ORIGINAL ARTICLE

Role of 3T MRI in Evaluation of Bone Marrow Changes in Spine in Various Diseases

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Abstract

Multiplanar MR imaging provides excellent spatial and contrast resolution necessary to differentiate the signal intensities of fatty (yellow) marrow elements from hematopoietic (red) marrow elements and hence it is useful for evaluation of various pathologies of bone marrow. Utilization of typical imaging features on conventional MR imaging techniques and other newer imaging techniques, such as diffusion-weighted imaging (DWI) and in- and out-of-phase MRI, for better characterisation of bone marrow pathologies has been highlighted.

Aims and Objectives

1. To determine the prevalence of various bone marrow pathologies in spine.
2. To study the MRI signal changes of bone marrow in various lesions such as anaemia, leukaemia, lymphomas and various bone marrow disorders.

Materials and Methods: A total of 100 patients who were investigated between November 2012 and October 2014 were included. MRI spine studies were done on a 3.0 Tesla Philips Achieva Medical Systems.

Observations and Results: In our study, out of 100 cases studied for various spinal pathologies, 48 patients were male and 52 were female indicating almost equal male to female distribution. Maximum cases were degenerative with most common site of involvement being lumbar followed by cervical region. There were only 3 cases of depletion disorder and no case with deposition disorder. The mean age group was 45.37 years, with the range being 9 years to 72 years. Maximum patients (n = 67) were found in the age group of 41-60.

Conclusion: Various bone marrow disorders were classified and evaluated separately. A systematic approach to its evaluation by categorization is essential with prudent use of both conventional and problem-solving techniques, such as CSI and DWI, for accurate diagnosis and appropriate patient management.

Conventional radiology depicts changes of an altered bony matrix while MRI displays changes at a cellular level and is well suited for imaging the bone marrow. MRI serves as a screening method in bone marrow disorders and the diagnosis is established in context with the clinical findings or by biopsy.

Introduction

Normal Bone Marrow

Bone marrow is divided into two main constituents, yellow and red marrow. "Yellow marrow" is considered as hematopoietically inactive and is mainly composed of fat cells while "Red marrow" in contrast, is characterized by a rich sinusoidal system and contains approximately 60% hematopoietic cells and 40 % fat cells. During growth, conversion of red to yellow marrow occurs following a predictable and orderly pattern until a balanced distribution pattern is reached by the age of 25. The exact pattern of marrow changes depend on many factors like sex, age and the health of the individual. With age trabecular bone is also decomposed and replaced by fat cells, hence the increase in fatty marrow with age is greater than the reduction in volume of red marrow. Sometime reconversion of yellow to red marrow takes place if a sudden rise in the demand for haematopoiesis occurs.

Disorders that affect bone marrow can be divided into following categories: Reconversion due to hyperplasia, Marrow infiltration or replacement disorders, Depletion of hematopoietic marrow, Depletion of myeloid elements with fibrosis and Deposition of metabolic products. This article reviews MRI protocols, including routine and non-routine pulse sequences such as diffusion-weighted imaging (DWI) and in- and out-of-phase MRI and outlines a systematic approach and typical imaging features of various pathologies based on available literature.

Materials and Methods

A total of 100 patients who were investigated between November 2012 and October 2014 were included. MRI spine studies were done on a 3.0 Tesla Philips Achieva Medical Systems.

Indications

A prospective study of 100 patients who presented to the OPD or Emergency department or admitted with clinically suspected pathology involving the axial skeleton underwent MRI of spine on an elective basis. Standard tests (history taking, physical examination, relevant blood investigations) were directed to all patients, whereas, the mode of additional imaging (x-ray spine or x-ray/CT chest and abdomen in patient with primary at other known location) was also carried out.

Inclusion Criteria

Clinical suspected pathology involving the axial skeleton.

