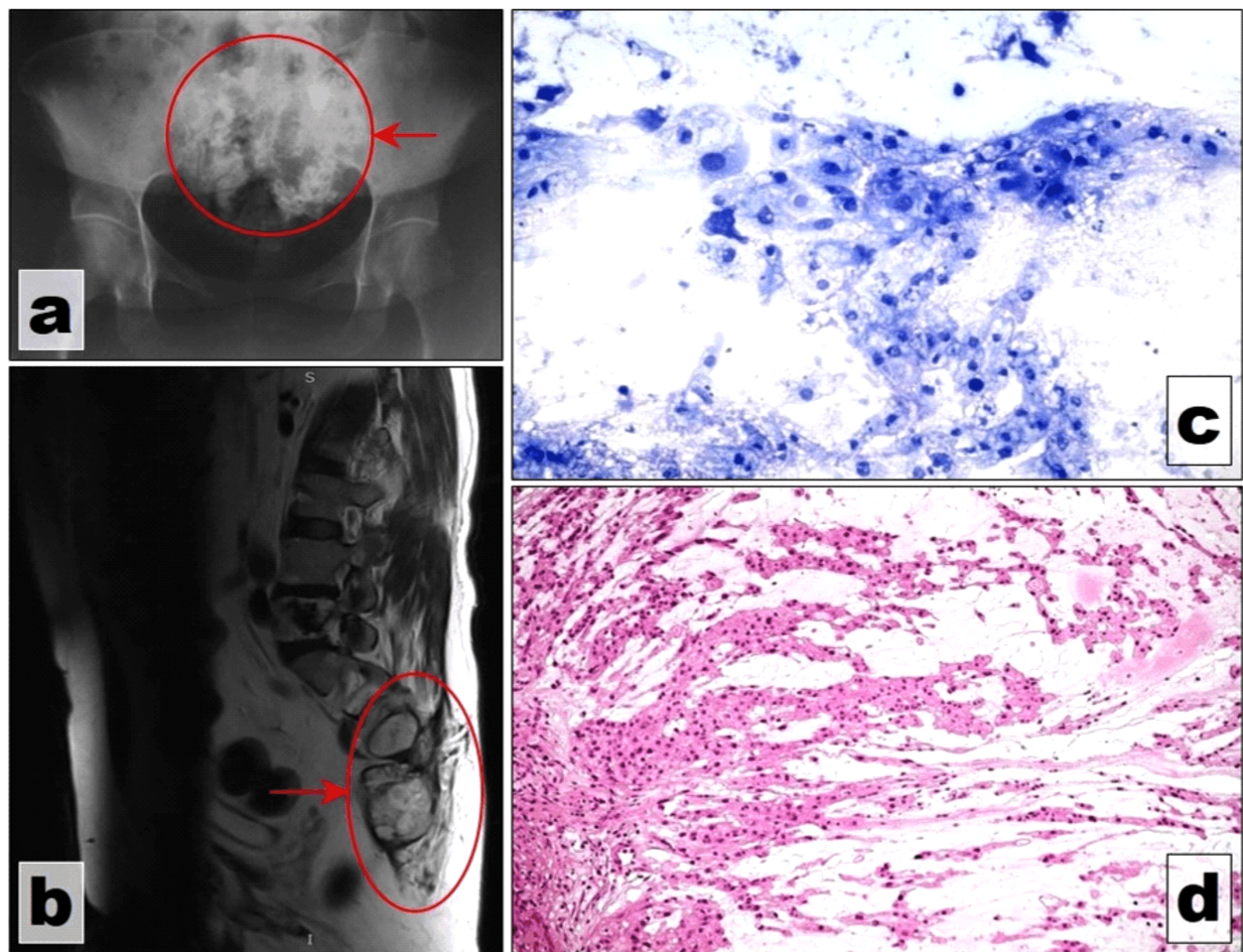


Figure 10 – Chordoma: (a) Giant sacral tumor – conventional X-ray; (b) Magnetic resonance imaging (MRI) examination of an operated, recidivated chordoma; (c) Frozen section – Toluidine blue staining, $\times 400$; (d) Histopathological aspect – Hematoxylin–Eosin staining, $\times 200$.

Histopathological examination performed during surgical intervention on frozen sections not only established a positive diagnosis but could also establish the margins of resection, further emphasizing the need for this type of intraoperative histopathological sampling. The characteristic aspect was suggested by the association of a well-contoured cytoplasmic membrane and a clear, vacuolated cytoplasm (Figure 10c).

Paraffin embedded sections stained with Hematoxylin–Eosin (HE) revealed the highly specific physaliphorous cells, with epithelial morphology, large, having centrally located, prominent, vesicular nucleus, vacuolated cyto-

plasm, disposed together in cords or lobules separated by fibrous septa with extensive myxoid stroma or isolated, floating in a mucous stroma (Figure 10d).

Schwannoma (Figure 11a) and Ewing's sarcoma (Figure 10, b and c), together, were diagnosed in more than a quarter of our subjects.

Schwannoma could easily be recognized by the alternation of Antoni A areas, consisting of compact spindle cells, highly ordered in palisades, forming Verocay bodies, with Antoni B, hypocellular areas with myxoid component (Figure 11a).

