



# Primary Intraosseous Synovial Sarcoma: Experience from a Tertiary Cancer Center

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South Asian J Cancer

## Abstract



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## Keywords

- ▶ synovial sarcoma
- ▶ bone
- ▶ intraosseous
- ▶ sarcoma
- ▶ bone tumor
- ▶ bone sarcoma

**Introduction** Primary intraosseous synovial sarcoma (PISS) is a rare cancer of the bone, with few reported cases across literature. Data from our institute reveals seven indigenous cases. This study aims to evaluate these PISS diagnoses, and to further investigate any histopathological findings and prognostic factors associated with patient survival.

**Materials and Methods** Data from patients diagnosed with PISS at the institute were obtained from January 1995 to December 2016, in the form of a retrospective study. Patient demographics, pathology locations, histological findings, surgical margins, and treatment modalities were audited as variables that can impact patient survival.

**Results** This research identified seven cases which fulfilled the diagnostic criteria and were subsequently classified as PISS of the bone. There were five men and two women among the cases, with ages ranging from 16 to 46 years, with a mean of 29.6 years. The study found that the lower limb was the most affected site in PISS, followed by the pelvis. Limb salvage was performed in six patients and one patient underwent amputation. Of these patients, six received adjuvant chemotherapy and four received adjuvant radiation as per institution guidelines. The study found that the 5-year disease-free and overall survival rate was 80 and 61%, respectively.

**Conclusion** PISS is a rare malignancy with limited cases in literature, and hence, there is no evidence for a standardized management protocol. The survival rates were similar between soft tissue and intraosseous synovial sarcoma among the case series.

## Introduction

Primary intraosseous synovial sarcoma (PISS) is an extremely rare tumor and was first described in the proximal tibia by Cohen et al in 1997.<sup>1</sup> Only few documented case reports on this rare entity have been described in literature, it primarily affects adolescents and young adults, with less than 10% of documented cases occurring over the age of 60.<sup>2-5</sup> We

present the largest series of seven cases and describe the clinical spectrum and review of the literature.

## Materials and Methods

We performed a retrospective analysis of all biopsy-proven synovial sarcoma (SS) who underwent treatment at our center from January 1995 and December 2016. Patients

DOI <https://doi.org/10.1055/s-0042-1757551> ISSN 2278-330X

**How to cite this article:** Ramanujan V, Soma S, Krishnan CK et al. Primary Intraosseous Synovial Sarcoma: Experience from a Tertiary Cancer Center. South Asian J Cancer 2022;00(00): 00–00.

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with histology-proven diagnosis, bone origin, and centrifugal spread of tumor as seen on magnetic resonance imaging (MRI) were included in the study. Patients treated elsewhere and presenting with local or systemic recurrences were excluded from the study. The historical records of eligible patient cohorts were reviewed, and all relevant clinical details including demographic profile, histological variants, and treatment and disease outcomes were collated and analyzed.

Upon confirmation of diagnosis, all patients had MRI of the involved extremity and metastatic workup included a chest computed tomography scan. Immunohistochemistry (IHC) and translocation studies were performed on postoperative specimen in all patients.

All statistical analyses were performed using SPSS software version 17.0 (SPSS Inc., IBM, Chicago, Illinois, United States). Student's *t*-test was used for nonparametric variables and the chi-square test was used for categorical variables with the level of significance set at *p* < 0.05. Actuarial overall survival was calculated from the date of diagnosis until the date of the last follow-up appointment using the Kaplan-Meier method.

### Results

There were 203 patients with a diagnosis of SS of which 7 cases were identified as PISS of the bone. The clinicodemographic profile of patients is given in [Table 1](#).

Four patients had open biopsies from bone or curettage done prior to presentation at our institute (15 days to 2 months prior) and had review of blocks. MRI images as depicted in [Fig. 1](#). Limb salvage surgery (LSS) could be performed in six patients with site-specific reconstruction. One patient underwent amputation as limb salvage was not feasible. Six patients had biphasic and one patient had monophasic type. IHC profile was performed on operative specimen and is shown in [Table 2](#) ([Fig. 2](#)).

Three patients received neoadjuvant chemotherapy (NACT). Two patients had pathological fractures on presentation, NACT was initiated to consolidate the fracture site. One patient (fibular tumor) had initial biopsy report suggestive of pleomorphic sarcoma and hence received NACT according to the osteosarcoma protocol (ifosfamide, Adriamycin, and cisplatin). A revised diagnosis of SS was made after evaluation of the final histopathological specimen with IHC correlation and translocation studies. Adjuvant chemotherapy was delivered after completion of radiation in five patients after limb salvage and one patient after amputation. One patient was deemed unfit for chemotherapy.

Adjuvant radiotherapy was delivered to the local site in all patients undergoing LSS except two patients with hemipelvectomies. The patient with acetabular PISS had significant wound morbidity because of a deep infection which needed multiple debridements. The patient with proximal femur PISS also had a wound breakdown, with a deep infection, and was treated through multiple wound debridements and antibiotic cement bead application.