Biochemical examination suggestive

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Table 1: Diagnosis and relative frequency of occurrence of various bone marrow disorders

Diagnosis	No. of patient
Degenerative disorders	60 (60%)
Infiltration/ replacement disorders	16 (16%)
Reconversion disorders	11 (11%)
Depletion disorders	3 (3%)
Deposition disorders	0 (0%)
Focal disorders of bone marrow	10 (10%)

of deranged haematological profile / Ineffective haematopoiesis (like in cases of thalassemia)

In patients with known primary malignancy presented with backache.

In patients with backache radiating to extremities without any previous significant past history.

In patients with hyperparathyroidism.

Exclusion Criteria

Patients not consenting for the study

Intracranial aneurysm clips (Unless the referring physician is certain that it is made of non-ferromagnetic material such as titanium)

Intra-orbital metal fragments

Any electrically, magnetically or mechanically activated implants

1. Including cardiac pacemakers, biostimulators, neurostimulators,
2. Cochlear implants and hearing aids.

Pregnancy (Risk Vs benefit ratio to be assessed).

Known h/o contrast allergy.

Other implanted medical devices (eg. Swan Ganz catheter).

Metal shrapnel or bullet.

For use of MR contrast (gadolinium):

1. Lactating women
2. Patients with moderate to severe renal insufficiency (i.e. with GFR<30ml/min or a S. creatinine> 2mg/dl)

Imaging Technique

The MRI appearance of the bone marrow depends on the pulse sequence used for its evaluation as well as on the relative amount of water, fat, protein and cells within the bone marrow. Among these the major determinants of the MR appearance of bone marrow are the fat and water content.

The routine spine evaluation on MRI typically includes T1-weighted,

Table 2: Age distribution of the bone marrow disorders

Age group (years)	No of patient (%)
0-10	01 (1%)
11-20	06 (6%)
21-30	07 (7%)
31-40	15 (15%)
41-50	33 (33%)
51-60	34 (34%)
61-70	03 (3%)
>71	00 (0%)

T2-weighted, and Short Tau Inversion Recovery (STIR) sequences. Post-contrast (intravenous gadolinium) fat-suppressed T1W imaging should always include pre-contrast baseline fat-suppressed T1W imaging in at least one plane. Several non-routine MRI sequences include T1 FLAIR Imaging, Diffusion-weighted imaging (DWI), in- and out-of-phase MRI, MR spectroscopy (MRS), and dynamic contrast enhanced MRI (DCE-MRI). These aid in enhancing contrast and visualize changes in the bone marrow at a molecular level.

Observation and Results

Prevalence of various bone marrow disorders

Out of 100 patient studied following diagnoses were made. Diagnosis and relative frequency of occurrence of various bone marrow disorders has been given below (Table 1).

Age distribution

The patients were divided on the basis of age group. Maximum patients (n = 67) were found in the age group of 41-60. Otherwise an equal distribution was seen in all age groups. The mean age group was 45.37 years, with the range being 9 to 68 years. Age distribution of the bone marrow disorders has been given below (Table 2).

Degenerative disorder

In our study of various spinal pathologies, there were 60 cases (60%) of degenerative changes of spine on MRI - Disc degeneration, Disc bulge, Disc herniation, Modic changes, Canal stenosis/Nerve root compression. Various types of degenerative changes and their frequency of distribution has been given below (Table 3).

Classification of Infiltrative / Replacement diseases

In our study of various spinal pathologies, there were 16 cases (16 %) of infiltrative / replacement disorders

Table 3: Various types of degenerative changes and frequency of distribution

Degenerative changes	Findings in patients with degenerative disorders
Disc degeneration	41 (68.3%)
Disc bulge	21 (35%)
Disc Herniation	28 (46.6%)
Modic changes	17 (28.3%)
Canal stenosis/nerve root compression	40 (66.7%)

of spine, of which most common pathology was metastasis found in 11 cases (68.7%). Marrow can be replaced by either neoplastic disorders or non-neoplastic disorders. Various neoplastic diseases include metastatic disease, lymphoma, leukemia, and multiple myeloma. These cases were confirmed pathologically with bone biopsy. Various types of infiltrative / replacement disorders and their frequency of distribution has been given below (Table 4).