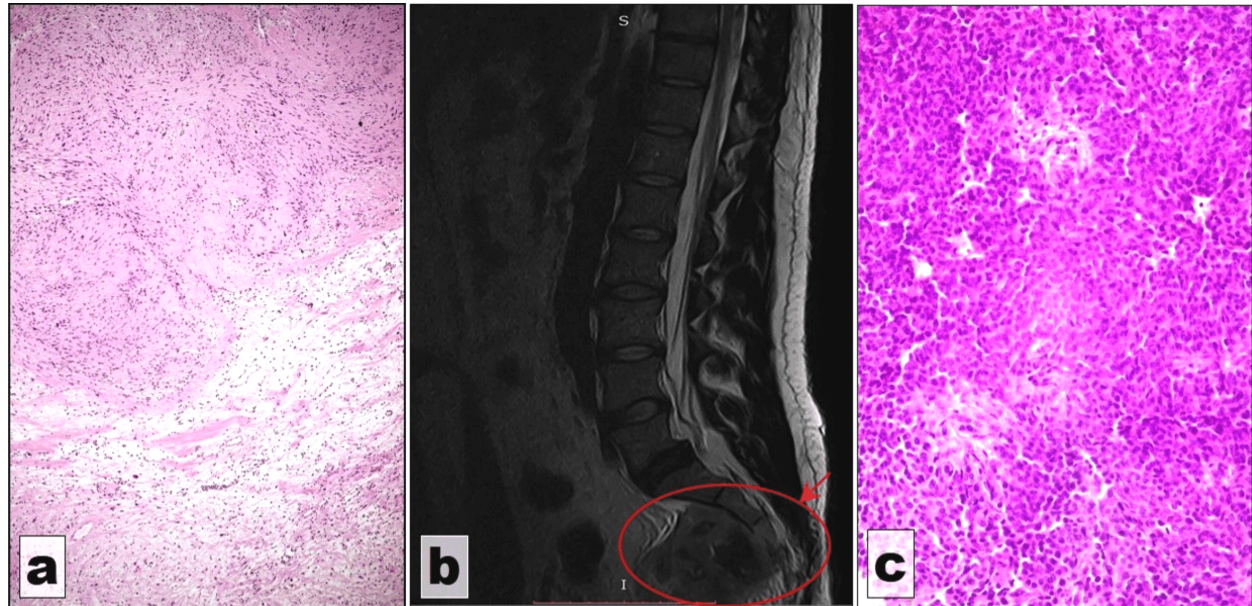


Figure 11 – (a) Schwannoma – proliferation of Schwann cells forming Verocay bodies in Antoni A regions (top left) and Antoni B regions (middle right), HE staining, $\times 100$; (b) Ewing's sarcoma – MRI examination: tumor with T1 low signal; (c) Ewing's sarcoma – histopathological aspect, HE staining, $\times 400$.

In its turn, the classical Ewing's sarcoma could be recognized by its appearance as compact sheets of small, round, uniform blue cells with scant clear cytoplasm and indistinct cell membranes, separated by delicate fibrous septa with rare perivascular disposition (Figure 11c).

Tarlov cysts were encountered in four cases, three of them arising at the S2 junction of the dorsal nerve root ganglion. Histological examination revealed an outer wall composed of vascular connective tissue, and an inner wall lined with flattened arachnoid tissue. Some of the lining nerve fibers contained ganglion cells.

Neurofibromas were present in three patients, two of them having large dimensions with tortuous enlargement of peripheral nerves. The histological examination showed proliferation of all elements of peripheral nerves with an infiltrative pattern and myxoid areas but with no Verocay bodies, no nuclear palisading and no hyalinized thickening of vessel walls.

We also found less frequent histopathological types such as epidermoid cyst (Figure 12a), plasmacytoma (Figure 12b), myxopapillary ependymoma (Figure 12c), non-Hodgkin's lymphoma (Figure 12d), osteoblastoma (Figure 12e).

In the two epidermoid cysts discovered, the patho-

gnomonic aspect of keratinized multistratified squamous epithelium with a core of keratin plates was seen (Figure 12a). Plasmacytoma, observed also in two cases, appeared as a solid mass composed of monomorphic population of neoplastic monoclonal plasma cells (extra-medullary) (Figure 12b).

Myxopapillary ependymoma, encountered in a 22 years old male patient, presents the typical histopathological aspect with trabecular bone lamellae destroyed by ependymal cells with predominant perivascular disposition and hyaline deposits in vascular walls. Fibrillary myxoid stroma containing cells with elongated cytoplasmic processes lying in a rosette-like pattern around central cores of myxoid to fibrillary type is seen (Figure 12c).

Another rare tumor, observed in a young woman, 22 years old, was the malignant non-Hodgkin's lymphoma. Histological examination revealed diffuse proliferation of lymphoid cells showing clear signs of malignancy (Figure 12d). Finally, in a 22 years old woman, we found an osteoblastoma whose histological aspect showed thin bone lamellae with irregular disposition, large osteoblasts with eccentric cytoplasm and perinuclear nuclei and vascular spindle cell stroma with osteoblasts and rare osteoclasts (Figure 12e).

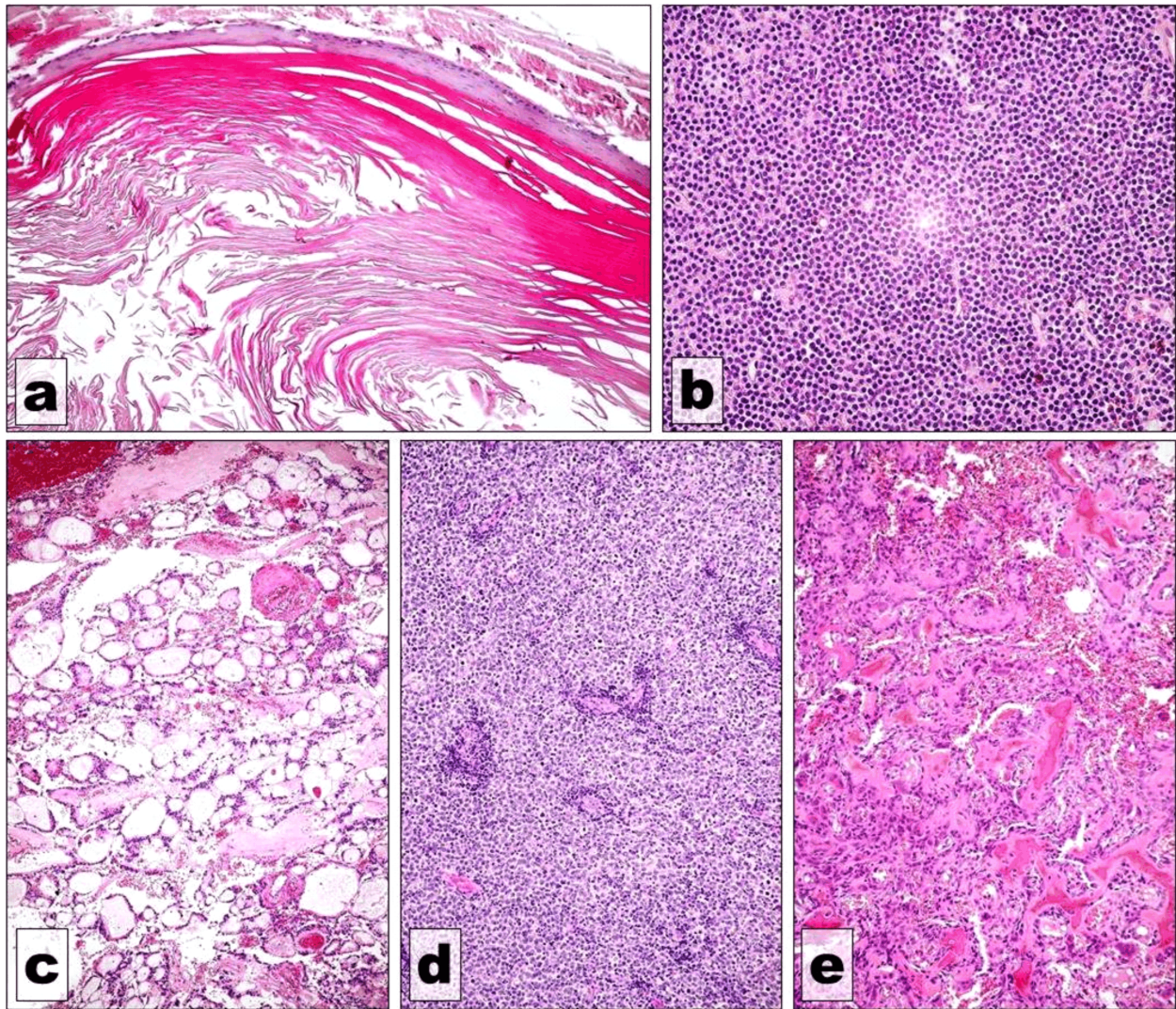


Figure 12 – (a) Epidermoid cysts; (b) Plasmacytoma; (c) Myxopapillary ependymoma; (d) Non-Hodgkin's lymphoma; (e) Osteoblastoma. HE staining: $\times 100$ (d and e); $\times 200$ (a–c).

