CORRELATION BETWEEN THE EXPRESSION OF POSTN AND CLINICOPATHOLOGICAL FEATURES, PROGNOSIS, AND DIAGNOSTIC EFFICIENCY OF CHONDROSARCOMA

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ABSTRACT

Objective: *To analyze the correlation between the expression of osteoperiosteal protein (PostN) and the clinicopathological features, prognosis, and efficacious diagnosis of chondrosarcoma.*

Methods: *A total of 86 patients with chondrosarcomas who did not receive radiotherapy or chemotherapy from January 2011 to January 2016 and 41 patients with chondromas that were surgically removed without radiotherapy or chemotherapy were recruited at the same time. The tumor histological grade, postoperative recurrence or metastasis, survival status, and other general information for all patients was recorded and all patients received follow-ups. The expression of PostN, proto-oncogene (c-Myc), and tumor protein p53 (tumor protein) in chondrosarcoma and chondroma were detected by immunohistochemistry. A Pearson linear correlation was used to analyze the correlation between PostN, c-Myc, and p53 levels. Univariate and multivariate Cox regression analyses were used to analyze the factors influencing the overall survival and disease-free survival of chondrosarcoma. An ROC curve was used to analyze the prognostic value of PostN protein expression in patients with chondrosarcoma.*

Results: *The high expression rate of PostN was 62.79% in the chondrosarcoma group overall, 52.17% in the low-grade chondrosarcoma group, and 75.00% in the high-grade chondrosarcoma group, all significantly higher rates than those in the chondroma group (26.83%, P<.05). The high expression rate of PostN was 42.50% in grade 1 chondrosarcoma patients, significantly lower than 81.25% and 78.70% in grade 2 and grade 3 chondrosarcoma patients, respectively. The high expression rate of PostN in the recurrent chondrosarcoma group was 86.11%, significantly higher than 48.08% in the non-recurrent chondrosarcoma group (P<.05). There was no significant difference in the high expression rate of PostN in patients with or without metastatic chondrosarcoma (P>.05). In the chondrosarcoma group, the high expression rate of PostN in c-Myc negative patients was 35.00%, significantly lower than that in c-Myc positive patients (86.96%); also in the chondrosarcoma group, the high expression rate of PostN in p53 negative patients was 44.90%, significantly higher than that in p53 positive patients (86.49%; P<.05). Univariate Cox regression analysis showed that the expression of PostN protein, tumor histological grade, and recurrence all affected the overall survival of patients with chondrosarcoma (P<.05 or <.01). Multivariate Cox regression analysis showed that the expression of PostN protein, tumor histological grade, and recurrence were independent risk factors affecting the overall survival of patients with chondrosarcoma (all P < .05). ROC curve analysis showed that the AUC of PostN in the diagnosis of chondrosarcoma was 0.859, the sensitivity was 88.95%, and the specificity was 82.41%.*

Conclusion: *The expression level of PostN protein in chondrosarcoma is significantly higher than that in chondroma. The expression of PostN protein is closely related to the histological grade and recurrence of chondrosarcoma and is significantly correlated with c-Myc, p53, and other prognostic factors. It can be used as a clinical evaluation factor for the prognosis of patients with chondrosarcoma.*

Keywords: *PostN protein, chondrosarcoma, clinical, pathological, characteristics, prognosis, correlation, diagnostic efficacy.*

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Introduction

Chondrosarcoma is one of the common primary malignant bone cancers, accounting for about 20% to 27% of primary malignant bone tumors, and seriously endangering patients' lives and health[(1)]. Clinical findings show that chondrosarcoma cells produce a relatively low proportion of extracellular matrix and divided cells and vascular distribution is uneven. Therefore, chondrosarcoma cells are not sensitive to radiotherapy, chemotherapy, or other treatments, and chondrosarcoma is mainly treated by extensive resection[(2)]. Because chondrosarcoma often occurs in the pelvis and long bones, surgery requires not only resection of the disordered bone tissue, but also resection of the adjacent neurovascular bundles

and even pelvic organs, resulting in a high rate of disability and low survival rate[3]. Early assessment of patients' prognosis is crucial for targeted treatment and the improvement of patients' quality of life[4]. Periosteal protein (PostN) is a secretory glycoprotein of the extracellular matrix that plays an important role in bone, tooth, and heart valve formation and maintenance[5]. Studies have found that PostN is abnormally expressed in chondrosarcoma tissue and may be closely related to the occurrence and development of cartilage tumors[6].

