

Hemophilic psuedotumor- is there a role of radiotherapy? Literature review and a case report

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ABSTRACT

We share the literature and management of an adult with moderate hemophilia a presented with a calcaneal psuedotumor and non healing ulcer by radiation therapy, factor VIII and cryoprecipitate supplement. Numerous literatures so far have quoted the satisfactory role of radiotherapy in hemophilic psuedotumor. We found it to be of great help as our case responded with radiotherapy, factor VIII and cryoprecipitate supplement and has a satisfactory 2 years follow up.

Keywords: Hemophilia, hemophilic psuedotumor, radiotherapy, factor VIII.

INTRODUCTION

Psuedotumor of bone in patients with hemophilia is rare, but well known and serious complications. This condition is seen in 1.0-2.0% of patients with either hemophilia A or B.¹

A hemophilic psuedotumor (HP) is recognized as a collection of chronic encapsulated blood initiated in most case by a minor traumatic injury. This is followed by recurrent extra-articular hemorrhage either into muscle, periosteum, or intraosseous spaces and development of a tough surrounding fibrous capsule. Psuedotumor are categorized as osseous and soft tissue lesions, on the basis of anatomic location.² The radiographic findings of a soft tissue mass with areas of calcification and adjacent bone destruction in a patient with hemophilia is usually sufficient to make the diagnosis of a pseudotumor.³ Conventional radiography, sonography, CT, and MRI each play an important role in the diagnosis, characterization and management.⁴⁻⁶ The mass usually grows in size over months or years and presents as features of compression of adjacent structures and increasing destruction of bone resulting into severe pain and deformity.

Treatment of this condition is difficult and requires multimodal approach. The treatment modality in each patient depends on the size of psuedotumor, site of involvement and the presence of inhibitors. Varying degrees of success with surgical resection,^{7,8} radiation therapy,⁹⁻¹¹ combination of radiation with factor replacement^{12,13} or embolization¹⁴ have been reported in literature. Non surgical mode of treatment is being tried in form of radiotherapy alone or combined with factor VIII. We evaluated the results of previous studies and

proceed further and found good result (Table-1). We suggest radiotherapy can be tried in HP especially where surgical treatment is less helpful and disastrous.

MATERIALS AND METHODS

A 23 year male, diagnosed case of moderate hemophilia A at age 4 (factor VIII approximately 4.0%) sustained a trivial trauma and developed swelling around left ankle 4 months back prior to our consultation. He was a registered member of hemophilia society and was under treatment from the same society. He was managed with light compression bandage followed by factor supplement. The acute episode of pain subsided though the swelling persisted. One month later he observed the spontaneous increase in size of swelling and pain in the ankle. With in few days he observed the color change around ankle followed by skin necrosis and discharging sinus below the lateral malleolus and medial malleolus, which progressed and later resulted into a non healing sinus. He was then referred to our center.



Fig. 1. Preradiotherapy, non healing ulcer lateral malleolus

Table-1: Outcome of patients with hemophilic pseudotumors treated with radiotherapy–review of literature