Metastatic tumors

Most cases of metastatic sacral tumors derived from adenocarcinomas, more precisely from colon adenocarcinomas (ADK) (53%; $p < 0.0001$). On the second place, came other types of carcinomas (C) (Figure 13).

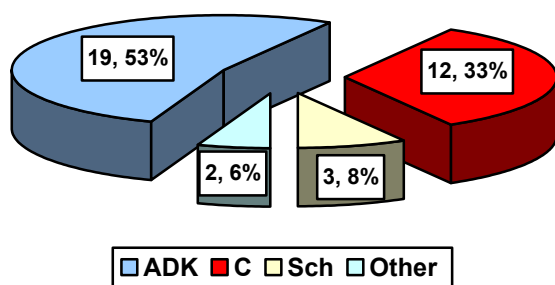


Figure 13 – Primitive tumor for metastatic sacral tumors.

In Figure 14 is presented such a metastasis of a lung moderately differentiated squamous lung carcinoma whose microscopic aspect shows increased proliferation of malignant epithelial cells, invading bone tissue. Less

frequent, sacral tumors derived from angiomyolipomas and medulloblastomas (reaching a percentage of 1.3% each).

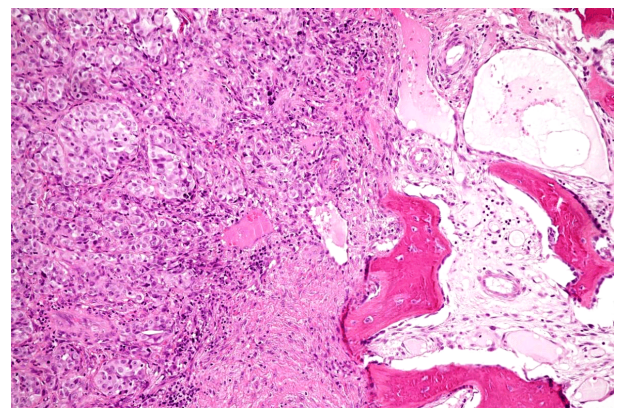


Figure 14 – Bone metastasis of lung carcinoma, HE staining, $\times 100$.

Therapeutic approach

Surgical approach

All subjects were undergoing surgery.

Posterior surgical approach was chosen in the majority of cases for all categories of sacral tumors (87.1%; $p<0.0001$), both for primitive and metastatic tumors (Figure 15a). **Transabdominal approach** (Figure 15b) was indicated for tumors higher than S4 vertebrae, without nerve root involvement.

Data analysis did not show a preferred level of resection. As far as the degree of resection was concerned, we were able to perform mainly partial resection for

primitive tumors (38 partial resections for primitive tumors, 34 partial resections for metastatic tumors; $p<0.077$).

In most of the patients with metastatic disease, the decision was to biopsy the metastatic site.

Total resection was performed in 11 subjects with primitive tumors and only one subject with metastatic disease ($p<0.0126$).

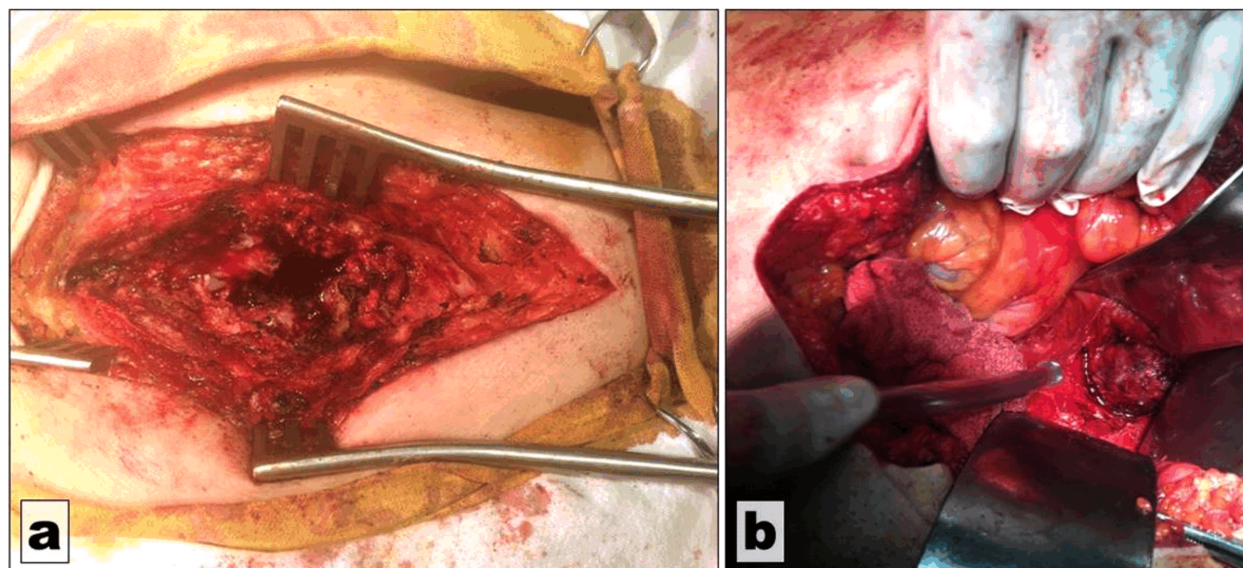


Figure 15 – (a) Posterior approach of a sacral tumor; (b) Anterior approach in a sacral Ewing sarcoma.

Patient outcome

All of the patients, whether experiencing only local or radicular pain prior to the surgical intervention, showed substantial postoperative pain relief. The *Visual Analog Scale* (VAS score) was significantly lower after surgical intervention (postoperative VAS=40 mm vs. preoperative VAS=60 mm; $p<0.0001$). On the other hand, the comparison between the *American Spinal Injury Association* (ASIA) *Impairment Scales* before and after surgical intervention did not show significant changes.

