



## EVALUATION OF AETIOLOGICAL FACTORS IN ADVERSE OUTCOME FOR NEUROSURGICAL INTERVENTION IN PATIENTS OF SOLITARY SPINAL PLASMACYTOMA WITH NEUROLOGICAL DEFICITS.

**Col (Dr) Sanjay Kumar**

Associate Professor, Department of Neurosurgery, Command Hospital (Southern Command) , Pune, India – 411040

**Col (Dr) Subir Dey\***

Associate Professor, Department of Neurosurgery, Command Hospital (Southern Command) , Pune, India - 411040 \*Corresponding Author

### ABSTRACT

**Aims & Objective:** Complications are known to occur in neurosurgical practice. But there are some complications which are beyond our understanding and do occur in patients postoperatively. Our aim was to analyse the cause and propose a theory for the rapidly fatal outcome in three patients of solitary spinal plasmacytoma with neurological deficits who underwent decompression along with instrumentation for stabilisation of the spine.

**Material and Methods:** Retrospective analysis of patients who were diagnosed as a case of solitary spinal plasmacytoma presenting with neurological deficits from a cohort of all patients with presenting with vertebral fractures managed at our centre During the period of aug 2014 to dec 2016 were included in the study. There were a total of 11 patients of solitary spinal plasmacytoma who underwent surgical intervention and 3 patients from this group of patients had a fatal outcome and expired within a period of 12 hours after the surgery. The preoperative haematological and biochemical parameters, renal function status, perioperative events with special emphasis on the episodes of hypotension, total intra-operative blood loss volume and volume of blood/blood products transfused in these 3 patients were analysed to elucidate the cause of adverse outcome in these subgroup of patients.

**Results:** The three patients of solitary spinal plasmacytoma who had adverse outcome were detected to have at least one episode of intra-operative hypotension, higher blood loss volume (>1000 ml) and large volume intra-operative transfusion of blood/blood products (>1000 ml). These three factors were which were not present in 8 of the other patients of solitary spinal plasmacytoma and hence were thought to be predictors of the adverse outcome in the 3 patients with similar preoperative profile in all the 11 patients.

**Conclusions:** This study revealed that in patients of solitary spinal plasmacytoma with neurological deficits having normal haematological, biochemical and renal parameters preoperatively can have adverse outcomes due to hitherto unknown factors. These study demonstrated that perioperative factors like episodes of hypotension, large volume intra-operative blood loss (>1000 ml) and large volume blood/blood products (>1000 ml) are important factors and lead to unmasking of the compensated state of renal function leading to adverse outcomes. The proposed mechanism for this outcome could be degradation products of blood, overload of proteins in the circulating blood which has a detrimental effect on the renal function and disturbance in the renin-angiotensin mechanism controlled by the kidneys causing refractory hypotension are causes of adverse outcome in a subgroup of patients with solitary spinal plasmacytoma.

**KEYWORDS :** Solitary spinal plasmacytoma, Complications in Neurosurgery, Renal dysfunction, Mortality, Renin-angiotensin mechanism, spinal stabilisation.

### INTRODUCTION

Solitary plasmacytoma of bone (SPB) is a malignant tumor and an independent subtype of plasmacytoma (1,2). Complications in neurosurgical practice are unavoidable and keep occurring from time to time during our surgical practice and remind us to improve our skills and guide us for better management in the future cases. However some complications baffle us and in spite of all the precautionary measures and correctness of the surgical procedure carried out, still occur and puzzle us. And if these complications are fatal, they trouble us more and we need to review our preoperative evaluation, surgical steps and the post operative management to isolate the problem and take remedial measures for the better outcome in our future patients.

Ours is a high volume tertiary care Neurosurgical centre where interventions and all types of instrumentation for spinal pathologies are carried out. During the period of Aug 2014 to Dec 2016 a total of 156 patients of vertebral fractures were managed at our centre, details of which are given as per table 1. Out of the total no of 47 patients with pathological fractures of the vertebral column, three patients with the final diagnosis of plasmacytoma on histopathological (HPE) evaluation had a fatal outcome that too on the first post operative day. The rapid downhill course and the outcome in these three patients was similar. Plasmacytoma of the spine is a systemic disease and the prognosis is guided by a lot of factors. However such rapidly fatal outcome has not been described in literature. This prompted us to evaluate the patient's clinical profile, preoperative evaluation carried out, surgical procedure carried out, peri-operative management and immediate post-operative care given in a bid to identify the risk factor or the step which would have led to such an outcome.