Year	No of cases	Age(yrs)	Bones involved	Treatment	RT dose	Outcome	Author
1942	1	30	Femur	RT	NA	Resolved	Muller <i>et al</i> ²⁶
1942	1	13	Tibia	RT	16Gy	Resolved	Echternacht <i>et al</i> ²⁷
1948	1	51	Femur	RT	NA	Noimprovement	Ghormley <i>et al</i> ²⁸
1959	1	65	Pubis	RT	23.50 Gy	Stable for 2 years	Horwitz <i>et al</i> ²⁹
1965	2	11, 13	Calcaneum and cuboid	RT	15.76Gy and 16.72 Gy	Resolved	Chen <i>et al</i> ³⁰
1968	2	11, 15	Mandible and fifth metacarpal	RT	8Gy and 10Gy	Resolved	Lazarovitis <i>et al</i> ³¹
1972	3	18, 13, 57	B/L tibia. Femur	F-VIII, Cyoprecipitate +RT	16Gy, 18Gy, 20Gy	Resolved	Brant <i>et al</i> ³²
1975	1	2	Femur	F-VIII+RT	7.5Gy	Resolved	Hilagartnet <i>et al</i> ¹⁶
1984	1	12	Mandible	F-IX+RT	6Gy	Resolved	Correra <i>et al</i> ¹¹
1985	1	14	Orbit	Proplex+RT	7.5Gy	Resolved	Meyers <i>et al</i> ³³
1991	2	3, 13	Mandible and fifth metacarpal	F-IX+RT	6Gy, 16Gy	Resolved	Castaneda <i>et al</i> ²⁴
1996	1	13	Tibia	RT	6Gy	Resolved	Ozbek <i>et al</i> ¹⁰
1998	1	15	Calcaneum	F-VIII, Cyoprecipitate +RT	15Gy/10days	Resolved	Kashyap <i>et al</i> ¹³
1998	1	14	Ankle joint	F-VIII, Cyoprecipitate +RT	14GY/7Fr	Resolved	Lal <i>et al</i> ³⁴
2001	1	20	PNS	F-VIII, Cyoprecipitate +RT	500cGy/10days	Resolved	Gupta <i>et al</i> ³⁵
2004	1	NA	Thumb	F-VIII, Cyoprecipitate +RT	NA	Resolved	Issaivanan <i>et al</i> ¹²
2005	1	30	Knee joint	F-enriched	25Gy/10Fr Cyoprecipitate +RT	Resolved	Kapoor <i>et al</i> ²¹
2007	1	NA	Hand	RT	2000cGy/10Fr	Stable	Subhasi <i>et al</i> ²²
2008	1	6	Orbit	RT	900cGy/5Fr	Resolved	Nongrum <i>et al</i> ²³
2009	1	23	Calcaneum	F-VIII, Cyoprecipitate +RT	15Gy/7days	Resolved	Laxman <i>et al</i> (current study)

On examination, there was a non healing ulcer of 3x3 cm just below the medial and lateral malleolus (Fig.1). Peri-malleolar swelling and change of skin color to dusky red. Slough and necrotic tissue with sero-sanguinush discharge was seen in the bed of ulcer but there was no frank pus. Hematological and radiological evaluation was done immediately after admitting the patient. Hematology confirmed the diagnosis of moderate

hemophilia A and imaging with X ray (Fig. 2) and MRI (Fig. 3) suggested large lytic lesion with heterogeneous internal contents (? Hemorrhage) in the calcaneum with cutaneous sinus on the medial and posterolateral aspect. The findings were consistent with HP with edema of talus and fluid in the ankle and subtalar joint.

The patient was started on factor VIII at dose of 2500 units every 12 hourly, supplemented with



Fig. 2. Pre radiotherapy X-ray showing calcaneal pseudotumor.

cryoprecipitate, regular dressing of the wound and light compression bandage was combined with external radiotherapy for 7 days. A total of 15 Gy/7 days was given and discontinued after a symptomatic relief. Post

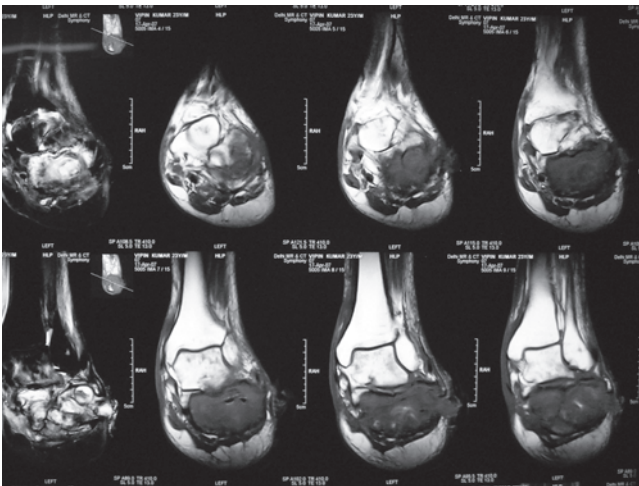


Fig. 3. Pre radiotherapy MRI section showing extent of lesion.