In this study, a total of 86 patients with surgically resected chondrosarcoma who had not received chemoradiotherapy from January 2011 to January 2016 were recruited as observation subjects to analyze the correlation between the expression of PostN protein and the diagnostic efficacy, clinicopathological features, and prognosis of chondrosarcoma.

Materials and methods

General information

A total of 86 patients with surgically resected chondrosarcoma who did not receive chemoradiotherapy from January 2011 to January 2016 were recruited.

The inclusion criteria were:

• Chondrosarcoma diagnosis by surgical pathological examination;

• Complete clinical patient data available;

• Patients and their family members signed the informed consent form.

During the same period, 41 patients with surgically resected chondroma who had not received chemoradiotherapy were recruited.

The inclusion criteria for chondroma were:

• Chondroma diagnosis by surgical and pathological examination;

• Complete clinical patient data available;

• Patients and their family members signed the informed consent form.

Patients in the two groups were excluded for the following reasons:

• The presence of other malignant tumors;

• Serious heart, liver, kidney, and other important organ dysfunction;

• Severe infection; patient refusal or termination of the experiment.

There were 86 patients in the chondrosarcoma group, including 45 males and 41 females, with an average age of 45.06±9.78 years old and an average BMI of 20.05±0.98 Kg/m^2. In the chondroma group, there were 41 patients, including 22 males and 19 females, with an average age of 45.11±9.89 years old and an average BMI of 20.12±1.05 Kg/m^2.

There was no significant difference in age, gender, or BMI between groups (P>.05).

Clinical data

Patients were followed for up to 5 years, and general data such as the tumor histological grade, postoperative recurrence or metastasis, and survival status were recorded.

Immunohistochemical method

The paraffin-embedded tissue samples of surgically resected chondrosarcoma patients treated with radiotherapy and chemotherapy were prepared for tissue microarray, immunohistochemical staining was performed, and the results of immunohistochemical staining were interpreted. The depth of tumor cell staining was used to evaluate PostN, c-Myc, and P53, among which P53 showed staining only of the nucleus. PostN showed staining of the cytoplasm and nucleus. The depth of stain was scored as 0 for no staining, 1 for light staining, 2 for medium staining, and 3 for dark staining. PostN staining was divided into two groups according to the scoring criteria: negative to weak positive (0 through 3 points) was considered low expression; moderate positive to strong positive (4 through 12 points) was considered high expression. P53 and c-Myc staining were assessed according to the above criteria. A score of less than 6 was considered negative, while a score over 6 was considered positive.

Statistical methods

The SPSS20.0 software package was used for the statistical analysis of the data in this study. The comparison of all measurement data was expressed as ($\bar{x}\pm s$), and a t-test was used for comparison between groups. Enumeration data were expressed as percentages, and the χ^2 test was used for comparison between groups. The relationship among PostN, c-Myc, and P53 levels was analyzed by Pearson linear correlation.

Univariate and multivariate Cox regressions were used to analyze the factors influencing the overall survival and disease-free survival of chondrosarcoma. An ROC curve was used to analyze the utility of PostN protein levels in the evaluation of chondrosarcoma patients' prognoses. The results were considered statistically significant if P<.05.

Results

Comparison of PostN protein expression between the two groups

The high PostN expression rate was 62.79% in the chondrosarcoma group, 52.17% in the low-grade chondrosarcoma group, and 75.00% in the high-grade chondrosarcoma group, all significantly higher rates than the 26.83% in the chondroma group (P<.05). See Table 1.

