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Diagnosis and surgical therapy of plasma cell neoplasia of the spine

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Presented is a retrospective analysis of 27 patients with plasma cell neoplasms of the spine treated by surgery. Multiple myeloma was confirmed in 22 (81%) and solitary plasmacytoma in 5 patients (19%), assessed at the time of surgery. Nineteen patients (70%) with the preliminary diagnosis of malignancy of unknown etiology were admitted for surgery. In 23 patients (85%) the essential symptom was back pain, which preceded surgery by an average of 4 months. Thirteen patients (48%) were bedridden due to tumor spinal cord compression, on average for 7 days before undergoing surgery. Only 5 out of 13 bedridden patients (38%) regained the ability to walk after surgery and 8 patients (62%) remained bedridden despite successful surgical decompression of the spinal cord. The difference of survival of the patients between bedridden and able to walk prior to surgery was statistically significant (Cox's F-Test = 0.005).

Key words: plasma cell neoplasia, spinal cord compression, late diagnosis, outcome

Plasma cell neoplasms comprise as much as 10% of all hematological malignancies and are one of the most common primary bone malignancies [1]. The highest incidence occurs between 60-70 years of age, with a slight predominance in men. The characteristic laboratory findings are a high sedimentation rate, usually mild anaemia and the presence of paraprotein in the serum and urine [2]. There is a significantly poorer prognosis in patients with multiple myeloma (MM) opposed to those with "only" solitary plasmacytoma (SP), in whom either surgery or radiotherapy may even be curative, if there are no signs of nervous system compression [3].

In the vast majority of patients the first clinical manifestation of spinal affliction is the localized back pain preceding other symptoms by a number of months [4]. A motor neurological deficit developed as a result of spinal cord compression due to further growth of tumor into the spinal canal or due to the occurrence of a vertebral body pathological fracture in approximately 10% of patients [5]. Due to the unspecific clinical symptoms the possibility of spinal involvement haematological malignancy is often not considered, diagnosis may be delayed and the patient reaches surgery bedridden with a severe neurological deficit. The patients' ability to walk before surgery is crucial in their future prognosis. In some patients with advanced clinical signs of spinal cord compression, despite successful surgical decompression of the spinal cord, damage to spinal cord function may be permanent. These patients remain permanently bedridden with a significantly lower quality of life and impaired self-sufficiency [6]. The aim of this paper is to analyze retrospectively the effect of delayed diagnosis on results of surgery in plasma cell neoplasia of the spine, especially in regard to regaining the ability to walk and length of survival.

Patients and methods

Twenty seven patients with plasma cell neoplasms of the spine treated by surgery in between 1997-2007 were retrospectively analyzed. Patients were divided into two groups based on preoperative knowledge of the underlying primary hematological malignancy and analyze the purpose of delayed diagnosis. Spinal tumors were categorized as either SP or MM based on histological and hematological findings. The basic characteristics of both groups in relation to surgery are presented in Table 1. A total of 22 patients diagnosed with MM and 5 patients with SP underwent surgery. In both groups males were prevalent, patients with SP were on average 10 years younger, and in comparison to the group

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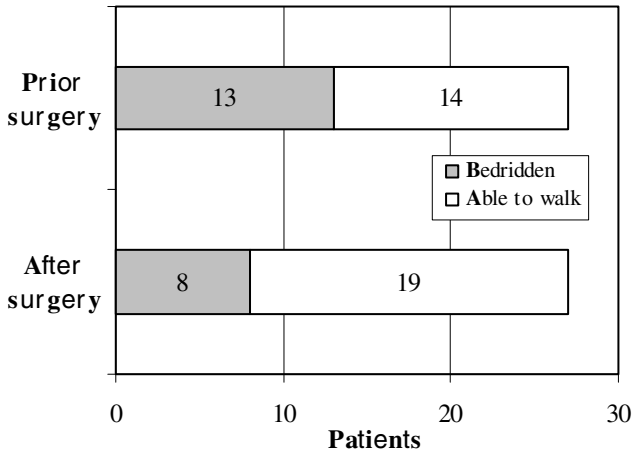

Figure 1. The ratio of patients able to walk/beddriden prior and after surgery.

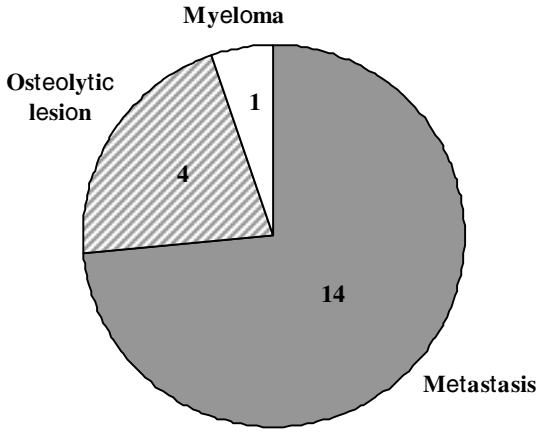

Figure 2. The role of radiological methods in determination diagnosis of haematological affliction of the spine prior to surgery (Number of patients).

of patients with MM the levels of serum paraprotein were lower.