radiotherapy follow up after 2 months showed decrease in swelling and healed sinus on the medial aspect and organized but small persistent dry sinus on lateral side just below the lateral malleolus (Fig. 4). He was

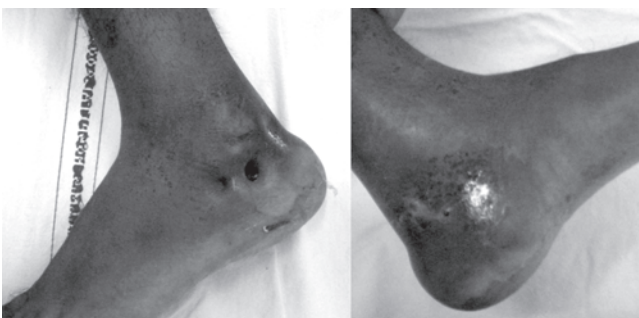


Fig. 4. Post radiotherapy healed sinus of medial and organized sinus of lateral malleolus

symptom free and was bearing weight over the affected limb comfortable. Two months post-radiotherapy X-ray (Fig. 5) and 6 months post-radio therapy MRI (Fig. 6) scans revealed reduction in the size of the lesion with some alteration in signal intensity due to evolution of the hemorrhagic products. A two years follow up is satisfactory, patient is ambulatory pain free and there is obliteration of sinus.

DISCUSSION

The diagnosis of HP is evident on the basis of clinical judgment, history of trauma, bleeding episodes, radio imaging and response of disease on treatment. Invasive methods to establish diagnosis like aspiration and biopsy are not favored for the fear of complication like; uncontrolled bleeding, skin necrosis, and non healing ulcers following procedures.

The mechanism of pseudotumor of bone is not understood well. Pathogenesis is unclear and several cases have been suggested : a) necrosis due to compression (bone destruction in the presence of hemarthrosis), b) subperiosteal or soft tissue hemorrhage with necrosis and bone destruction followed by bone formation and c) intraosseal hemorrhage, followed by cyst alterations with bone destruction and subsequent hemorrhage.^{15,16}

The bony destruction in imaging is similar to sarcoma, tuberculosis, multiple myeloma, and metastatic conditions.¹⁷

The different classification is based upon localization of injuries. First of them distinguishes three types according to anatomical layout, secondary osseal alteration and radiological correspondence.¹⁸

Another classification distinguishes between proximal HP and more frequent in adults and located in femur and pelvis and distal HP located in hands and feet, multiple more frequent in children and with better prognosis.¹

Magallon *et al*¹⁹ reviewed patient diagnosed with hemophilia A and B and other coagulopathies from 1965-1990. Of the 1831 patients, only 21 patients had pseudotumor, located mainly in the appendicular skeleton and the pelvis. Total number of patients with hemophilia A was 1108, of which only 16 patients (1.4%) had pseudotumor. Total number of patients with hemophilia B was 172, of which 4 (2.3%) had pseudotumor. The number of patients with other coagulopathies was 551, of which only 1 patient (0.2%) had pseudotumor. In the series, replacement therapy and surgery gave the good results, especially in cases that surgery was electively chosen.¹⁹

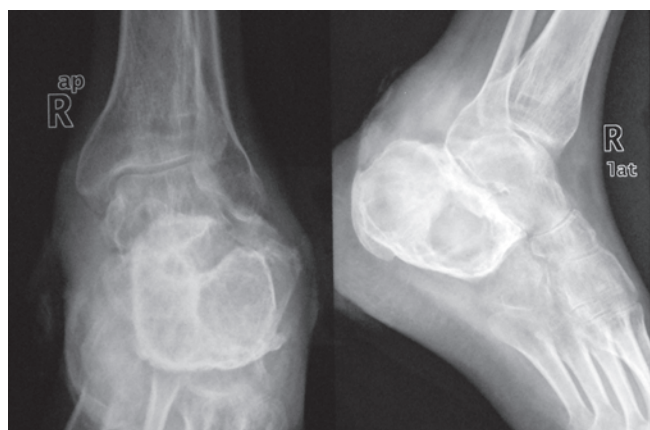


Fig. 5. Post radiotherapy X-ray showing healed lesion with sclerosis (2 months follow up).