Classification of Reconversion disorder

Reconversion disorders can be classified in to the chronic anemia, hyperparathyroidism and miscellaneous conditions (Heavy smoking, increase oxygen requirements), there were total 11 (11%) cases of reconversion disorders of spine in our study, of which most common was chronic anaemia due to thalassemia accounting for approximately 45.5% (5 cases) of all reconversion disorders. Cases of thalassemia and sickle cell disease were proven with clinical correlation, blood parameters and Hb electrophoresis. Cases of hyperparathyroidism were proven clinically and with blood parameters viz S. PTH, calcium and phosphate levels. Various types of reconversion disorders and their frequency of distribution has been given below (Table 5).

Classification of Depletion disorders

In our study, there were 3 (3%) cases of depletion disorders. Various depletion disorders can be classified in to depletion disorders secondary to radiotherapy, chemotherapy, idiopathic and depletion disorders with fibrosis (myelofibrosis), aplastic anaemia and tabulated below. Various types of depletion disorders and their frequency of distribution has been given below (Table 6). Bone biopsy was performed for confirmation.

Table 4: Various types of infiltrative / replacement disorders and frequency of distribution.

Infiltrative / replacement disorders	No of patients
Metastasis	11 (68.7%)
Lymphoma	2 (12.5%)
Leukemia	0 (0%)
Myeloma	0 (0%)
Non-neoplastic disorders	3 (18.8%)

Table 5: Various types of reconversion disorders and frequency of distribution

Reconversion disorders	No of patients
Chronic anaemia : Sickle cell anaemia	1 (9.09%)
Chronic anaemia : Thalassemia	5 (45.4%)
Hyperparathyroidism	2 (18.1%)
Others (Heavy smoking, increase Oxygen requirements)	3 (27.2%)

Table 6: Various types of depletion disorders and frequency of distribution

Depletion disorders	No of patients
Unknown cause	1 (33.33%)
Myelofibrosis	1 (33.33%)
Aplastic anaemia	1 (33.33%)
Secondary to chemo or radiotherapy	0 (0%)

Table 7: Various types of focal disorders and frequency of distribution

Focal disorders of bone marrow	No. of patients
Focal edema(Infection)	6 (60%)
Ischemia	0 (0%)
Trauma	4 (40%)

Distribution of focal disorders of bone marrow

In our study, there were 10 (10 %) cases of depletion disorders. Various focal disorders of bone marrow in spine are focal edema, ischemia and trauma. Various types of focal disorders and their frequency of distribution has been given below (Table 7).

Discussion

The role of diagnostic imaging is to provide accurate anatomic information and to affect the management decision making.[1] This cross-sectional hospital based study used MRI to diagnose various bone marrow pathologies in spine as it has better tissue differentiation and it can show bone marrow changes at an early stage as compared to other imaging techniques (such as CT Scan and radiographs). Other advantages of MRI include a) no known side effects or morbidity, b) no radiation exposure and is c) non-invasive.[2,3] Despite its high sensitivity, few of the marrow changes are observed on many MRI scans in asymptomatic subjects, thus questioning its specificity.