The most common intraoperative incident was bleeding (Figure 16) with similar need for blood transfusion for primitive and metastatic tumors (mean need for blood transfusion of 2.2 and 2.15 units respectively).

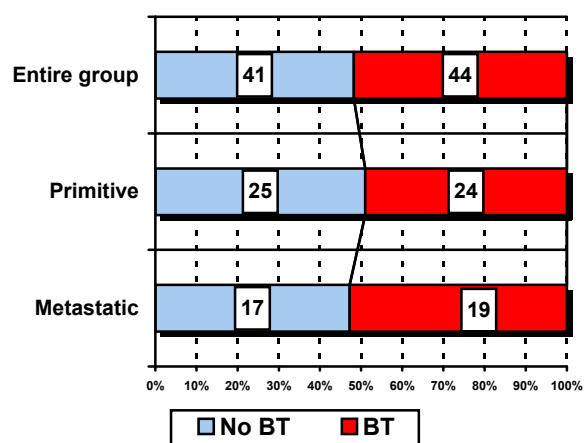


Figure 16 – Distribution of blood transfusion (BT) need.

Incidental dura mater opening was reported as the second most common intraoperative incident in nine subjects suffering from primitive sacral tumors. Contrariwise, this incident was reported in only one patient with metastatic sacral tumor ($p=0.330$) (Figure 17).

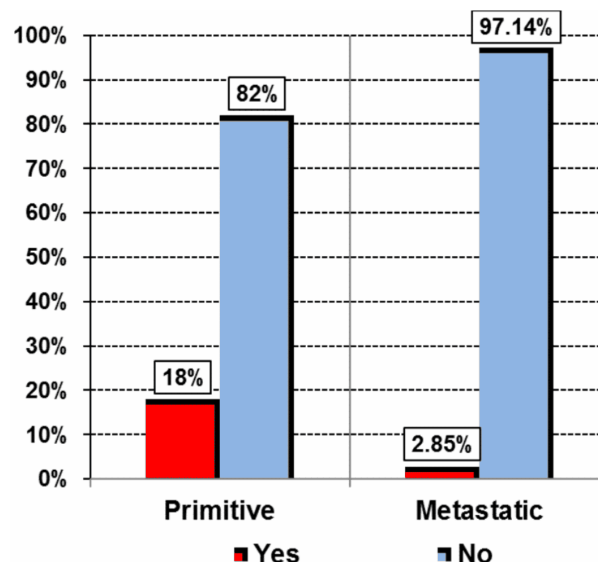


Figure 17 – Opening of the dural sac.

The subject's outcome was quantified utilizing the postoperative neurological status. Postoperative neurological status was carefully assessed and was not clear-cut favorable neither for primitive nor for metastatic sacral tumors.

The overall prognosis of subjects suffering from primitive tumors was clearly favorable compared to

subjects with metastatic disease (10 patients with primitive tumors were declared cured compared to only one patient with metastatic disease; $p < 0.0190$).

The need for postoperative oncological treatment was lower in primitive sacral tumors compared to metastatic tumors as primitive sacral tumors were mostly benign (17 patients with primitive tumors did not require oncological treatment after definitive histopathological diagnosis).

Clinical morphological correlations

Gender–histopathological type

Histological classification did not reveal a preferential occurrence of any of the histopathological types in male or females.

Age–histopathological type

Studying age-specific prevalence of each histopathological type, we discovered that chordoma is appeared more likely between 45 and 63 years, with a mean age of 54 years.

It was followed by schwannoma (both primitive tumors and metastases of a malignant schwannoma) with a mean age of 52 years but a larger range (between 38 and 78 years).

Meanwhile, Ewing's sarcomas were present in younger patients, with a mean age of 36 years and a range between 21 and 53 years (Figure 18).

Metastases from both adenocarcinomas and carcinomas had a mean age of 63 years, higher than all the primitive tumors and also ranges of cases starting from 49–50 years and going to 80 years (Figure 18).

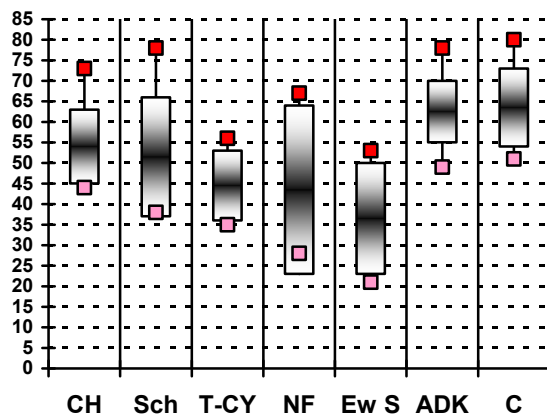


Figure 18 – Mean age in different histopathological types of primitive tumors.

In isolated malignant tumors, except non-Hodgkin's lymphoma, found in a young patient, all the other tumors appeared in adults and elderly, even the patient with metastasis of a medulloblastoma (Table 2).

Among benign tumors, those arising from immature cellular lines appeared in young patients, whereas the rest appeared usually after 51 years, including the patient with angiomyolipoma.

The non-neoplastic conditions had no preference for any age group except hamartomas, who were found in patients younger than 40 years.

Table 2 – Patients' ages in isolated cases of sacral tumors

Sacral tumor	No. of cases	Age [years]
MALIGNANT		
Rhabdomyosarcoma (R)	2	41, 59
Plasmacytoma (P)	2	45, 72
Primitive neuroectodermal tumor (PNET)	1	54
Medulloblastoma (metastasis)	1	49
Non-Hodgkin's lymphoma (NHL)	1	22
BENIGN		
Giant cell tumor (Gct) (Osteoclastoma)	2	37, 51
Fibrolipoma (F)	1	54
Teratoma (T)	1	61
Angiomyolipoma (metastasis)	1	55
Osteoblastoma (O)	1	20
Myxopapillary ependymoma (Me)	1	22
NON-NEOPLASTIC CONDITIONS		
Epidermoid cyst (Epc)	2	28, 67
Hamartoma (H)	2	27, 37
Endodermal cyst (Enc)	1	63

Site–histopathological type

Only few tumors developed on the ventral side of the sacrum (10.6%), with no predominant histological type in this group. Furthermore, the study of various histopathological types did not reveal preferential tumor topography within the sacrum for any of the encountered entities.

Radicular involvement–histopathological type

Radicular involvement varied with histopathological features in primitive sacral tumors, many of them having bilateral or unilateral root involvement (Table 3).

