

Importance of Hyaline Material in Herniated Lumbar Disk Pathology: Predicting the Presence of Hyaline from Preoperative Magnetic Resonance Imaging and its Clinical Significance

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ABSTRACT

Aim: To conduct a prospective study to assess whether we can predict the presence of hyaline material in the extruded disk from preoperative magnetic resonance imaging (MRI) in patients with lumbar disk herniations and its clinical significance.

Materials and methods: Hundred patients posted for micro-lumbar discectomy were included in the study. They were assessed preoperatively for severity of symptoms using visual analog scale (VAS). Detailed radiological assessment was done using MRI. Following surgery, extruded disk specimens were sent for histopathological examination. The presence of hyaline material in biopsy was correlated with specific MRI findings and postoperative outcome assessed based on the VAS score.

Results: Out of the 100 patients, there were 58 males and 42 females between the age of 18 and 55 years. Histopathology of herniated disk material showed annulus fibrosis in 15% of patients, nucleus pulposus in 78% and a combination of both in 7%. Hyaline cartilage was found in 24% of patients. Extend of Modic changes more than 50% of vertebral end plate in MRI was indicative of the presence of hyaline in biopsy ($p < 0.001$). Preoperative MRI finding of vertebral end plate defect (VEPD) was associated with the presence of hyaline in 92.8% of cases. Presence of hyaline was correlated with the improvement in mean VAS score postoperatively.

Conclusion: In this study, the importance of hyaline in the extruded disk with its clinical significance is emphasized. We conclude that the presence of hyaline, as predicted from MRI findings like VEPD and extend of Modic changes, is a predictor of good postoperative outcome.

Keywords: Hyaline, Modic, Vertebral end plate.

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INTRODUCTION

Although disk herniation is a common disease, few data are available in literature discussing histopathology and composition of herniated material including presence of hyaline and granulation tissue.^{1,2} Importance of knowing tissue composition in herniated disk material is that inflammatory responses are different for each leading to varied symptomatology.^{1,3} Hyaline material, which is common in avulsion type of herniations, has the property of inhibiting the natural healing mechanism by neovascularization. Hyaline thus, reduces the chances of spontaneous resolution of extruded disk.⁴⁻⁶ Our aim was to conduct a prospective study to assess the histopathology of extruded disk material and whether we can predict the presence of hyaline in the extruded disk from preoperative magnetic resonance imaging (MRI) findings and its clinical significance.

MATERIALS AND METHODS

Patient Selection

We conducted a prospective observational study on 100 patients, who underwent microsurgical removal of extruded lumbar disk between 2013 and 2015 in Government Medical College, Kottayam, Kerala. Patients with recurrent disk herniation and failed back syndrome were excluded from the study. Patients were assessed preoperatively for severity of clinical symptoms using visual analog scale (VAS) score. A proper neurological examination was done. Detailed radiological assessment was done using MRI spine (1.5 Tesla) with T1-weighted and T2-weighted sequences. Disk herniation with adjacent vertebral end plate involvement was graded according to Modic types. Quantitative assessment of end plate destruction along the anteroposterior diameter of end plate was done as < 25 , $25-50$, $50-75$ and $> 75\%$. We looked specifically for vertebral end plate defect (VEPD). Vertebral end plate defect was defined as discontinuity in end plate of adjacent vertebra in MRI.

Those patients planned for surgery underwent routine preoperative investigations. After obtaining informed written consent, patients were taken-up for laminectomy

and discectomy. Approval was obtained from Institutional Review Board (IRB) for enrolling patients in the study.

All surgeries were done with the aid of operating microscope. During surgery, all epidural and submembranous part of disk herniation were removed. Intradiscal space was examined thoroughly and loose parts of disk were removed in order to prevent reherniation. Extruded parts were separately placed in 5% formalin solution and sent for histopathological examination.

Histopathology was intended to assess as follows:

- Presence of hyaline material in herniated disk
- Composition of extruded material
- Presence or absence of neovasculariation or granulation tissue.

Specimen was first assessed macroscopically and then microscopically. The specimen was sectioned using microtome and stained with hematoxylin and eosin to specifically look for composition of herniated material annulus fibrosis was identified as consisting of fibrocartilage with fascicular collagen fibers. Nucleus pulposus contained bland cartilage in mucoid matrix and cartilaginous endplate contained hyaline cartilage in matrix. Along with this, the presence of neovascularization and granulation were also assessed. Both preoperative and postoperative VAS scores were compared and the outcome was assessed. Postoperatively, patients were followed-up for 6 months to assess clinical outcome.