### MATERIAL AND METHODS:

A retrospective analysis of records of all patients with dorsolumbar fractures managed at our centre for the period of Aug 2014 to Dec 2016 was carried out. aetiological data of the patients was as mentioned in table 1.

**Table 1: Aetiological diagnosis of patients of vertebral fractures during the period of study (Aug 2014 to Dec 2016).**

Diagnosis	No of patients
Traumatic fractures of spine	109
<b>Pathological fractures</b>	47
Metastasis from solid organs	24
Multiple myeloma	12
Solitary spinal plasmacytoma	11

The patients with pathological fracture were included in the study. Of the patients with pathological fractures the outcome in patients who were finally diagnosed as plasmacytoma were only included in this study with the aim of analysing the predictive value of pre-operative investigations and perioperative issues which were responsible for an adverse outcome in these subgroup of patients. The demographic clinical profile of these patients is as given in table 2.

**Table 2: Demographic and clinical profile of patients with solitary spinal plasmacytoma (n=11).**

Clinical factors	No of patients (n=11)
<b>Age</b>	N = 11
20-30 years	1
31-40 years	2
41-50 years	4
51-60 years	4
<b>Sex</b>	N = 11
Males	5
Females	6
<b>Symptoms</b>	N = 11
Pain	10
Weakness of limbs	11
Sphincter involvement	3

All the patients underwent haematological, biochemical and

radiological investigations with contrast enhanced MRI and NCCT of the spine for evaluation of degree of compression and instability of the spine. The known factors which are known to have an adverse outcome in patients with solitary spinal plasmacytoma who undergo neurosurgical intervention are as mentioned in table 3.

**Table 3: Known pre-operative factors which may have adverse outcome in post-operative patients of solitary spinal plasma cytoma.**

Factor	Present /absent
Hemoglobin <10	Absent
Elevated B.Urea	Absent
Elevated S.Cr	Absent
Urinary light chains	Absent

The degree of neural compression of the spinal cord as demonstrated on CE MRI and degree of bony destruction as seen on CT is given in table 4.

**Table 4: Imaging findings in the 3 patients who had an adverse outcome in the post-operative period.**

Patient	CT findings	CE MRI findings	Skeletal survey
Patient 1	Pathological fracture involving LV 3	Enhancing soft tissue lesion involving the vertebral body with pathological fracture. Epidural mass compressing the thecal sac	No other lesions
Patient 2	Osteoblastic lesion of the LV1 and posterior elements	Enhancing soft tissue component replacing the vertebral body Epidural component causing severe cord compression	No other lesions
Patient 3	Osteoblastic lesion of DV12 with pathological fracture involving body	Enhancing soft tissue component replacing the body of vertebra Epidural component causing severe cord compression	No other lesions

The patients also underwent skeletal survey to rule out any other lesions in the body before labelling them as a case of solitary spinal plasmacytoma. The representative images of one two patients is as depicted in figure 1a-1c & figure2a-2c.



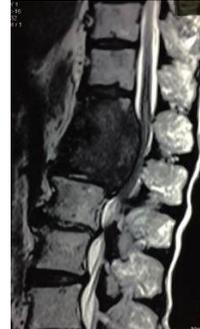
**Figure 1a: T1W MRI Brain showing osteoblastic lesion involving LV3 compressing the thecal sac**



**Figure 1b: NCCT spine sagittal section depicting compression fracture of LV3 with retropulsion in the spinal canal**



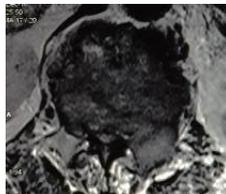
**Figure 1c: Retropulsed bony fragment causing canal compromise on NCCT spine axial section**



**Figure 2a : T2W MRI sagittal image showing lesion involving the vertebral body and epidural soft tissue component compressing the thecal sac**



**Figure 2b: NCCT spine sagittal image showing osteoblastic lesion of vertebra involving both anterior and posterior elements with canal compromise.**



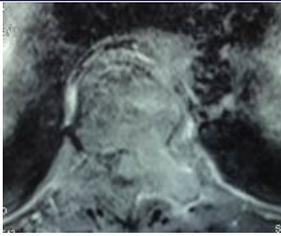
**Figure 2c: MRI SPINE axial image showing the lesion involving vertebral body. Lamina with severe canal compromise.**



**Figure 2d: NCCT spine axial image showing osteoblastic lesion of vertebra involving both anterior and posterior elements with canal compromise**