Table 3 – Frequency of bilateral nerve roots involvement

Primary sacral tumor	No. of cases	%
Chordoma	11(11)	100
Tarloc cyst	4(4)	100
Epidermoid cyst	2(2)	100
Rhabdomyosarcoma	2(2)	100
Endodermal cyst	1(1)	100
Myxopapillary ependymoma	1(1)	100
Fibrolipoma	1(1)	100
Neurofibroma	2(3)	66.7
Schwannoma	5(8)	62.5
Ewing's sarcoma	3(6)	50
Carcinoma	1(2)	50
Hamartoma	1(2)	50
Plasmacytoma	0(2)	0
Giant cell tumor	0(2)	0
Non-Hodgkin's lymphoma	0(1)	0
Osteoblastoma	0(1)	0
Primitive neuroectodermal tumor (PNET)	0(1)	0
Teratoma	0(1)	0
Total	34(51)	66.67

Local extension–histopathological type

Primitive and metastatic sacral tumors were equally extensive in the nearby structures. However, differences

were recorded in the group of primitive tumors. Thus, the majority of tumors did not differ in subclinical extension, whereas the greater extension of chordomas and Ewing sarcomas (especially in the small pelvis) was highly significant ($p=0.00118$).

Surgical approach–histopathological type

Whether the tumor was resected entirely or only a partial resection or biopsy was performed, we found no preferred topography of the resection in any of the histopathological types. Moreover, there was no apparent correlation in this series between the tumor localization and extension and the histological type.

We did not encounter any histopathological type associated with increased resectability. No differences in resectability were demonstrated in various tumors. Less extensive tumors were proved to be as hard to resect as more extensive tumors, because of their constant nervous invasion despite maybe smaller dimensions. Furthermore, the subjects having a less extensive tumors for which the surgical team was able to perform a wider resection did not show significant improvement in postoperative neurological status.

Blood loss was not correlated with the patient's age and genre. An evaluation of intraoperative blood loss for each histopathological type was performed. Amongst sacral tumors, carcinomas recorded the highest blood loss (mean need for blood transfusion of 4.5 units; $p<0.0001$) (Figure 19).

Among the isolated tumors, the patients with PNET, osteoclastoma, myxopapillary ependymoma, teratomas and hamartomas needed an important intraoperative blood supply (Table 4).

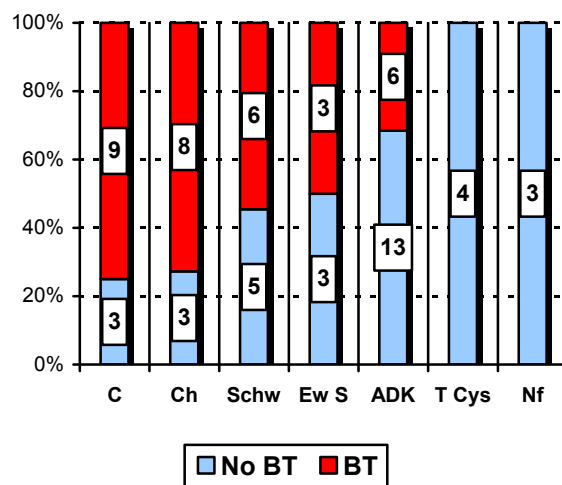


Figure 19 – Blood transfusion (BT) need in different histopathological types of tumors.

Table 4 – Blood transfusion (BT) need in isolated histopathological types of tumors

Sacral tumor	No. of cases	BT (AV)
MALIGNANT		
Primitive neuroectodermal tumor (PNET)	1	3
Rhabdomyosarcoma (R)	2	1.5
Plasmacytoma (P)	2	1
Medulloblastoma	1	1
Non-Hodgkin's lymphoma (NHL)	1	No

Sacral tumor	No. of cases	BT (AV)
BENIGN		
Giant cell tumor (Gct) (Osteoclastoma)	2	No, 5
Myxopapillary ependymoma (Me)	1	3
Teratoma (T)	1	3
Fibrolipoma (F)	1	No
Osteoblastoma (O)	1	No
NON-NEOPLASTIC CONDITIONS		
Hamartoma (H)	2	2.5
Epidermoid cyst (Epc)	2	No
Endodermal cyst (Enc)	1	No

Discussion

Given the fact that they are rare, and with a high variety of histopathological types, sacral tumors remain a diagnostic and therapeutic challenge [10].

In the study group, median age of patients was 53.3 years (minimum 20, maximum 80) with a predominance of females (56 vs. 29 males; $p=0.0034$). Because of the substantial extension of the tumor at the time of the diagnosis, in the majority of cases with bilateral radicular involvement and nearby organs invasion, subjects were symptomatic, presenting with sciatica, low back pain, coccydynia, buttock pain, perianal pain and radicular pain. The symptoms were significantly reduced after surgery. Thus, results showed statistically significant differences between preoperative and postoperative pain (VAS score). Preoperative and postoperative motor deficit did not differ significantly (ASIA score).

Primitive tumors

More than half of patients (58%) had primitive sacral tumors, value consistent with those presented in the literature according to which two-thirds of sacral tumors are primitive [1].

Chordoma

The most frequent malignant tumor is represented by chordoma [11–14]. Chordoma is also the most common primitive sacral tumor, representing 40% of all sacral tumors [7]. The incidence of sacral chordoma is approximately 0.02–0.03 per 100 000 people being more common in male patients over 40 years of age [6].

Our study group analysis showed the appearance of chordoma in subjects older than 44 years, with an equal gender repartition and a slightly lower frequency compared to other studies (22.6% of primitive sacral tumors).

Schwannoma

Schwannomas, also named as neurinomas or neurilemmomas, are well defined, encapsulated, round or fusiform benign tumors characterized by a low growth rate. [15]. They originate from Schwann cells being classified as histological grade I [16]. They can reach dimensions up to 10 cm [17] and represent 8% of total intracranial neural tumors, 85% of cerebellopontine angle tumors and 29% of root nerve tumors, 4% of them being associated with type 2 neurofibromatosis [16].

In our study, schwannoma represented slightly more than 16% of all primitive sacral tumors, with a peak in

incidence between 38 and 78 years of age (mean age 52 years), but more common in women (six women vs. two men).

Surgical treatment is required when they become symptomatic and recurrence can raise suspicion of malignant transformation [18].

Extremely rare in children, they reach a peak of incidence between 40 and 60 years [6], with no clear consensus on predilection for one of the genders. Some studies note that schwannomas are equally distributed across different gender [19], while other studies [6] show a heavier predominance of males.

Ewing sarcoma

Ewing sarcoma is even rarer tumor, often diagnosed in young patients, in the first two decades of life [20].

In our study, Ewing sarcoma is the third most frequent primitive tumor. It appeared in majority of cases in women, with a mean age of 36 years (with the youngest patient being 21 years of age and the oldest patient being 53 years of age).

Tarlov cyst

This type of tumor has a reported prevalence of 4–9%, mostly in women, often being clinically silent [21]. Four of the patients suffering from primitive sacral tumors had Tarlov cysts. All of them were women, with a medium age of 44 years.