The presence and length of neurological symptoms and signs before undergoing surgery were evaluated. Neurological deficit caused by spinal cord compression was assessed with an emphasis on motor deficit, quantified using the Frankel scale and divided into two groups able to walk or bedridden, prior to surgery and 1 week after surgery [7].

The follow up of the presented cohort was 6 to 120 months. Patient survival was compared using Kaplan-Meier's empirical curve. The statistical significance of patient survival was evaluated using Cox's F-Test.

Results

Neurological symptoms and signs before surgery. Localized back pain was the manifesting symptom in 23 patients (85%), appearing on average 16 weeks before surgery. Fourteen patients (52%) were able to walk preoperatively (Frankel E and D); however, the remaining 13 patients (48%) were bedridden (Frankel A, B and C), on average for 7 days before being admitted for surgery (Fig. 1).

Determination of diagnosis prior surgery. Spinal affliction was the first manifestation of hematological disease in 19 out of 27 patients (70%). In 14 out of 19 patients (74%) imaging findings were described by the radiologist as secondary spinal metastases as the most likely diagnosis. In another 4 patients (21%) an osteolytic focus together with a pathological fracture was described without any further specification as to etiology. In only 1 case (5%) the lesion was described as suspicious of MM (Fig. 2). In this group with diagnosis of malignancy of unknown etiology imaging methods (CT and MRI) did not contribute to establishing the hematological origin of the disease before surgery. The definitive diagnosis was established postoperatively based on histological and hematological findings.

Multiple myeloma and solitary plasmacytoma. MM was confirmed in 22 patients (81%) and SP in 5 patients (19%), assessed at the time of surgery. In all patients with SP the diagnosis was established by peroperative histological examination. In 14 out of 22 patients (64%) with MM the underlying haematological disease was established after surgery. During the follow up at 5 and 40 months, 3 patients with SP were reclassified as MM. The length of survival of patients with

Table 1. Group of patients with multiple myeloma and solitary plasmacytoma – basic facts.

	Plasmacytoma	Multiple myeloma
Total number of patients	5 (19%)	22 (81%)
Male to female ratio	4:1	18:8
Age distribution(median)	52 years (28 – 65)	62 years (39 – 69)
Stage according to Durie and Salmon		2x IIB, 10x IIA,9x IIIA
Paraprotein type	4x IgG kappa,1x nonsecretory	9x IgG-κ, 5x IgG-λ, 3x IgA-κ, 2x IgA-λ, 1x free chains κ, 1x nonsecretory MM
Paraprotein type entrance levels (median)	5,2 g/l (0 – 38,2)	21,8 g/l (0 – 54,7)
Bone marrow infiltration (median)		15,0% (1 – 60)

Note. In one case we did not succeed to retrieve the entrance data from archives (staging, type and quantity of PP and extent of bone marrow infiltration).

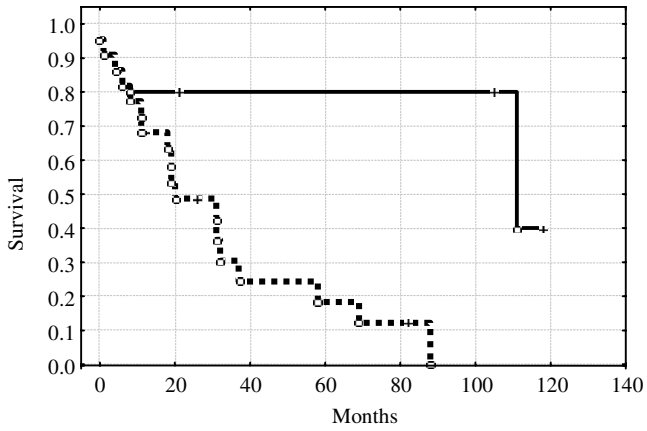

Figure 3. Kaplan-Meier's empirical curve of survival of patients with diagnosis multiple myeloma (interrupted line) and solitary plasmacytoma (full line).

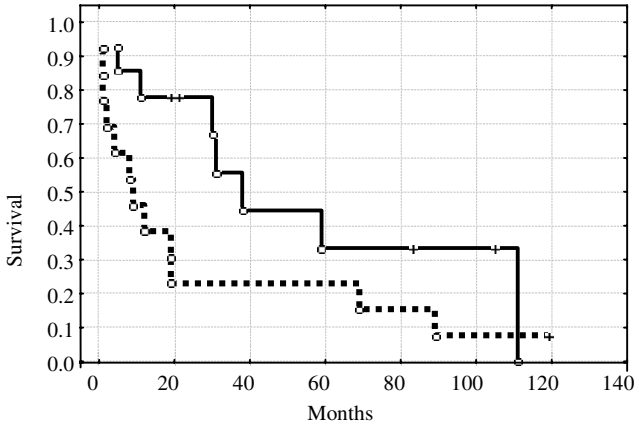

Figure 4. Kaplan-Meier's empirical curve of survival of patients bedridden (interrupted line) and able to walk prior surgery (full line).