STATISTICAL ANALYSIS

Data were collected in a prewritten proforma. Collected data were entered in Microsoft Excel spreadsheet and analyzed using statistical package for social sciences (SPSS, Version 16, and Chicago SPSS Inc). Basic descriptive data were presented in distribution tables. To compare distribution of two dichotomous variables, we used Fischer exact test. Categorical data were analyzed using Chi-square test and a $p < 0.05$ was taken as significant. And wherever necessary, non-parametric test were also applied. If data were not normally distributed, Mann-Whitney test was used to compare between the two groups and Wilcoxon test was used to compare within the two groups. Two tailed significance was kept at < 0.05 .

RESULTS

Demographics

Out of 100 patients who participated in the study, there were 58 males and 42 females between the age group of 18 and 55 years (mean age: 37.5 ± 7.75 years). The composition of herniated disk material showed annulus fibrosis in 15% of patients, nucleus pulposus in 78% and combination of

both in 7%. Hyaline material was found in 24% of biopsy specimens. The tissue composition in biopsy showed a progressive change from nucleus pulposus to annulus fibrosis as age advances more than 35 years ($p < 0.001$) (Table 1). In patients less than 25 years, all the extrusion contained nucleus pulposus whereas in patients with age more than 45 years, majority of extrusion (10 out of 20) contained only annulus fibrosis. Composition of extruded disc material among various age group is shown in Table 1. Disk extrusions with hyaline was highest (11 out of 40 patients) in the middle age group (36–45 years) ($p = 0.26$). Number of disk biopsy specimens containing hyaline material and its relation to various age groups is shown in Table 2.

MAGNETIC RESONANCE IMAGING FINDINGS PREDICTING HYALINE IN BIOPSY

1. *Modic changes*: Modic changes in adjacent vertebra were found in all patients. A total of 58% of patients had type 1 Modic change, 30% had type 2 change and 12% had type 3 change. Patients with type 1 changes were younger compared to type 2 Modic change where majority (12 out of 30) belong to 36 to 45 years age group (Fischer exact test $p = 0.350$). Relationship between Modic change and age is shown in Table 3. Extend of Modic changes along vertebral end plates

Table 1: Composition of herniated material in different age groups

Age	Annulus fibrosis	Nucleus pulposus	Annulus and nucleus pulposus	Total
<25	0	6		6
26–35	1	33		34
36–45*	4	35	1	40
>45	10	4	6	20
Total	15	78	7	100

* $p < 0.001$

Table 2: Correlation of hyaline material in disk biopsy specimens in various age groups

		Age				Total
		<25	26–35	36–45*	>45	
Hyaline**	Present	1	10	11	2	24
	Absent	5	26	27	18	76
Total		6	36	38	20	100

* $p = 0.26$, **Hyaline material in biopsy specimens

Table 3: Modic changes along adjacent vertebra among various age groups

Age		Modic**			Total
		Type 1	Type 2	Type 3	
<25		5	1	0	6
26–35		23	9	2	34
36–45*		22	12	6	40
>45		8	8	4	20
Total		58	30	12	100

* $p = 0.35$, **Modic changes in vertebral end plate

were greatest (40%) in the middle age group (36–45 years) with 86 % having more than 50% of vertebral end plate involvement ($p < 0.001$). Relationship between extend of Modic changes in MRI and age is shown in Table 4.

In 16 out of 58 patients with type 1 changes, 6 out of 30 patients with type 2 changes and 4 out of 12 patients with type 3 changes, the extruded disk contained hyaline material (Fischer exact test, $p = 0.615$). Assumption that extend of Modic changes more than 50% along anteroposterior diameter of vertebral end plate had hyaline in biopsy, was statistically significant ($p < 0.001$). Sixty-eight percent of disk biopsy specimens with hyaline cartilage had Modic changes involving more than 50% of vertebral end plate in MRI, whereas patients with less than 50% involvement of vertebral end plate had hyaline only in 4% of biopsy specimens. Histogram showing relationship between presence of hyaline and extension of Modic changes along vertebral end plates are shown in Graph 1.