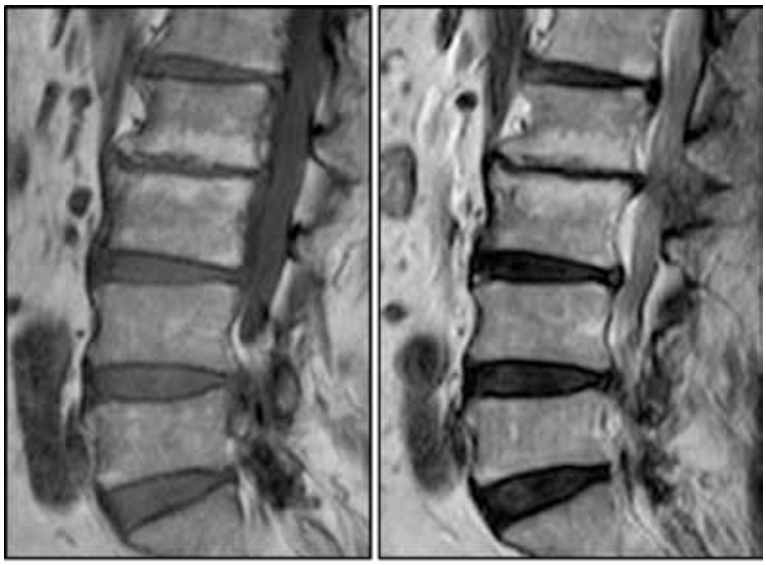


Fig. 1: Endplates adjacent to the L2-L3 intervertebral disc showing hyperintense signal on T1 W (A) and T2 W (B) imaging s/o Type II Modic changes. There is also decrease disc space involving L2-L3 level with posterior disc bulge

Prevalence of bone marrow pathologies

In our study of 100 patients of various spinal pathologies, around 60% were degenerative disorders. Among the various bone marrow pathologies, after excluding degenerative changes, most common pathology was infiltration/replacement disorder (16%) of which most common was metastasis. Second most common pathology was reconversion disorder (11%) followed by focal disorders of bone marrow (10%). Least common pathologies were Depletion disorders and Deposition disorders. Vogler et al, have grouped the bone marrow disease conditions according to common pathophysiological patterns in to reconversion disorder, infiltration disorders, depletion disorders, bone marrow edema and bone marrow ischemia.[4]

Age Distribution

In our study patients were found in all age groups with the mean age group being 45.3 years, with the range being 9 years to 68 years. The mean age group of above 45 is expected considering that a major cause of various marrow pathologies are degenerative and infiltrative / replacement disorder of which most common is metastasis, which tend to occur in elderly population.

Degenerative Disorder

Degenerative changes were observed in majority of patients examined i.e. in 60 patients (60%). Though degenerative changes of the disc begin early in life and are partly a consequence of aging, the actual cause is not known but many factors (autoimmune, genetic, re-absorption and biochemical) have been implicated in accelerating the process. Disc degeneration was the most frequent finding observed in 41 (68.3%) patients in our study followed by disc bulge, disc herniations and Modic changes (Figure 1 A, B). The prevalence was observed to increase with age. Proportion of degenerated discs progressively increases at lower spinal levels, and that most common part of spine involvement is lumbar region, in particular L4-L5 and L5-S1 levels.[5-7]

Infiltrative / Replacement Disorders

Most common neoplastic processes that involve the spine is metastatic disease which was consistent with our study. Followed in order were lymphoma, and plasma cell dyscrasia, either solitary plasmacytoma or multiple myeloma.[8]

Metastasis

Replacement of the bone marrow always appears hypointense relative to normal marrow on T1-weighted images.[9,10] On T2-weighted images; metastatic lesions are usually much brighter than bone marrow due to

Fig. 2: In this k/c/o carcinoma prostate, multiple hyperintense lesions are seen scattered throughout the dorsal vertebral bodies and appear hyperintense in in-phase sequence (A) and do not suppress on out-phase sequence (B) s/o infiltrative disorder

Fig. 3: In this k/c/o Thalassemia major patient, vertebral bodies show diffuse hypointensity on T1 W (A), T2 weighted (B) sequences compared to intervertebral disc s/o Marrow Reconversion

their high water content. Metastases often (but not consistently) have a rim of bright T2 signal around them (a halo sign).[11] The halo sign and diffuse signal hyperintensity were shown to be a strong indicator of metastatic disease. In our study, all patients with metastasis had hypo to isointense signal on T1 and heterogeneously hyperintense signal on T2 with 4 out of 11 were showing halo sign and 6 out 11 were showing the post contrast enhancement. Hence, findings were almost consistent with previous data. Dual-FFE sequence was done in only 5 patients with metastasis; increased signal was noted in all the 5 patients on out phase (Figure 2 A, B).