MM and SP was compared using Kaplan-Meier's empirical curve at the time of surgery (Fig. 3). The difference of patient survival was statistically significant (Cox's F-Test = 0.017).

Surgical results. Out of all 13 preoperatively bedridden patients 8 patients (62%) remained bedridden despite successful surgical decompression of the spinal cord. The main cause of such unsatisfactory results was the delayed diagnosis. The remaining 5 patients (38%) regained the ability to walk after surgery – all of whom were from the MM group. All 14 patients able to walk preoperatively were able to walk after surgery and 5 patients regained the ability to walk after surgery – 19 patients were able to walk after surgery in total (Fig. 1).

The length of survival of patients bedridden and able to walk before surgery was compared using Kaplan-Meier's empirical curve (Fig. 4). The difference of patient survival was statistically significant (Cox's F-Test = 0.005).

Discussion

Plasma cell neoplasms are primary bone tumors which affect the spine in up to 45% of cases [4]. Their growth behavior is similar to that of metastases of malignant tumors creating osteolytic lesions in the vertebrae. Due to the clinical similarities, plasma cell neoplasms are often grouped together with spinal metastases. Despite this plasma cell neoplasms have a better prognosis than secondary spinal malignancies due to their radiosensitivity and chemosensitivity [9, 10, 11].

Localized back pain is present in up to 94% of patients with spinal malignancies, developing an average of 3 months before the diagnosis is established [8]. Durr notes that out of 27 patients with MM of the spine all had back pain which developed over an average period of 5,8 months [9]. In our study, 23 out of 27 patients (85%) presented with back pain which developed over an average period of 4 months before the diagnosis was established. In patients back pain is a common symptom of degenerative disease of the spine and the possibility of a hematological malignancy is seldom considered in the differential diagnosis.

Another factor leading to delayed diagnosis is the fact that clinical symptoms of plasma cell neoplasms in the spine are often the first manifestation of malignant hematological disease. Pascal described a group of patients with MM in which symptoms of spinal involvement were the first manifestation of hematological disease in 10 out of 15 patients [12]. Omnibus described a similar group in which the first manifestation occurred in the spine in 10 out of 18 patients with MM and SP [13]. In our study, the spine affliction was the first manifestation of malignant haematological disease in 19 patients (70%). This is considerably higher than the incidence of metastases of unknown origin in the spine, which is estimated to be between 6-33% [10, 14].

Patients with neurological deficits of unknown etiology are admitted to hospital for further investigation. In this phase delays in establishing the correct diagnosis occur due to several reasons, hence leading to a delay in necessary adequate treatment. Durr, in a group of 27 operated patients with spinal affliction of MM found that 21 patients had normal preoperative neurological findings and in 6 cases a preoperative neurological deficit had developed [9]. In Levack's group of 248 patients with metastatic disease of the spine, of which 10% were MM, 82% of patients were not able to walk independently once the diagnosis was established [8]. In our study 13 patients (48%) were admitted bedridden prior to surgery. Patients admitted for surgery with severe neurological deficit have a small chance of improvement of spinal cord function, despite successful surgical decompression of the spinal cord.

MRi is superior in imaging with high specificity and sensitivity, myeloma lesions appear as typical hypointense lesions in T1 sequences and hyperintense in T2 and STIR sequences

[15, 16]. Out of 19 patients with uknown etiology the first manifestation of plasma cell neoplasm in the spine almost $^3/_4$ findings were described as secondary metastatic lesions. These radiological conclusions partially influence the surgeon's decisions as to the radicality of the procedure. The treatment of choice for MM is usually systemic – chemotherapy and radiotherapy according to hematooncologists' orders. However, in our study, only 8 patients (30%) had a known hematological malignancy prior to surgery.

An important prognostic factor in return of neurological function caused by compression of the spinal cord by a malignant tumor is the patient's ability to walk prior to surgery [14]. The basis of satisfactory outcomes and neurological improvement is swift diagnostics and decompression of the spinal cord before irreversible damage occurs. Omnibus, in his group of 18 patients with hematological affliction of the spine, of which 7 had a preoperative neurological deficit, was able to achieve a postoperative neurological improvement in 5 patients, but in 2 patients the neurological deficit persisted [13]. Durr demonstrated in his group of 27 haematological patients, 6 of whom had a preoperative neurological deficit that all patients improved following surgery and began to walk again [9]. In our group out of preoperatively 13 bedridden patients only 5 patients (38%) regained the ability to walk after surgery. The main cause of such unsatisfactory surgical results is the delay in diagnosis of plasma cell neoplasia of the spine. The postoperative neurological outcomes are similar to other studies, but there are minor differences depending the severity of the preoperative neurological deficit [6, 8, 12, 13, 14, 19].

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