2. *Vertebral end plate defect:* On evaluating VEPD on MRI, we found that 92.8% of patients (26 out of 28) with VEPD had hyaline material in biopsy and 6.8% of patients without VEPD in MRI had hyaline in biopsy. The assumption that presence of vertebral end plate defect had cartilaginous material in extruded disk was statistically significant (Fischer exact test $p < 0.001$). Thus, VEPD in MRI had 92.85% sensitivity and 97.2% specificity in predicting presence of hyaline in extruded disk. Relationship between VEPD and presence of hyaline in extruded disk material is shown in Table 5.

Thus, the extend of Modic changes $> 50\%$ of vertebral end plate and presence of VEPD on MRI were predictive of the presence of hyaline material in extruded disk specimens ($p < 0.005$). But the mere presence of Modic changes alone were not significantly associated with presence of hyaline in biopsy specimens ($p = 0.615$).

INFLUENCE OF HYALINE IN GRANULATION TISSUE FORMATION

The presence of granulation tissue in disk material was less (16.66%) in patients with hyaline in biopsy specimen

as compared to those without (97.2%) ($p < 0.001$). The relationship is shown in Graph 2.

IMPORTANCE OF HYALINE IN PREDICTING CLINICAL OUTCOME

The patients with hyaline in extruded disk had higher preoperative VAS score (mean VAS = 6.76) as compared to mean VAS of 6.43 in the patients without hyaline (Wilcoxon signed rank test $p < 0.05$). Postoperative VAS score was 3.07 in group 1 (hyaline present) compared to 3.17 in group 2 (hyaline absent). Preoperative and postoperative VAS scores in each groups are shown in Graph 3. Even though preoperative symptoms were severe in patients with presence of hyaline in extruded disk, postoperative outcome was found good.

From our study, it was also observed that patients with VEPD and Modic changes more than 50% of vertebral end plate in MRI are more symptomatic preoperatively (mean VAS = 6.8). Patients with above findings had hyaline in the extruded disk and had better post surgical patient satisfaction as measured by lower mean VAS score of 3.0 compared to 3.19 in patients without the above findings. (paired t-test, $p < 0.05$).

Thus, presence of hyaline in biopsy as predicted by MRI finding of VEPD and extend of Modic changes was thus associated with a better clinical outcome even though associated with severe preoperative symptoms.

DISCUSSION

Mechanism of Disk Herniation

The mechanism of disk herniation involves degenerative changes in the disk with concentric and radial tears of the annulus fibrosis. The nucleus pulposus herniates through the tears as a result of increased internal pressure and produce sciatica due to mechanical compression on the nerve root. Mechanical pressure may not be the only cause of sciatica biochemical, vascular and immunological factors can also produce sciatica without severe mass effect.^{7,8}

Avulsion Type of Disk Herniation and Presence of Hyaline in Biopsy

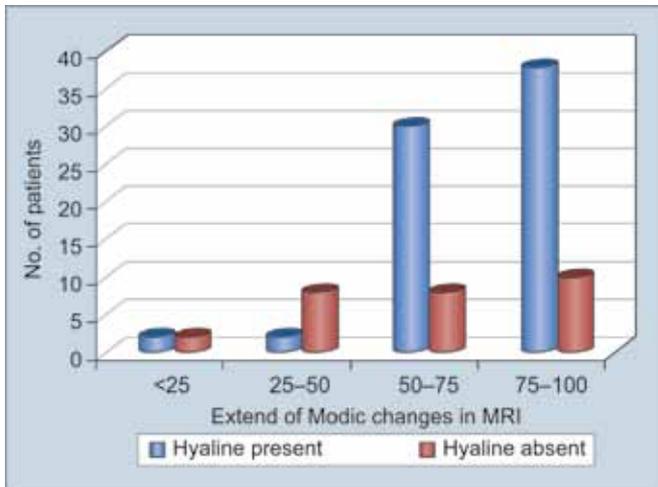
Tanaka M⁹ reported avulsion type disk herniation in elderly. Avulsion type of disk herniation can also occur

Table 4: Extension of Modic changes along adjacent vertebral body among various age groups

