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Research Article

Differential Diagnostics of Hematogenous Osteomyelitis and Malignant Neoplasm of Bone

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Abstract

Objectives: To identify the criteria for differential diagnosis in hematogenous osteomyelitis and malignant neoplasms of the bone, evaluate them in quantitative terms and develop a mathematical model.

Methods: A retrospective analysis of data on 127 patients who underwent differential diagnosis between hematogenous osteomyelitis and malignant bone tumors was performed. The accuracy of the initial diagnosis at the outpatient stage was 59.8% (76 observations). Information on 96 patients who were subsequently diagnosed with hematogenous osteomyelitis was compared with data on 31 patients with morphologically confirmed malignant neoplasms of bone. The method of sequential analysis was used.

Results: When studying about retrospective group, a database was created that became the basis for the development of a mathematical model for the differential diagnosis of hematogenous osteomyelitis and malignant bone disease. 14 prognostic criteria were identified, each of which is defined in quantitative terms. These criteria included the age of the patient, gender, concomitant pathology, localization of the pathological process, indicators of laboratory studies, etc. An algorithm for the differential diagnosis of hematogenous osteomyelitis and malignant neoplasms of the bone was developed.

Conclusion: During a prospective study (63 cases), differential diagnosis model was tested. As a result of this, the accuracy of the initial diagnosis at the outpatient stage was 88.9% (56 patients), which made it possible to shorten the examination time and refer patients to specialized hospitals.

Keywords: *Hematogenous Osteomyelitis; Malignant Bone Lesion; Differential Diagnosis*

Introduction

Hematogenous osteomyelitis (HO) for a long time remains an urgent problem of surgery. The number of patients with HO do not have a steady downward trend and amounts to 14.8 - 28.8% of all cases of osteomyelitis [1-4]. Diagnosis of HO with a vivid clinical picture is not difficult. At the same time, in the absence of pronounced symptoms, with atypical laboratory parameters and questionable interpretation of X-ray data, there are certain difficulties in making a final diagnosis [5-7]. A very important role plays the microflora that causes

HO, the spectrum of which changes regularly [8]. Often, these difficulties arise at the stage of outpatient care in main hospitals, as well as at district hospital level [9].

Currently, most often differential diagnosis of infectious lesions of bone tissue, including HO, is carried out with bone tumors, which today are not uncommon and, like osteomyelitis, can develop at any age: from early childhood to senile, without having a typical clinical picture [10-12]. Errors in the diagnosis of hematogenous osteomyelitis and malignant neoplasms of the bones (MNB) lead to incorrect treatment tactics and, as a result, to unsatisfactory results [13].

In recent years, the number of publications on differential diagnosis between osteomyelitis and bone tumors has been steadily growing [14-18]. At the same time, these works mainly, are descriptive, and the data on their practical application are contradictory. The authors have no single point of view regarding the types and weight of differential diagnostic criteria. In this regard, the study of aspects related to the development of methods for the differential diagnosis of HO and MNB can be considered an urgent topic of scientific medical research.

The purpose of the study was to identify the criteria for differential diagnosis in HO and MNB, evaluate them in quantitative terms and develop a mathematical model.

Material and Methods

The study was conducted with permission of the ethical committee. In the department of orthopedics services hospital lahore (hereinafter referred to as the clinic) in 2017 - 2019. 213 patients with similar diagnoses were hospitalized. 159 of them were diagnosed with HO and 34 had a MNB. Among 159 patients with HO, 63 (39.6%) had clinical symptoms and a typical x-ray picture with laboratory signs characteristic of this pathological condition, which did not require additional differential diagnosis measures. These 63 observations were excluded from further research.

Of 54 cases of MNB in 23 patients (42.6%), the diagnosis was not in doubt. In all these observations, a metastatic lesion of bone tissue was detected with a histologically proven diagnosis of primary lesion at a different location. Only 31 patients who required differential diagnostics with other pathological conditions were included in the further study.

Thus, the study included 96 patients with HO and 31 cases with MNB (a total of 127 people), i.e. only those cases in which additional studies were required to make a final diagnosis. A comparative analysis of clinical, laboratory, radiological and immunological data in patients of these two groups was carried out using the method of sequential analysis by A. Wald (1960) [19]. Identification of markers of HO and malignant bone lesions significant for differential diagnosis was carried out. The weight of each of the analyzed markers was evaluated in quantitative terms. Based on these rating values, identified retrospectively, a differential diagnosis model of HO and MNB was created.

The effectiveness of the differential diagnostic technique was evaluated in 148 patients (87 of them were hospitalized in the clinic and 61 went to outpatient clinic).