Neurofibroma

Neurofibromas pertain to the class of neurogenic benign tumors (along with perineurinoma and schwannoma). They may appear as unique entities or with multiple localizations. As far as histological grading is concerned, neurofibromas pertain to grade I. They have a small potential of proliferation, being able to be cured with surgical resection. Surgical resection may result however in postoperative neurological deficit [16]. The study of the resected tissue shows Schwann cells, “perineural-like cells” and fibroblasts [8, 16]. Three of the primitive sacral tumors in our group were neurofibromas, two of them belonging to men and having no preference for an age group.

Other tumors

Epidermoid cysts are rare cystic tumors resulting from dysembryogenesis, mostly diagnosed in middle aged women. They are benign and unilocular [22]. Contrary to what we might expect from studying other articles written on this pathology, epidermoid cysts occurred equally in both genders, a 28 years old woman and a 67 year old man.

Retro-rectal cystic hamartoma (tailgut cyst) is a benign congenital tumor of the presacral space (retrorectal space). It has a high potential of malignant transformation into adenocarcinoma or carcinoid tumor. This occurs especially in male subjects, frequently being asymptomatic and therefore hard to diagnose [23]. They appear mostly as well defined tumors, with thin walls. They may be uni- or multi-locular [24]. Two of primitive tumors in our group were hamartomas, being equally distributed by gender. They were diagnosed mainly in young subjects (mean age of 32 years).

Plasmacytoma is a rare tumor, associating, in most patients, a systemic latent disease. It may be singular counterpart of multiple myeloma [25]. We encountered plasmacytomas in two patients between one man of 45 years old and one woman of 72 years old, in which electron microscopy showed eccentric nuclei and characteristic “clock face” chromatin pattern.

Primitive rhabdomyosarcoma of the sacrum represents less than 2% of total sarcomas in adults [26]. Histological examination of the tumor usually shows proliferation of spindle-shaped cells intermingled in a fascicular and storiform growth pattern too. Tumor cells, named rhabdomyoblasts are recognized by their immunoreactivity for desmin, vimentin, sarcomeric actin, muscle-specific actin, CD99 and alpha-smooth muscle actin [27]. Two of the diagnosed primitive sacral tumors were rhabdomyosarcomas. They were diagnosed at one 40-year-old male patient and a 59-year-old woman.

Giant cell tumor (GCT) is the most frequent benign tumor of the sacrum [28]. It represents a relatively frequent osseous tumor. When localized in the spine, it is mostly present in the sacrum [6, 7]. In our group, GCT was present in two of patients with primitive sacral tumors, appearing between 30 and 55 years of age and being equally distributed by gender.

Endodermal spinal cysts are congenital lesions. Usually, they are incidentally diagnosed at young adults without a typical clinical picture [29]. Among our subjects, we diagnosed only one case of sacral endodermal cyst (male, 63-year-old), so being confirmed the rare appearance of the lesion.

Myxopapillary ependymoma is a rare type of neoplasm, mostly localized in *cauda equina* and *filum terminale*, being characterized by production of mucin and formation of papillae. Even though it has benign features, disseminations and metastases have been localized along the cerebrospinal axis, sometimes at a certain distance one from another [30]. In our series, we identified such a tumor in a 22 years old woman.

Fibrolipomas belong to non-neurogenic benign tumors, along with lipomas, *myositis ossificans* and hemangiomas [31]. Fibrolipoma of the *filum terminale* is a congenital asymptomatic lesion (this implies a differential diagnosis with intradural lipomas which are symptomatic), incidentally discovered at children and adults, both genres [32, 33]. Among our patients, a female patient, aged 54 was diagnosed with fibrolipoma.

Chondrosarcoma is the second most frequent malignant bone tumor in adults, with an incidence of 0.8 per 100 000 people [34]. Of total chondrosarcomas, 5% are located in the sacrum. Another entity is represented by primary pelvic chondrosarcomas that invade the sacrum (25% of the total number of chondrosarcomas). Survival rate is influenced by the histological grade, the tumors localization. Generally speaking, pelvic and sacrum chondrosarcomas have a poor prognosis [35, 36]. We encountered no subjects pertaining to this histopathological type.

Perineurinomas are neurogenic tumors, together with neurofibromas and schwannomas. They represent benign rare tumors, reaching a total of 5% of neural tumors [37]. Their origin is in perineural cells, more precisely

in cellular layer proliferation in the endoneurium, determining a specific aspect of "onion bulb" [38]. They pertain to histological grade I [16]. They reach a high incidence in children and young adults, without predisposing a certain genre [39]. The treatment consists in surgical resection followed by a low rate of recurrence [40]. In the group of neurogenic tumors, the malignant entity is called malignant peripheral nerve sheath tumors (MPNSTs) [41].

Primitive neuroectodermal tumor (PNET) of the spine was recently included in the family of Ewing's sarcomas due to the way it develops, biological traits and histological similarities including the expression of p30/32 glycoprotein (CD99) [42]. Recent studies mention few cases of PNET/Ewing's sarcoma with sacral localization [43–46]. Due to high addressability for rare vertebral tumors at our Center, we were able to register one case of PNET, in a 54-year-old patient.

The most frequent primitive sacral tumor in young subjects is **teratoma** [47]. Unexpectedly, in our study group, teratomas did not occur in young patients. Our case of teratoma was a 61-year-old female.

Other types of neoplasms such as hemangiomas, angiosarcomas, nerve sheath tumors, multiple myeloma and lymphoma may also appear as primitive sacral tumors [5].

Many other types of osseous tumors such as osteoblastomas, osteosarcomas or osteochondromas may be localized in the sacrum. Sacral **osteoblastomas** represent 7–17% of all osteoblastomas [48]. Among our patients, we diagnosed one case of osteoblastoma in a 20-year-old female.

Metastatic tumors

Metastatic vertebral tumors are localized in the thoracic and lumbar spine, followed by lumbosacral junction and sacrum [49]. Almost half of sacral tumors are metastases originating from pulmonary tumors, sarcomas, breast cancer, prostatic tumors and rectal tumors [8]. Sacral metastases are often osteolytic, excepting metastasis from lung cancer. Breast cancer represents another entity generating osteoblastic lesions [50].

We found 42% metastatic tumors amongst all sacral tumors. The majority of primary tumors were adenocarcinomas, followed by carcinomas, MPNSTs, medulloblastoma and angiomyolipoma.

Adenocarcinoma

Colon adenocarcinomas with osseous metastasis are usually associated with unfavorable prognostic [51]. More than half of our patients with metastatic tumors had sacral tumors derived from a colon adenocarcinoma. Feiz-Erfan *et al.* conducted a study on 25 patients over a period of 12 years. They found that renal carcinoma is the main primary tumor for sacral metastasis [52].