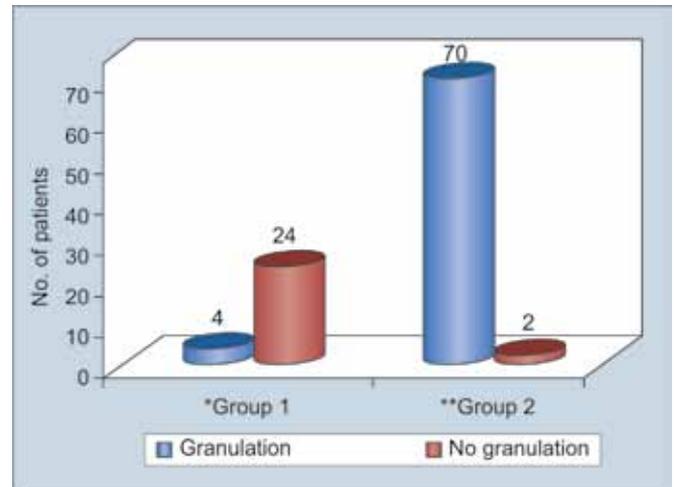
		Age				
		<25	26–35	36–45	>45	Total
Extend of Modic change**	<25	2	2	0	0	4
	25–50	0	0	0	10	10
	*50–75	2	11	19	6	38
	*75–100	2	21	21	4	48
Total		6	34	40	20	100

* $p < 0.001$, **Extend of Modic changes along anteroposterior diameter of vertebral body





Graph 1: Histogram showing relationship between extension of Modic changes in MRI and the hyaline material in biopsy of extruded disk



Graph 2: Histogram showing relationship between hyaline and granulation in biopsy of extruded disk, *group 1: patients with hyaline in biopsy, **group 2: patients without hyaline in biopsy

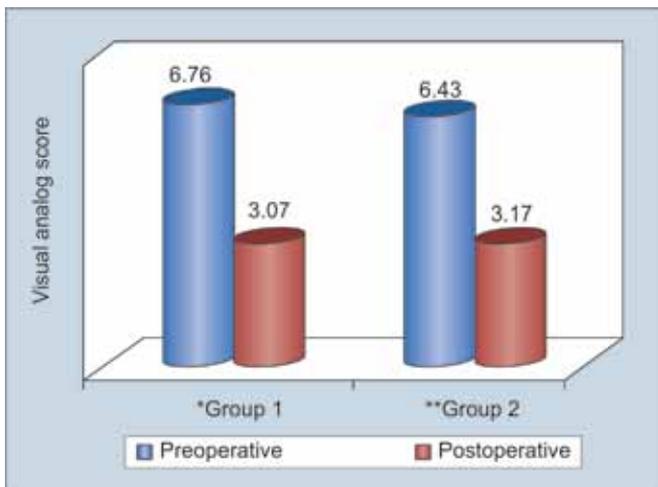
Table 5: Relationship between presence of hyaline material in extruded disk material and vertebral end plate defect

	Hyaline [†]		Total
	Present*	Absent	
VEPD**	N	N	
Present	26	2	28
Absent	5	67	72
Total	31	69	100

*p<0.001, **VEPD: Vertebral end plate defect, †Hyaline material in biopsy

Composition of Extruded Disk Material

Few investigators had evaluated the presence and effect of various amount of histological material in extruded lumbar disk.² In one study, the tissue almost always exclusively contained annulus fibrosis.¹⁰ In another study of 100 cases, free fragments consisted mainly of nucleus pulposus in 54%, and endplate material in 44%.¹ Thus, there are conflicting ideas. In our study, the composition of herniated disk material showed annulus fibrosis in 15% of cases, nucleus pulposus in 78 and 7% had combination of both. A total of 26% of biopsy specimens showed presence of cartilaginous end plate.



Graph 3: Histogram showing relationship between preoperative and postoperative VAS score, *group 1 (with hyaline), **group 2 (without hyaline)

Role of Hyaline in Granulation Tissue Formation and Neovascularization

There was evidence from experimental studies that blood vessels from the surrounding fibrovascular tissue infiltrate into herniated annulus and not into herniated cartilaginous material.^{1,5} Animal study confirmed that annulus induces vascular sprouting and subsequent decrease in annulus material.^{1,5} When they implanted both annulus and end plate material, inflammation was suppressed probably due to inhibitors of neovascularization in cartilage.⁴ Presence of hyaline in extruded disk material gives more knowledge on its role on neovascularization and natural healing mechanism.⁴ In our study, the presence of granulation tissue in disk material was significantly less in patients with hyaline material in biopsy specimen which supported the above evidence in literature.

in substantial percentage in young patients. The authors found that there was only loose connection between cartilaginous end plate and subchondral bone. There was a strong connection between inner fibers of annulus and cartilaginous end plate. In this type, cartilaginous end plate rupture was found. Our study showed presence of hyaline material in patients with vertebral end plate fracture which supports the the above evidence.