Group	PostN		χ^2	*P*
	Low expression	High expression		
Chondrosarcoma	32 (37.21%)	54 (62.79%)	13.615	.001
Chondroma	29 (70.73%)	11 (26.83%)		
Low-grade chondrosarcoma	22 (47.83%)	24 (52.17%)	5.397	.020
High-grade chondrosarcoma	10 (25.00%)	30 (75.00%)	18.061	.001

Table 1: Comparison of PostN protein expression between the two groups (cases, %).
Note: A indicates that, compared with the normal group, P<.05; B indicates that, compared with the pneumonia group, P<.05.

Comparison of PostN protein expression in patients with different clinicopathological characteristics

In the chondrosarcoma group, the high expression rate of PostN in grade 1 patients was 42.50%, significantly lower than 81.25% and 78.70% in grade 2 and grade 3 chondrosarcoma patients, respectively. Also in the chondrosarcoma group, the high expression rate of PostN was 86.11% in the recurrence group, which was significantly higher than 48.08% in the non-recurrence group (P<.05).

There was no significant difference in the high expression rate of PostN in patients with or without metastatic chondrosarcoma (P>.05). See Table 2.

Group		POSTN		χ^2	*P*
		Low expression	High expression		
Histological grade	Grade 1	23 (57.50%)	17 (42.50%)	13.208	<.001
	Grade 2	6 (18.75%)	26 (81.25%)		
	Grade 3	3 (21.43%)	11 (78.57%)		
Recurrence	No	27 (51.92%)	25 (48.08%)	13.298	<.001
	Yes	5 (13.89%)	31 (86.11%)		
Metastasis	No	20 (32.79%)	41 (67.21%)	0.649	<.001
	Yes	6 (24.00%)	19 (76.00%)		

Table 2: Comparison of PostN protein expression in patients with different clinicopathological characteristics (cases, %).

Correlation analysis of PostN protein expression and prognostic factors for chondrosarcoma

In the chondrosarcoma group, the high PostN expression rate of c-Myc-negative patients was 35.00%, significantly lower than that of c-Myc-positive patients (86.96%; P<.05).

The high expression rate of PostN in the P53-negative group was 44.90%, which was significantly higher than that in the P53-positive group (86.49%; P<.05). See table 3.

Group		PostN		χ^2	*P*
		Low expression	High expression		
c-Myc	Negative	26	14 (35.00%)	24.720	<.001
	Positive	6	40 (86.96%)		
P53	Negative	27	22 (44.90%)	15.606	<.001
	Positive	5	32 (86.49%)		

Table 3: Correlation analysis of PostN protein expression and prognostic factors for chondrosarcoma.

Analysis of related factors for poor prognosis of chondrosarcoma

Univariate Cox regression analysis showed that PostN protein expression, tumor histological grade, and recurrence all affected the overall survival of chondrosarcoma patients (all P<.05 or <.01). Multivariate Cox regression analysis showed that PostN protein expression, tumor histological grade, and recurrence all affected the overall survival of patients with chondrosarcoma.

PostN protein expression, tumor histological grade, and recurrence were independent risk factors affecting the overall survival of chondrosarcoma patients (all P<.05). See Table 4.

Factors	Univariate analysis			Multivariate analysis		
	95% CI	HR value	*P*-value	*95% CI*	HR value	*P*-value
PostN	1.456-12.088	4.194	.006	1.010-9.017	3.017	.047
Histological grade	1.558-3.870	2.53	.001	1.159-3.426	1.992	.012
Recurrence	1.578-6.720	3.258	.001	0.620-5.312	1.785	.285
c-Myc	0.521-2.516	1.168	.720	-	-	-
P53	0.078-3.251	1.526	.289	-	-	-

Table 4: Analysis of factors associated with poor prognosis of chondrosarcoma.

Analysis of the prognostic efficacy of PostN protein in chondrosarcoma cases

ROC curve analysis showed that the prognostic efficacy of PostN protein in chondrosarcoma patients was 0.859, the sensitivity was 88.95%, and the specificity was 82.41%. See Table 5.