Lymphoma

When lymphoma involves the spine, it is more commonly found isolated to the epidural space as a result of secondary spread. Tumour location within the epidural space can vary, but there is a proclivity for the thoracic levels.[12,13]

On MRI, Spinal lymphoma is typically hypointense on T1 and in homogenously hyperintense on T2WI.[14] In our study, in patients with lymphoma, lesions were hypointense on T1 and hyperintense on T2. There was no significant post contrast enhancement in either of the patients.

Reconversion Disorder

11 cases of reconversion disorders of spine seen in our study, of which most common was chronic anaemia due to thalassemia followed in order were hyperparathyroidism and sickle cell anaemia and other causes like increase oxygen requirements and heavy smoking.

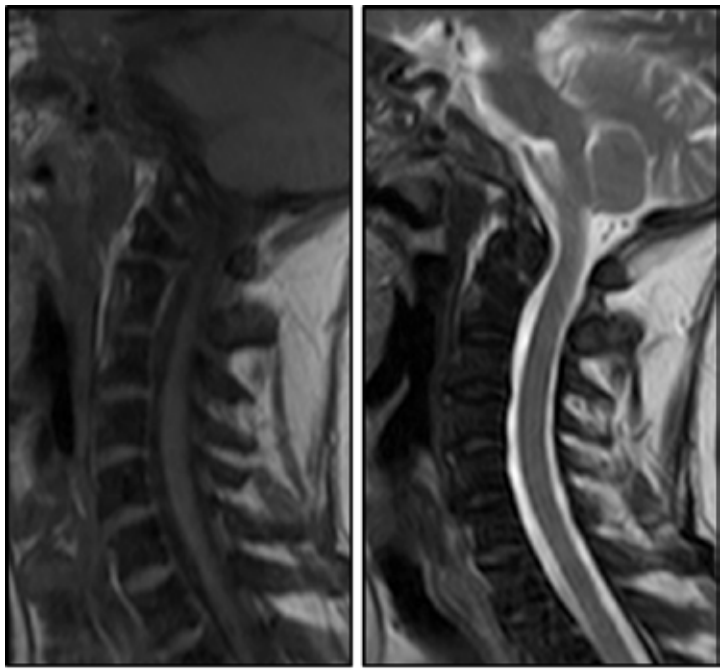
Hemolytic Anaemia- Thalassemia

Signal characteristics of marrow were compared with those of surrounding muscle and fat. Fatty marrow (isointense with subcutaneous fat) was compared with red marrow (hypointense to fat and slightly hyperintense to muscle). Marrow hypointense to muscle was identified as iron deposition within red marrow.

There are only a few studies addressing marrow SI in transfusion-dependent patients with thalassemia[15,16] and sickle cell anaemia[17,18] by using T1- and T2-w SE sequences. They report the presence of hypointense bone marrow in both T1- and T2-w images as attributed to iron deposition.[15-18] In our study, we found that 3 out of 5 patients (60%) with thalassemia had diffuse bone marrow hypointensity in all MR sequences (Figure 3 A, B). 2 out of 5 patients (40%) had hypointensity on the T2*-W GRE sequence alone without any significant hypointensity on T1 and T2.