Radiotherapy with or without factor VIII supplement has established better results in the previous studies. The mechanism of action of radiation is postulated to be the derangement of micro vascular architecture of the psuedotumor, resulting in increased fibroblastic activity leading to fibrosis.^{16,20} Secondary calcification occurs in four weeks and complete healing occurs in 8-12 weeks. Literature provides evidence that low dose radiation for hemophilic psuedotumor is sufficient.

Medline database search of patients with HP receiving radiotherapy with or without factor VIII replacement yielded a case report and review article of 22 cases by Kapoor *et al.*²¹ Which included the study by Magallon *et al* also. In the subsequent years two more cases Subhasi *et al*²² and Nongrum *et al*²³ were reported who were treated by radiotherapy. The most common site of involvement was the femur 5/25 (20.0%), followed by tibia 4/25 (16.0%), mandible 3/25 (12.0%), calcaneum 3/25 (12.0%), orbit 2/25 (8.0%), hand 2/25 (8.0%), pubic bone 1/25 (4.0%) and ankle joint 1/25 (4.0%), Para nasal sinus involvement was seen in 1/25 (4.0%) . Fourteen of 22 (56.0%) patients only received radiotherapy while 11/25 (44.0%) received radiotherapy and replacement factors. In 23/25 (92.0%) patients, the lesion had either resolved or were in the process of resolving, 1 (4.0%) patient did not show any improvement, and 2/25 (8.0%) patients had stable diseases. Castaneda *et al*²⁴ have reviewed 17 psuedotumor treated with radiation either alone or in combination with factor replacement. The radiation dose varied between 750 cGy to 2350 cGy. Fourteen of 17 (82.0%) patients showed complete resolution, while 3/17 (18.0%) patients with factor VIII inhibitors also responded to radiotherapy and factor VIII therapy. Krill *et al*²⁵ reviewed eight cases of hemophilic hemarthrosis over a period of seven years and showed that the patient treated with radiotherapy had rapid resolution of tumor without any recurrence. Dose as low as 600 cGy to as high as 2300 cGy with or without factor VIII replacement has shown good response.

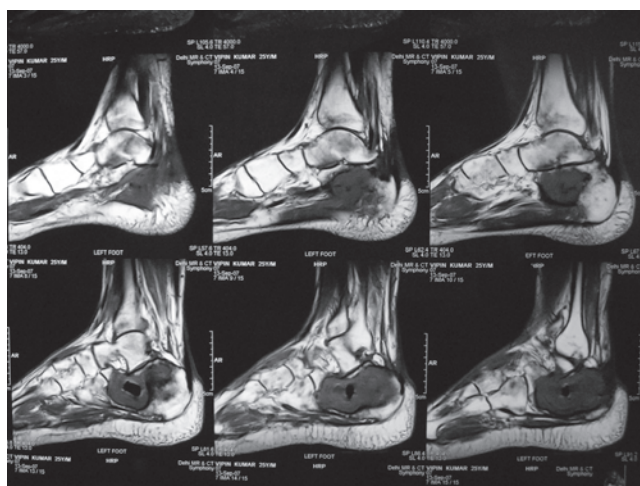


Fig. 6. Post radiotherapy MRI section showing the healed lesion (6 months follow up MRI)

In our case we preferred the combination therapy and the patient was started on factor VIII at dose of 2500 units every 12 hourly, supplemented with cryoprecipitate, regular dressing of the wound and light compression bandage was combined with external radiotherapy for 7 days. A total of 15 Gy/7 days was given and discontinued after a symptomatic relief. Two months clinico-radiological (X-ray) follow up revealed dramatic clinical recovery and 6 months later clinico-radiological (MRI) follow up suggested healed lesion. Now after 2 years of clinical follow up lesion has healed and he is asymptomatic even on full weight bearing.

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