Index	*AUC*	*95% CI*	*P*	Sensitivity	Specificity
PostN protein	0.859	0.801-0.909	<.001	88.95%	82.41%

Table 5: PostN protein prognostic efficacy analysis in chondrosarcoma.

Discussion

Chondrosarcoma is a common malignant connective tissue tumor, the main pathological feature of which is the differentiation of tumor cells from chondrocytes and the formation of a chondrocyte matrix. Chondrosarcoma is insensitive to radiotherapy and chemotherapy and presents a serious danger to the life and health of patients, with typically poor prognoses[7]. Developing a method of early diagnosis and prognosis evaluation is crucial to effective treatment, improving patients' quality of life and longevity.

PostN is a stromal-associated protein that regulates differentiation and adhesion of osteoblasts and is abnormally expressed in osteosarcoma, ovarian cancer, prostate cancer, and other tumors[8]. Studies have shown that the overexpression of PostN can promote serosal cavity invasion and lymph node metastasis and increase the aggressiveness of cancer by promoting epithelial–mesenchymal transformation, leading to poor prognoses in cancer patients[9]. Recent studies have found abnormal expression of PostN in chondrosarcoma cancer tissues[10], and this study hypothesized that PostN could promote the occurrence and development of chondrosarcoma to a certain extent. In this study, the high PostN expression rate in the chondrosarcoma group overall was 62.79%, the high PostN expression rate in the low-grade chondrosarcoma patients was 52.17%, and the high PostN expression rate in the high-grade chondrosarcoma patients was 75.00%, all significantly higher rates than the 26.83% in the chondroma group (P<.05). The high PostN expression rate in the grade 1 chondrosarcoma group (42.50%) was significantly lower than those in the grade 2 and grade 3 chondrosarcoma groups (81.25%, 78.70%; P<.05).

The high PostN expression rate in the recurring chondrosarcoma group (86.11%,) was significantly higher than that in the non-recurring chondrosarcoma group (48.08%; P<.05). These results suggest that PostN protein is highly expressed in chondrosarcoma carcinoma tissues, varies with the clinicopathologic stage and recurrence of chondrosarcoma, and may be involved in the occurrence and development of chondrosarcoma. C-Myc is a transcriptional regulatory factor that can occur in the growth, proliferation, differentiation, angiogenesis, and even apoptosis of tumor cells, and is often used in the clinical evaluation of the prognosis of patients with malignant tumors[11, 12]. P53 is widely present in all malignant tumors and can increase their aggressiveness.

Increased P53 levels often indicate a poor prognosis for patients[13, 14]. In this study, the high PostN expression rate in the c-Myc–negative chondrosarcoma patients was 35.00%, significantly lower than the 86.96% in the c-Myc–positive chondrosarcoma patients (P<.05). The high expression rate of PostN in P53-negative chondrosarcoma patients was 44.90%, significantly higher than that in the P53-positive chondrosarcoma patients (86.49%; P<.05). These results suggest that changes in PostN protein levels are closely related to the prognosis of chondrosarcoma, as Shooshtarizadeh et al found[15].

To further analyze the relationship between PostN protein and chondrosarcoma, univariate and multivariate Cox regression analyses showed that PostN protein expression, tumor histological grade, and recurrence all affected the overall survival of patients with osteosarcoma. ROC curve analysis showed that the prognostic efficacy of PostN protein in chondrosarcoma patients was 0.859, the sensitivity was 88.95%, and the specificity was 82.41%. PostN has a good predictive value in evaluating the prognosis of chondrosarcoma, which allows physicians to evaluate the prognosis of chondrosarcoma early and take corresponding measures, and is crucial for the effective treatment of patients.

In summary, PostN protein expression levels were significantly higher in chondrosarcomas, and PostN protein expression correlates with the histologic grade of chondrosarcoma, as well as with recurrence and prognostic factors such as c-Myc and P53 levels. PostN levels can be used for clinical evaluation of the prognosis of patients with chondrosarcoma.

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