**Figure 3a: MRI SPINE axial image showing the lesion involving vertebral body. & lamina with severe canal compromise.**

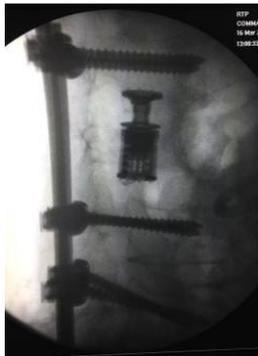


**Figure 3b: MRI SPINE axial image showing contrast enhancing lesion involving vertebral body. & lamina with severe canal compromise.**

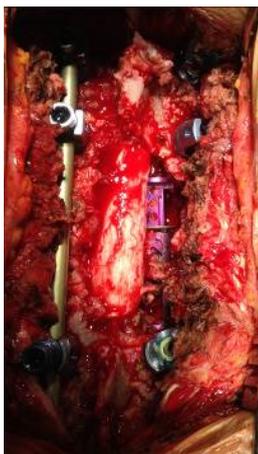
All patients who were diagnosed as a case of solitary spinal plasmocytoma with neural compromise resulting in neurological deficits and features of bony instability underwent surgical decompression and skeletal stabilisation with instrumentation. Of the total of 11 patients who underwent surgery, five underwent posterior decompression with laminectomy and pedicle screw and rod fixation, 5 patients underwent transpedicular corpectomy (figure 3a – b) with placement of expandable cage placement and 1 patient underwent left anterolateral thoracotomy with retro pleural approach, corpectomy & expandable cage placement.(figure 4a-b)



**Figure 3a: Intraoperative image depicting the resected tumor with thecal sac and implants after resection of the tumor in patient 1**



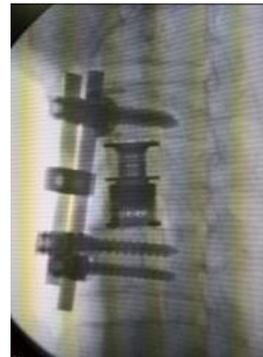
**Figure 3b Intraoperative lateral image of C-arm depicting implants after resection of tumour in patient 1.**



**Figure 4a: Intraoperative image depicting the resected tumor with thecal sac and implants after resection of the tumor in patient 2**



**Figure 4b: Intraoperative lateral image of C-arm depicting implants after resection of tumor in patient 2.**



**Figure 4c: Intraoperative lateral image of C-arm depicting implants after resection of tumor in patient 3.**



**Figure 4d: Intraoperative AP image of C-arm depicting implants after resection of tumor in patient 3.**

The duration of surgery, blood loss, episodes of intra-operative hypotension, intra-operative urine output, and transfusion of blood/ blood products was noted as mentioned in table 5.

3 patients out of the 11 patients who had an immediate fatal outcome within 12 hours of surgery were further analysed with poor prognostic factors like haemoglobin, renal function status, B-2 microglobulin, serum calcium level, M-component & urine light chains. (table 5)

**Table 5: Preoperative prognostic factors in the 3 patients who had a fatal outcome.**

Patient	Hb (gm %)	B.urea mg/dl	S. Cr mg/dl	S. Ca mg/dl	M-component (IgG <5g/dl, IgA <3 g/dl)	Urine light chains
Patient 1	10.6	35	0.9	8.7	IgG – 3.2 IgA – 1.8	Absent
Patient 2	11.5	29	1.0	9.1	IgG – 2.8 IgA – 1.1	Absent
Patient3	11.8	21	0.8	9.6	IgG – 3.9 IgA – 2.1	Absent

**RESULTS:**

11 patients who were diagnosed as a case of solitary spinal plasmacytoma who underwent neurosurgical intervention for included in this study. None of these 11 patients had poor prognostic markers in serum or radiological imaging as mentioned in literature were present. There was no significant difference in the pre-operative prognostic markers between the 8 patients with good outcome and the 3 patients with fatal outcome (table -5). Mean age of patients with good outcome was ---- and with fatal outcome was. The patients with fatal outcome had on an average 2 episodes of intra-operative hypotension with MAP below 60 mmHg. The total amount of blood loss in was 1800ml, 1450ml and 1600ml in patients 1, 2 & 3 respectively. The mean duration of surgeries was 5.4 hours in the patients with fatal outcome. Whereas it was 3.6 hours in the patients who had a good outcome. The total amount of blood & blood products was 1500ml, 1250ml & 1500ml respectively in the three patients with fatal outcome whereas it was 450 ml (mean) in the patients with good outcome. We compared the perioperative profile of similar metastatic tumours to the spine other than solitary spinal plasmacytoma and it was noticed that these patients with similar profile of duration of surgery, blood loss & blood/blood products had good outcome as compared to the three cases of solitary bone plasmacytoma with fatal outcome.