Magnetic Resonance Imaging Findings Predicting Presence of Hyaline Material in Biopsy

Bone erosion and vertebral corner defect as a source of cartilage material had been studied.¹¹ Likelihood of presence

of cartilage material in the herniated disk increases when a vertebral corner defect was found.¹¹ Modic classified adjacent bone marrow changes in vertebra into three types.¹² The process of osteochondrosis starts with internal derangement of disk space, fissuring of end plate and sprouting of granulation tissue into bone marrow. In one study, these Modic changes had a low prevalence in asymptomatic young patients.¹³ To be of use in patient treatment, amount of hyaline should be predicted on the basis of vertebral end plate abnormalities on MRI. Usually such abnormalities are seen in elderly but may also be found in younger.¹¹ Our results showed that extend of Modic changes more than 50% of vertebral end plate and presence of vertebral end plate defect (Figs 1A to C) on MRI predict the presence of hyaline material in biopsy. From our study, the presence of VEPD in MRI has 92.85% sensitivity, 97.2% specificity in predicting presence of hyaline. This again supported the literature.

Association of Presence of Hyaline and Clinical Outcome

We found that patients with hyaline in extruded lumbar disk, as predicted by extend of Modic changes and the

presence of VEPD in MRI, had greater postoperative clinical improvement surgical satisfaction even though preoperative symptoms are severe. Relation of clinical outcome with presence of hyaline in biopsy was not well addressed in earlier studies.

CONCLUSION

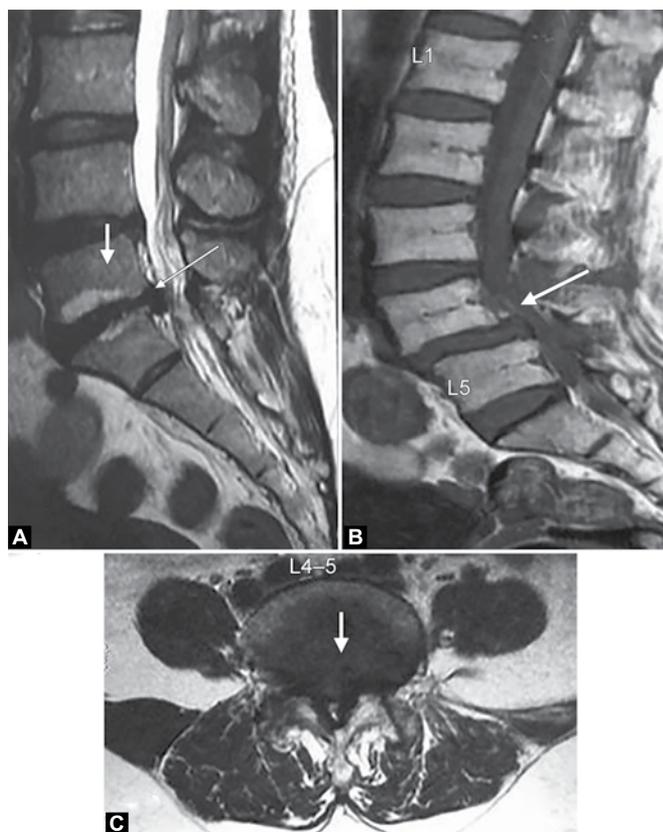
Our study had extensively assessed the composition of disk material, the presence of hyaline material and granulation tissue in biopsy specimen of extruded lumbar disk. From our study, we found that hyaline inhibits granulation tissue formation around extruded disk correlating with the severe preoperative symptoms, which is not addressed in the earlier studies. Presence of hyaline was also associated with good postoperative outcome. We found that, preoperative MRI findings like extend of Modic changes, and the presence of vertebral end plate defect are predictive of hyaline in the extruded disk material. Thus, presence of hyaline material in extruded disk, as indicated by specific MRI findings, can preoperatively predict which all patients improve following surgery.

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Figs 1A to C: (A) Sagittal T2-weighted image showing Modic change (thick white arrow) and vertebral end plate defect at upper dorsal aspect of L5 vertebra (shown in long thin white arrow), (B) sagittal T1-weighted MRI showing vertebral end plate fracture (shown in white arrow) and (C) axial T2-weighted image showing VEPD on the dorsal aspect of vertebral body (shown in white arrow)

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