Carcinoma

Carcinomas appear in the sacroccocygeal area as result of rectal tumors directly invasive into the sacrum, usually invasive rectal carcinomas [5]. Jaureguizar *et al.* discovers in newborn up to 21% malignant tumors, including embryonal carcinoma, in a study conducted

for 15 years [53]. In our group, carcinomas were the second most frequent tumors generating sacral metastases in one third of the metastatic tumors.

The patients had a medium age of 57 years, being both males and females.

Malignant schwannoma

Malignant schwannoma, also known as **malignant MPNST**, is a rare tumor with an incidence of 1:100 000 developing from pre-existent neurofibromas after spontaneous mutations [54]. It originates from the extremities and trunk, usually the sciatic nerve, brachial plexus, and sacral plexus, the sacral incidence being the lowest [55].

They may sometimes have similar macroscopic aspect as neurofibromas, the malignant transformation being suggested by rapid growth of a structure with irregular margins, heterogenic composition, infiltrating the surrounding tissues, with adjacent edema [56].

MPNST develops metastasis in the lungs, bones and pleura [57]. We found three patients with MPNST metastases.

Medulloblastoma

Medulloblastoma is a primitive-neuroectodermal tumor (PNET). It is the most frequent malignant tumor of the brain in children [58]. It metastases mainly in the pelvis followed by the femur, vertebrae and ribs. Its sacral localization is exceptional [59]. One of our patients with metastatic tumor, 49-year-old woman, had a secondary medulloblastoma.

Angiomyolipoma

Angiomyolipoma is a tumor generally localized in the kidneys and in the retroperitoneum, followed by different bones [60]. We found in the literature a single case of epithelioid retroperitoneal angiomyolipoma with hepatic metastasis and bone metastasis in an 80-year-old woman [61]. Examinations of tissue samples in our subjects found one case with specific features of angiomyolipoma. Our patient was 55-year-old woman, suffering from a sacral metastatic tumor.

Clinical morphological considerations

Patients with metastatic tumors were significantly older compared to those presented with primitive tumors (mean age 60 years old vs. 47.5 years old; $p < 0.0001$). So, we should suspect a metastatic sacral tumor in an old patient with history of cancer, associating general symptoms like weight loss and fever.

Sacral metastases did not differ significantly from primary tumors as far as the localization is concerned; no differences were observed in different histopathological types. Studies regarding sacral tumors localizations mention that giant cell tumors are mainly with eccentric localization, in the proximal sacrum [62], whereas teratomas mostly develop as exophytic masses between the anus and the coccyx, with subsequent extension in the sacrum [63].

Only few tumors (10.6%) developed in the presacral space. We did not encounter the predominance of a certain histopathological type. Studies shows that nearly 50% of presacral tumors are malignant, being often solid masses, rarely cystic (60% solid masses vs. 10% cystic

masses) [64, 65]. They are characterized by a slow growth. In time, the patient develops pain in the perianal region. Other symptoms may include: constipation, urinary incontinence or fecal incontinence, sexual dysfunctions [66]. Refractory perianal suppurations or suppurations of the sacrococcygeal area non-respondent to treatment may have underlying retrorectal tumors. Yet, retrorectal tumors are known to be often asymptomatic for a long period of time, being mostly discovered incidentally [64, 67], fact that was consistent with our group. The patients we had with this pathology were pauci- or asymptomatic, their tumors being discovered incidentally.

As far as the histopathological examination is concerned, presacral tumors, also called retrorectal masses, are generally neurogenic tumors, non-neurogenic tumors being less frequent and often malignant (metastases) [38]. In our patients, unlike other studies, regarding presacral masses, the benign and malign tumors were equally distributed.

As far as extension in the nearby structures is concerned, no significant differences were found in metastatic tumors compared to primitive tumors. In primitive tumors, chordoma and Ewing sarcoma showed a significant extension in the nearby structures, especially in the small-pelvis, compared to other histopathological types, consistent with results of other studies [68].

The resections topography did not differ in primitive tumors vs. metastatic tumors and was not influenced by the tumors extension or by the type of resection (similar results being obtained for total resection, partial resection or biopsy). This is due to the fact that most of the patients undergoing surgery were in an advanced stage of the disease, having a major extension in the nearby structures, unlike patients presented in other studies that had small tumors, localized in a certain area of the sacrum, fact that dictated a certain topography in performing the resection, topography that sometimes differs with the histopathological type [67].

Furthermore, the advanced stage of the disease may be the explanation for with in the majority of cases only partial resection or biopsy (in case of metastatic disease) was performed. We were able to perform 11 total resections for primitive tumors and one metastatic tumor, without observing an easier resectability for a certain histopathological type in contrast to other studies in with benign sacral tumors were associated with a higher resectability rate [69].

More than that, the resectability rate was not influenced by the tumors extension, as opposed to results published by Fusch & Boos [70]. Also, it did not produce a major effect on postoperative outcome. This may be due to the large number of partial resections and biopsies often performed for large tumors with significant nerve root invasion. Studies mention cases in which a total tumor resection determined a significantly favorable postoperative outcome [71].

For primitive tumors, the grade of nerve root invasion depends on the histological type, bilateral lesions being more frequent. Schwannomas and chordomas produced bilateral root involvement, result that was consistent with other studies [72].

In order to determine the exact radicular involvement,

imaging of the sacrum is essential. Conventional X-ray was previously used for establishing positive diagnosis (Figure 10a), having the capability to show only certain specific signs like presacral occupation with bony destruction in case of chordoma [73], the “scimitar sign” (for anterior meningocele) [74] or retrorectal calcifications (for teratoma) [75].

More complex imaging techniques [computed tomography (CT) and/or MRI] offer the possibility to establish the exact extension and invasion, suggesting a certain pathology, which is vital in choosing the optimal surgical approach [76].

MRI can give better anatomic delineation of the bone, soft tissues showing nerve invasion more [77]. Colonoscopy and barium enema might be useful in selected cases [78]. Fine needle biopsy might be used in order to obtain a tissue sample for histological sampling in subjects presented with large, unresectable tumors associating severe comorbidities that contraindicate surgical treatment [79]. Afterwards these patients may be referred for oncological treatment.

Surgery is usually the main treatment for the majority of sacral tumors, whether for resection or just for biopsy and/or decompression. For benign tumors, especially those situated on the anterior surface of the sacrum, a surgical intervention is indicated even in the absence of symptoms because of the high risk of malignancy or infection (for meningoceles and cystic lesions) [80].

For all categories of sacral tumors, the posterior surgical approach was preferred due to the facility in applying this particular approach, the sacrum being easily accessible with minimum dissection. This is why the posterior approach is the method of choice even in highly specialized centers. Contrary to results published in other studies [5, 81], we found no significant differences between surgical approaches in various histological types of sacral tumors.