The patients of solitary bone plasmacytoma had a rapidly deteriorating course with renal shutdown, refractory hypotension not responding to inotropic support significantly raised albumin the post operative urine evaluation and succumbed within 12 hours of the surgical intervention. Such rapid deterioration and mortality of these patients prompted us to re-evaluate all the preoperative parameters which could have had an adverse outcome in these patients, perioperative factors as outlined above which could have caused such a rapid deterioration.

Analysis of all the factors revealed that in spite of not having any abnormal preoperative poor prognostic markers, these patients mortality could be attributed to the episodes of intra-operative hypotension, higher blood loss & transfusion of blood/blood products in the intraoperative period.

These patients although had normal preoperative prognostic markers and in spite of this the poor outcome in these subset of patients can be attributed to the fact that these patients are in a state of compensated renal function and the perioperative adverse events would have unmasked the compensated renal function leading to rapid deterioration of renal function which were the cause of the poor outcome. The refractory hypotension in these patients could be attributed to the failure of HPA – axis involving the kidney – adrenals-pituitary which was disturbed by the failure of renal functions.

After taking in to consideration we finally arrived to the conclusion that episodes of intra-operative hypotension, large volume blood loss (> 1000ml) and large volume blood/blood products transfusion in the intraoperative period are the main factors responsible for poor outcome in patients of solitary bone plasmacytoma with neurological deficits who undergo neurosurgical intervention for alleviating the neural compression and stabilisation of the spine. Physiological basis for this outcome is most likely the unmasking of compensated status of the renal function in patients of solitary spinal plasmacytoma because of the three perioperative factors outlined above and disturbance of the HPA axis & renin-angiotensin mechanism which are responsible for the maintenance of blood pressure in a normal individual.

**DISCUSSION:**

Solitary plasmacytoma is a localised osseous tumour of a single focus of plasma cells.(3-5). Solitary plasmacytoma of bone (SPB) represents only 5% of all plasma cell malignancies and is a heterogeneous condition(6,7,8). A firm diagnosis of a solitary plasmacytoma could be made in the presence of four features,2 including (i) histological evidence of the lesion; (ii) absence of other lesions as confirmed by a complete skeletal survey; (iii) negative bone marrow examination, and (iv) absence of dysproteinemia and Bence Jones proteinuria. Since the solitary lesion may often disseminate, a complete skeletal survey and immunological as well as biochemical studies during follow-up (extending at least for 10 years) are important.(4). Myelomatous tumours, including solitary plasmacytomas, have a predilection for the vertebral body, frequently involving both the anterior and middle columns. A review of 84 cases of solitary spinal plasmacytoma by McLain and Weinstein (5) showed that 61% of the tumours occurred in

the thoracic vertebrae while 18% were detected in the lumbar spine. Cervical spine involvement was only 8%. Bullough and Boachie-Adjei (9) suggested that a solitary spinal plasmacytoma is more likely to cause spinal cord complications than multiple lesions. McLain and Weinstein (4) have described that in eight of 12 cases of their own series an objective neurological deficit was found.

Radiotherapy remains the primary modality of treatment for patients with solitary bone plasmacytoma in patients without significant neural compromise. Surgical intervention for solitary spinal plasmacytoma is recommended for patients in whom it is easy to remove and patients primarily presenting intractable pain due to vertebral involvement, instability and neurological deficits.(2,12) These subgroup of patients respond well to post operative radiotherapy and surgical resection with radiotherapy can be curative (10,11).

The procedure which are performed in solitary spinal plasmacytoma depends on the extent of involvement of structures and may vary from decompression with laminectomy & pedicle screw fixation, thoracotomy with corpectomy and instrumentation, transpedicular corpectomy with instrumentation and so on. The aim of these procedures is to adequately decompress the neural structures and supplemented with instrumentation for stabilisation of the spine. The outcome depends on the adequacy of the surgical intervention and generally patients will recover well. The complications noticed in our three patients with a rapid downhill course have not been reported in literature. The procedures carried out in all these three patients were standard procedures with transpedicular corpectomy –expandable cage placement with pedicle screw and rod fixation. There were no complications related to the procedure and the instrumentation itself and the preoperative status of the patients wrt renal function were the same as in other patients included in the study. The search of literature did not revealed known factors which could explain the rapidity of the onset of renal shutdown and refractory hypotension leading to mortality with 12 hours of the surgery. On considering all the perioperative factors and the peri-operative considerations we can hypothesize that, episodes of hypotension, large volume blood loss (>1000ml) and large volume blood transfusion are important consideration in overall outcome in patients of solitary spinal plasmacytoma undergoing decompression and stabilisation surgery of the spine. The possible explanation for this can be the unmasking of the compensated renal dysfunction due to the episodes of hypotension, blood loss and transfusion of blood/blood products. Refractory hypotension could be ascribed to the disturbance of the renin-angiotensin mechanism subsequent to the renal dysfunction.