**Table 1** Demography and treatment profile of the patients

Serial no.	Age (y)	Sex	Site	Prior surgery	NACT	Type of surgery	Margin	Adjuvant treatment	Recurrence	Follow-up duration
1	22	Male	Right ilium	Nil	No	Type 1 + 4 internal hemipelvectomy	Negative	Chemo + RT	Solitary lung (operable)	84
2	46	Female	Right acetabulum	Nil	No	Type 2 internal hemipelvectomy with prosthesis reconstruction	Negative	Nil	No	24
3	20	Male	Left tibia	piecemeal excision	Yes	Wide excision + free fibula transfer	Positive	Chemo + RT	No	62
4	30	Male	No	open biopsy	Yes	Above knee amputation	Negative	Chemotherapy	No	77
5	44	Male	Right radius	excision	No	Wide excision + ulnar translocation	Negative	Chemo + RT	Bilateral lung (inoperable)	19
6	16	Male	Right fibula	curettage	No	Wide excision + free flap	Negative	Chemo + RT	No	55
7	14	Female	Right proximal femur	Nil	No	Extra-articular proximal femur reconstruction with type 2 internal hemipelvectomy and a mesh pseudoarthrosis	Negative	Chemotherapy	No	13

Abbreviations: NACT, neoadjuvant chemotherapy; RT, radiotherapy.

**Table 2** Immunohistochemistry profile of the patients

Serial no.	Vimentin	EMA	Bcl-2	SMA	Desmin	Keratin	CD99	Ki-67
1	++	+	+	+	-ve	+	+	15–20
2	++	++	+	NA	-ve	+	+	10–15
3	++	+	NA	-ve	NA	-ve	+	40
4	+	-ve	NA	NA	NA	+	-ve	NA
5	++	++	++	NA	-ve	-ve	++	NA
6	++	-ve	NA	NA	NA	-ve	++	40
7	NA	+	+	NA	-ve	+	++	NA

Abbreviations: EMA, epithelial membrane antigen; NA, not available; SMA, smooth muscle actin.

The patient with radius PISS had wound breakdown with infected nonunion of the translocated ulna following radiotherapy. This case warranted complete implant removal and external fixator application with an abdominal wall flap.

No patient developed local recurrence. Two patients developed systemic recurrence (lung) (→Table 1). One patient developed multiple bilateral pulmonary metastases at 17 months after completion of treatment and was offered only best supportive care. The other patient developed solitary lung metastasis 19 months following completion of adjuvant therapy, for which the patient underwent lung metastasectomy with negative margins and has been disease-free at 84 months after surgery.

The disease-free survival and overall survival at 3 years was 71.42 and 85.71%, respectively. Age, sex, surgical margins, use of neoadjuvant therapy, and location of primary site did not influence survival. The only significant factor negatively influencing survival was distant metastasis ( $p = 0.03$ ).

The mean follow-up duration was 47.57 months (range: 12–84 months).

## Discussion

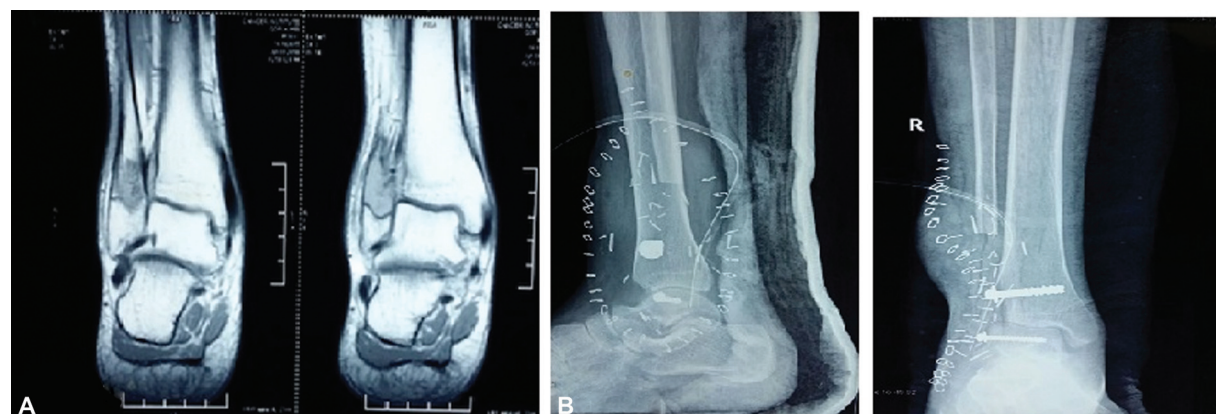
SS was originally coined in 1936 by Knox and was thought to be of synovial cell origin<sup>1</sup>; however, SS has been found to also originate in locations where no synovial tissue is present. SS has also been reported to arise in a variety of other locations such as in the head and neck, chest, and abdomen.<sup>6</sup> The

diagnosis of SS can be confirmed genetically with the detection of t(X;18) (p11.2;q11.2). This translocation involves the SS18 (i.e., SYT) gene on chromosome 18 and either the SSX1, SSX2, or rarely the SSX4 gene on the X chromosome.<sup>7</sup> This translocation occurs in more than 90% of all SSs.<sup>8</sup>