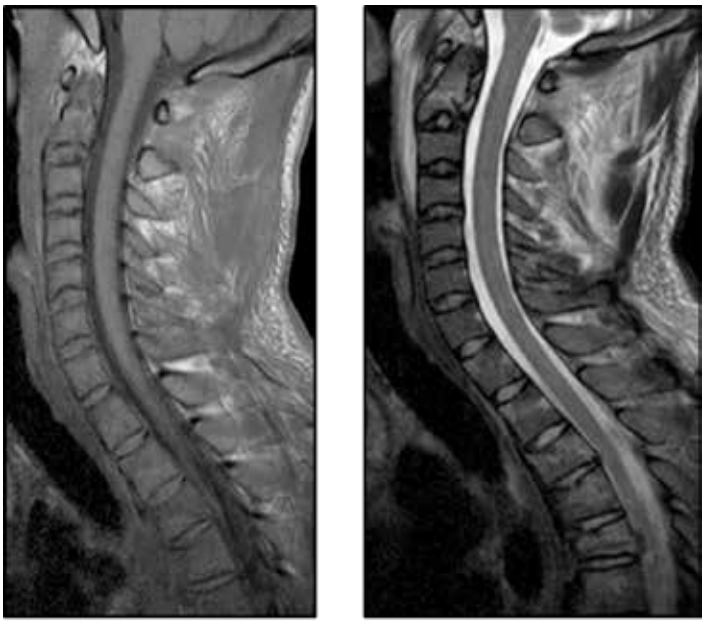
Hemolytic Anaemia-Sickle cell anaemia

There was only one case of sickle cell anaemia found in our study and findings were diffuse hypointense signal noted on T1 involving entire



A: T1 W sequence B: T2 W sequence

Fig. 4: There is diffuse hypointensity noted on both T1 W (A) and T2 weighted (B) sequences involving the vertebral bodies compared to intervertebral disc resulting in a "black marrow"



A: T1 W sequence B: T2 W sequence

Fig. 5: Fracture line appears hypointense on T1 W (A), T2 weighted (B) sequences and hyperintense signal of marrow on T2 weighted sequence indicating marrow edema

spine consistent with findings of anaemia without any complications of osteomyelitis.

Depletion Disorders

Only 3 cases of depletion disorders were found in our study .Various depletion disorders can be classified into depletion disorders secondary to radiotherapy, chemotherapy, idiopathic and depletion disorders with fibrosis (myelofibrosis), aplastic anaemia.

In study conducted by Gupta et al., Magnetic resonance imaging of the thoracolumbar spine revealed multiple focal low signal intensity lesions involving most of the thoracic and lumbar vertebral bodies[19]. In our study there was diffuse T1 and T2 hypointensity noted in all patients with depletion disorders (Figure 4 A, B).

Focal Disorders of Bone Marrow

Trauma

In our study, out of 4 patients with trauma to spine, 3 patients had injury and associated vertebral fracture involving cervical vertebra while rest 1 had fracture involving the thoracic region.

In study conducted by us, there were 4 patients of benign traumatic fractures; all had diffusely hypointense signal on T1-weighted images and hyperintense signal on FSE T2-weighted fat-suppressed images and contrast given to 1 patient showed contrast enhancement (Figure 5 A, B).

Infection (Tuberculous spondylitis)

Thoracolumbar spine is most common site of involvement in Tuberculous Spondylitis (50% of patients). Each of cervical spine and lumber spine are involved in 25% of patients.[20] In our study, there were 6 patients of Tuberculous Spondylitis out of which 5 had thoracolumbar spine involvement (i.e. 83.33%) and 1 had multiple level diffuse involvement (16.67%).

Conclusion

Bone marrow lesion can be seen as a non-specific finding in a variety of conditions. A systematic approach to its evaluation by categorization is essential with prudent use of both conventional and problem-solving techniques, such as CSI and DWI, for accurate diagnosis and appropriate patient management.

Conventional radiology depicts changes of an altered bony matrix while MRI displays changes at a cellular level and is well suited for imaging the bone marrow. It is very sensitive, although the specificity of MRI findings is not always without fallacies. Hence MRI serves as a screening method in bone marrow disorders and the diagnosis is established in context with the clinical findings or by biopsy.

In Hodgkin's lymphoma marrow involvement is detected more often with MR than with marrow biopsy. In low-grade NHL the involvement is diffuse and biopsy is superior. In high-grade lymphomas the involvement is more focal and MRI is more efficient. Also, the nodular nature of

lymphomatous marrow deposits allow MR mapping to select the site of biopsy because blind bone marrow biopsy may give false negative results.