Further research is required to isolate and define pre-operative factors apart from the known entities which can elicit the compensated status of renal dysfunction so that such fatal complications can be avoided in patients of solitary spinal plasmacytoma undergoing surgery for decompression and stabilisation of the spine.

**CONCLUSION**

Solitary spinal plasmacytoma is a relatively rare disease involving the vertebral column. The subgroup of patients presenting clinically with neurological deficits and instability of the spine are best managed by decompression of the neural structures, stabilisation of the spine with instrumentation and postoperative radiotherapy for the best outcome. However in spite of having normal haematological, biochemical and renal function, a subgroup of patients may have a rapidly fatal outcome due to unknown factors. Peri-operative factors like episodes of hypotension, large blood loss volume (>1000 ml) and large volume intra-operative blood/blood products transfusion (>1000 ml) are important factors in the outcome in a subgroup of patients. The proposed mechanism could be unmasking of compensated renal function and refractory hypotension due to the disturbance of the renin-angiotensin mechanism are likely to be the cause rapidly fatal outcome in a subgroup of patients of solitary spinal plasmacytoma with neurological deficits undergoing surgery. Further research is required for elucidating unknown preoperative factors which could predict the adverse outcome to surgical interventions so that mortality could be avoided. Pre-operative renal biopsy in patients of solitary spinal plasmacytomas planned for surgical intervention may fill in the gap in our knowledge to assess the renal function status which are not detected in existing protocols of non-invasive evaluation of renal function by haematological, biochemical and urinary analysis. However the question of carrying out renal biopsy in all patients of solitary spinal plasmacytoma undergoing surgical intervention is a debatable issue which needs validation by further studies.

CONFLICT OF INTREST: None

## REFERENCES:

1. Dumesnil C, Schneider P, Dolgoplov I, Radi S, Leluyer B, Vannier JP. Solitary bone plasmacytoma of the spine in an adolescent. *Pediatric Blood Cancer*. 2006;47:335-8.
2. Tsutsumi S, Yasumoto Y, Ito M. Solitary spinal extradural plasmacytoma: a case report and literature review. *Clin Neuroradiol*. 2013;23:5-9.
3. Fechner RE, Mills SE. Solitary (plasma cell) myeloma. In: *Atlas of Tumor Pathology: Tumors of the Bones and Joints*. Armed Force Institute of Pathology: Washington DC, 1992, pp 218-19.
4. Huvos AG. Multiple myeloma, including solitary osseous myeloma. In: *Bone Tumors: Diagnosis, Treatment, and Prognosis*. 2nd ed, WB Saunders: Philadelphia, 1991, pp 653-76.
5. McLain RF, Weinstein JN. Solitary plasmacytomas of the spine: a review of 84 cases. *J Spinal Disord* 1989; 2: 69-74.
6. Chakraborti C, Miller KL. Multiple myeloma presenting as spinal cord compression : a case report. *J Med Case Rep* 4 : 251, 2010
7. Dimopoulos M, Kyle R, Fermand JP, Rajkumar SV, San Miguel J, Chanan-Khan A, et al. : Consensus recommendations for standard investigative workup : report of the International Myeloma Workshop Consensus Panel 3. *Blood* 117 :4701-05, 2011
8. Greipp PR, San Miguel J, Durie BG, Crowley JJ, Barlogie B, Bladé J, et al. : International staging system for multiple myeloma. *J Clin Oncol* 23 : 3412-20, 2005
9. Bullough PG, Boachie-Adjei O. Solitary myeloma. In: *Atlas of Spinal Disease*. JB Lippincott: Philadelphia, 1988, pp 192.
10. Lin L, Wang YF. Progress on extramedullary plasmacytoma. *Guo Ji Shu Xue Ji Xue Ye Xue Za Zhi*, 2012, 35: 543-545 (in Chinese).
11. Soutar R, Lucraft H, Jackson G, et al. Guidelines on the diagnosis and management of solitary plasmacytoma of bone and solitary extramedullary plasmacytoma. *Clin Oncol (R Coll Radiol)*, 2004, 16: 405-413.
12. Sinha PK, Paul R, Bandhopadhyay R, Roy A, Solitary plasmacytoma of the axis vertebra presenting as severe neck pain. *J Assoc Physicians India* 2011;59:334-5.