A review of literature revealed a total of 13 cases of PISSs in various sites,<sup>1–5,9–11</sup> with differing treatment. Since the first reported case in 1997, confirmed cases of PISS of the bone have been reported in the elbow,<sup>9</sup> sternum,<sup>12</sup> sacrum,<sup>13</sup> distal tibia,<sup>14</sup> and mandible.<sup>15</sup> To our knowledge, this is the largest series of PISSs to be published.

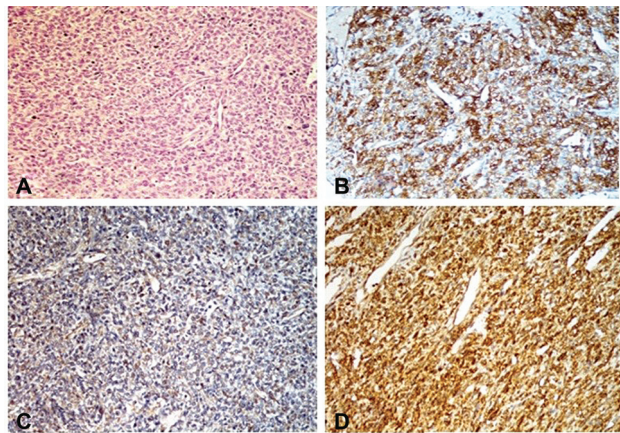
SS generally arises in the soft tissues of the extremities and rarely has an intraosseous origin. SS accounts for about 5 to 10% of all soft tissue sarcomas.<sup>2</sup> It commonly affects adolescents and young adults and has a mean age of onset of 30 years.<sup>3</sup> Males have been shown to be more commonly affected for the soft tissue primary site and the rarer intraosseous primary site. Lower extremities are most commonly affected. In our study, there was male preponderance (5:2) with mean age of onset at 27 years with 6 of 7 arising in the lower extremity.

The treatment for PISS in our study has been extrapolated from studies done for soft tissue SS. Due to high local recurrence rate of 63% with surgery alone, radiotherapy and chemotherapy has been added to the treatment protocol. In our series, four patients received adjuvant radiation with total dose used being 50 to 55 Gy. We have used six cycles of ifosfamide and Adriamycin chemotherapy in our patients and have used in adjuvant setting except



**Fig. 1** Magnetic resonance imaging (MRI) showing primary intraosseous synovial sarcoma (PISS) lesion in the distal fibula (A) and postresection (B).





**Fig. 2** (A) Photomicrograph of hematoxylin and eosin stain ( $5\times$ ) showing ovoid to spindle cells arranged in fascicles and hemangiopericytomatous pattern with interspersed blood vessels. (B) Photomicrograph showing CD99 membrane positivity ( $5\times$ ). (C) Photomicrograph showing epithelial membrane antigen (EMA) cytoplasmic positivity ( $5\times$ ). (D) Photomicrograph showing Bcl2 cytoplasmic positivity ( $5\times$ ). Magnetic resonance imaging (MRI) showing primary intraosseous synovial sarcoma (PISS) lesion in the distal fibula (A) and postresection (B).

when indicated as mentioned previously. When compared with other authors, only Cao et al<sup>16</sup> used adjuvant chemotherapy for PISS of thoracic spine and reported recurrence-free survival of 1 year. Other authors who used either surgical modality alone or combined with chemotherapy had mixed results with both local and distant recurrence reported.<sup>11</sup>

One patient with PISS of the tibia had positive marrow margin and received adjuvant radiation and chemotherapy and continues to be disease free at last follow-up.

The overall survival rates appear to be consistent with the survival rates of soft tissue SSs with the advent of multimodal treatment. Campbell et al<sup>17</sup> proposed good prognostic factors in the management of soft tissue SS, which included female gender, age < 50 years, location in the hand or foot, size < 5 cm, biphasic histologic pattern, *SYT/SSX2* translocation, and negative resection margins. However, none of these factors were found to be significant in our series, probably due to small size. In our study, the presence of recurrence significantly reduced the overall survival.

## Conclusion

PISS is extremely rare and accounts for 0.03% of all SSs treated at our institute. The treatment of choice is multidisciplinary management with wide-margin surgical resections alongside chemotherapy and radiotherapy. The survival rates appear to be consistent with that of soft tissue SS and the presence of primary disease in bone is not a relatively poorer prognostic factor. Distant recurrence is a poor prognostic factor for survival.

## Ethical Approval

The study has been approved by the Institutional Ethics Committee of the Cancer Institute, Approval Number: IEC/2020/Nov 10.

## Funding

None.

## Conflict of Interest

None declared.

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