References

1. Modic MT and Ross JS. Lumbar degenerative disc disease. *Radiology* 2007; 245:43-61.
2. Modic MT, Obuchowski NA, Ross JS, et al. Acute low back pain and radiculopathy: MR imaging findings and their prognostic role and effect on outcome. *Radiology* 2005; 237:597-604.
3. Shobeiri E, Khalatbari MR, Taheri MS, Tofighirad N and Moharamzad Y. Magnetic resonance imaging characteristics of patients with low back pain and those with sciatica. *Singapore Medical Journal* 2009; 50:87-93.
4. Vogler JB, 3rd and Murphy WA. Bone marrow imaging. *Radiology* 1988; 168:679-93.
5. Cheung KM, Karppinen J, Chan D, et al. Prevalence and pattern of lumbar magnetic resonance imaging changes in a population study of one thousand forty-three individuals. *Spine* 2009; 34:934-40.
6. Ong A, Anderson J and Roche J. A pilot study of the prevalence of lumbar disc degeneration in elite athletes with lower back pain at the Sydney 2000 Olympic Games. *British Journal of Sports Medicine* 2003; 37:263-6.
7. Takatalo J, Karppinen J, Niinimaki J, et al. Prevalence of degenerative imaging findings in lumbar magnetic resonance imaging among young adults. *Spine* 2009; 34:1716-21.
8. Rodallec MH, Feydy A, Larousserie F, et al. Diagnostic imaging of solitary tumors of the spine: what to do and say. *Radiographics : a review publication of the Radiological Society of North America, Inc* 2008; 28:1019-41.
9. Daffner RH, Lupetin AR, Dash N, Deeb ZL, Sefczek RJ and Schapiro RL. MRI in the detection of malignant infiltration of bone marrow. *AJR American Journal of Roentgenology* 1986; 146:353-8.
10. Baur A, Stabler A, Bruning R, et al. Diffusion-weighted MR imaging of bone marrow: differentiation of benign versus pathologic compression fractures. *Radiology* 1998; 207:349-56.
11. Schweitzer ME, Levine C, Mitchell DG, Gannon FH and Gomella LG. Bull's-eyes and halos: useful MR discriminators of osseous metastases. *Radiology* 1993; 188:249-52.
12. Lyons MK, O'Neill BP, Marsh WR and Kurtin PJ. Primary spinal epidural non-Hodgkin's lymphoma: report of eight patients and review of the literature. *Neurosurgery* 1992; 30:675-80.
13. Epelbaum R, Haim N, Ben-Shahar M, Ben-Arie Y, Feinsod M and Cohen Y. Non-Hodgkin's lymphoma presenting with spinal epidural involvement. *Cancer* 1986; 58:2120-4.
14. BN Lakhkar MA, Jose J. Pictarial essay : MR appearances of osseous spine tumors. *Indian Journal of Radiology and Imaging and Imaging* 2002; 12:383-90.
15. Levin TL, Sheth SS, Ruzal-Shapiro C, Abramson S, Piomelli S and Berdon WE. MRI marrow observations in thalassemia: the effects of the primary disease, transfusional therapy, and chelation. *Pediatric Radiology* 1995; 25:607-13.
16. Brasch RC, Wesbey GE, Gooding CA and Koerper MA. Magnetic resonance imaging of transfusional hemosiderosis complicating thalassemia major. *Radiology* 1984; 150:767-71.
17. Levin TL, Sheth SS, Hurlet A, et al. MR marrow signs of iron overload in transfusion-dependent patients with sickle cell disease. *Pediatric Radiology* 1995; 25:614-9.
18. Kaneko K, Humbert JH, Kogutt MS and Robinson AE. Iron deposition in cranial bone marrow with sickle cell disease: MR assessment using a fat suppression technique. *Pediatric Radiology* 1993; 23:435-8.
19. Gupta G, Robertson P and Szer J. Focal lesions on magnetic resonance imaging in aplastic anaemia: multiple metastases or haemopoietic marrow. *Australasian Radiology* 2007; 51 Spec No.: B110-4.
20. Wheeless CR. *Wheeless' Textbook of Orthopaedics*. 1996.