Also, the fact that we found in our subjects few tumors developed on the anterior surface of the sacrum is an additional argument for choosing in most cases the posterior approach. The majority of our patients were in a local advanced stage of the disease for which only biopsy or partial resection could be performed, surgical interventions that are more easily performed using this particular approach. Moreover, this approach is preferred because it allows optimal nerve root dissection.

The optimal surgical approach (abdominal or anterior, transsacral or posterior or combined) is chosen after a multidisciplinary team meeting between a neurosurgeon, a general surgeon, an orthopedic surgeon and sometimes a plastic surgeon [82–84]. Studies also mention the transrectal or transvaginal approach but used with a significantly lower prevalence [85]. An “en bloc” resection significantly improves overall survival and also reduces the risk of local recurrence [86]. Jao *et al.* conducted a study on 120 patients with sacral tumors (69 benign, 51 malignant), for a period of 20 years. In 79 cases, posterior approach was chosen, for 21 patients anterior approach was preferred and in only two patients combined surgical approach was considered optimal. The resectability rate was 85% [87]. A recent study, conducted by Wang *et al.* on 45 patients (23 suffering from benign tumors, 22

suffering from malignant tumors), showed a higher prevalence of the anterior approach (24 cases) *versus* the posterior approach (13 cases) or combined approach (six cases). The resectability rate was 95% [88]. If sacrectomy is imperative, at least one S2 nerve root must be preserved in order to avoid postoperative bladder and bowel dysfunction [64].

Transabdominal approach, indicated usually for tumors higher than S4 vertebrae, without nerve root involvement [9] has the advantage of a good exposure of pelvic structures, iliac vessels and ureters [89]. Subumbilical midline incision is routinely used. Recent studies confirm that laparoscopic approach can offer an efficient exposure for an appropriate resection but only for benign lesions [90].

For large tumors, with extension above and below S4 vertebrae, combined approach is preferred, starting with the anterior approach (for selected cases it can be done laparoscopically), possibly continued with a perineal approach, if rectal resection with a very low anastomosis is required, afterwards adding a posterior approach if needed. [91]. Perineal approach can be used for distal benign tumors of the sacrum [92].

Posterior approach is generally used for benign lesions without extension above S4 vertebrae [5]. Different studies show that a lesion whose upper pole can be felt by rectal examination may be totally resected using only a posterior approach [1]. Coccyx resection may be indicated both for obtaining a better exposure and for excision of potential fistulous trajectories. It is sometimes mandatory for cystic lesion and teratoma excision [93, 94]. The major disadvantages of posterior approach are the lack of vascular control and the risk of producing injuries on the nervous structures in the pelvis [95]. These risks may be diminished by a careful selection of patients, being practically null for benign cystic tumors with imagistic showing the lesions origin or penetration into the sacrum [94].

The most frequent intraoperative incident was bleeding. Average blood transfusion need was around 2.1 units, similar for both primitive and metastatic tumors. Age and gender did not produce a significant influence on mean blood loss in our subjects, unlike results published by Tang *et al.* [96]. He reported excessive bleeding in male patients, with highly vascularized tumors, extended beyond S2 vertebrae and having a tumor volume greater than 200 cm³. In these cases, operative time was significantly longer [96]. For giant cell tumors of the sacrum, Zhou *et al.* performed preoperative embolization thus decreasing intraoperative blood loss and facilitating resection [97].

Of all sacral tumors, carcinomas were associated with the highest intraoperative blood loss (mean necessary of blood transfusions 2.5 units; $p < 0.0001$). Some studies report a lower blood loss in cases where "en bloc" excision was performed (300–650 mL – in average 460 mL) compared to subtotal resections (350 – 2800 mL – in average 1695 mL) [71].

Incidental lesion of dura mater is the second most frequent intraoperative incident reported, more common in primitive tumors. This is probably due to the tumors origin, primitive sacral tumors being adherent to the

dura mater. This observation is consistent to results obtained in other studies [98].

The subject's outcome quantified by studying the postoperative neurological status was not clearly favorable neither for primitive sacral tumors nor for metastatic sacral tumors in our study group. Studies show that benign tumors of the sacrum have a favorable outcome, often being totally resected [99]. For malignant tumors, the prognosis depends on the histopathological type. For example, the 5-year survival rate for chordoma varies between 67% and 84%. Although recurrence rate is high (41/32), it can be lowered with postoperative radiotherapy [100]. Other histopathological types have a poorer prognosis [81, 101].

The general prognosis was significantly better for primitive tumors, with 10 patients suffering from primitive sacral tumors being declared healed after surgical intervention *vs.* only one patient suffering from metastatic disease that was declared healed after surgical resection.

Postoperative oncological treatment was beneficent for metastatic sacral tumors and was applied in 91.42% of cases. In the group of primitive sacral tumors, postoperative oncological treatment was less necessary (being applied in 35% of cases), mainly because the majority of primitive sacral tumors were benign lesions.

Knowing the specific features of each histopathological type of sacral tumor is mandatory. We must be aware of some specific locations within the sacrum of certain histopathological entities as well as of the targeted population. The team must be wise in choosing the right investigations in order to obtain a complete and correct diagnosis. Afterwards a proper surgical approach must be chosen. The best therapeutically plan is the one not only proved to be efficient in clinical studies but also respecting the multidisciplinary approach desiderate, being efficient for both surgeons and oncologists. We must be fully aware of the potential of recurrence of each tumor in order to develop an efficient follow up protocol.

✎ Conclusions

Patients suffering from sacral tumors often present in advanced stages of the disease, with large tumors, extended throughout the sacrum and invading nearby structures. Histopathological analysis of the resected tissue showed a large variety of histopathological types, with a predominance of primitive sacral tumors, metastatic disease being less frequent and more likely to appear in older subjects.

For both primitive and metastatic sacral tumors, posterior surgical approach is preferred in most cases, a high majority of surgical interventions being partial resections and biopsies. Performing a total resection at all cost, in patients with advanced disease, neglecting vascular and nervous involvement may result in severe bleeding, postoperative neurological deficit or postoperative sphincter deficiency, thus determining or aggravating physical disablement.

Thus, in order to achieve a proper management of the complex and controversial pathology that are sacral tumors, histopathological sampling, initially intraoperatively, followed by complementary histopathological

studies is essential. It not only helps establish positive diagnosis and the type of malignancy but is mandatory in choosing the best therapeutic approach, starting with choosing the right surgical tactics and continuing with helping conduct a correct oncological treatment, while focusing on the rehabilitation process, whilst paying high attention on the patient's quality of life.

Conflict of interests

The authors declare that they have no conflict of interests.

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