Results

76 parameters were analyzed reflecting the condition of the patient, data of their clinical symptoms, laboratory and instrumental examination. These included information on the general and local (gender, age, comorbidity, body mass index, etc.). Separately, a number of indicators of laboratory and instrumental studies were analyzed. The risk factors used for the differential diagnosis of HO and MNB are parameters that have significant differences ($p < 0.05$) in the study groups, as well as prognostic criteria, the probability of error in

which (p-level) exceeded the generally accepted norm, but it was revealed the tendency for differences to appear (at least 1.5 times in percentage terms). At the same time, there was an expert assessment of other researchers, where the p-level of the analyzed risk factor was statistically confirmed.

Thus, 14 prognostic criteria were selected for the program. As an example, we present data on the distribution of patients, taking into account the location of the fracture, as one of the risk factors for the development of Surgical Site Infection (SSI) (Table 1).

Type of Bone affected	Number of Observations			
	HO (n = 96)		MNB (n = 31)	
	No.	%	No.	%
Long Tubular Bones	75	78.1	17	54.8
Cancellus bone	14	14.6	10	32.3
Spine	3	3.1	2	6.5
Others(Rib,Clavicle)	4	4.2	2	6.4
Total	96	100.0	31	100.0

Table 1: *Distribution of patient groups according to type of affected bone.*

As follows the data from table. 1, in the group with HO in 78% of cases, long tubular bones were affected, and among patients with MNB in most cases (55%), the pathological process was localized in the trabecular bones. In a statistical analysis, the number of degrees of freedom is 3. The value of the $\chi 2$ criterion is 12.126. The critical value of $\chi 2$ at a significance level of $p < 0.01$ is 11.345. The relationship between factor and effective traits is statistically significant at a significance level of $p < 0.01$. Thus, the appearance of the affected bone was taken into account when developing a mathematical model for differential diagnosis. Similarly, other criteria were selected.

After forming a complete list of significant differential diagnostic factors, the ratio index and the prediction coefficient were calculated. The correlation index was the quotient between the frequency of occurrence of the symptom in the group of patients with HO and the frequency of its occurrence among patients with MNB.

The forecast coefficient was a natural logarithm (ln) of the ratio index increased, for the convenience of calculations, by 10 times. As a result, the prognosis coefficient for lesions of the long tubular bone was "+3.5", with localization of the process in the spongy bones "- 7.9", in the spine - "7.4", in other bones - "4.2". This allowed us to conclude that the diagnosis "Hematogenous osteomyelitis" with a localization of the process in long tubular bones is more likely.

Subsequently, all forecast coefficients known at the time of the survey were summarized. The result obtained was the total index of prognosis (PI). This parameter was determined at different stages of examination and treatment of the patient with a confidence interval from "–14" to "+14" conventional units (c.u).

If the total PI was at the level of "+14"c.u and more, with a probability of more than 80%, it was assumed that the patient had HO. When the parameters of the PI is less than "-14" c.u, with the same probability a MNB could be assumed. If the PI indicators were in the range from "-14" to "+14"c.u, the diagnosis was considered uncertain for a given level of reliability. A complete list of prognostic criteria with the calculation of the differential diagnosis coefficients is presented in table 2.

Prognostic criteria	Frequency of observations (%)		The ratio index	Coefficient of prognosis
	HO	MNB		
1	2	3	4	5
Pre-operation				
1. Sex:				
Male	77	42	1,833	6,1
Female	23	58	0,397	-9,2
2. Age in years:				
18 – 29	6	32	0,188	-16,7
30 – 44	27	16	1,688	5,2
45 – 59	40	26	1,538	4,3
60 – 74	26	26	1,000	0
75 – 89	1	-	-	-
3. Work capacity:				
working	72	48	1,500	4,1
not working, taking pension	28	52	0,538	-6,2
Concomitant diseases:				
4. Respiratory System				
COPD (present)	6	16	0,375	-9,8
COPD (absent)	94	84	1,119	1,1
5. Cardio-vascular system IHD, Hyperten-				
sion	51	16	3,188	11,6
present	49	84	0,583	-5,4
IHD, Hypertension absent				
6. Digestive system	45	26	1,731	5,5
present	55	74	0,743	-3,0
absent				
7. Excretory system				
Chronic pyelonephritis	12	6	2,000	6,9
present	88	94	0,936	-0,7
Chronic pyelonephritis absent				
8. History of recent trauma	35	10	3,500	12,5
present	65	90	0,722	-3,3
absent				

9 .History of Viral Hepatitis				
present	12	6	2,000	6,9
absent	88	94	0,936	-0,7
10. Allergy (food or drugs)				
present	20	10	2,000	6,9
absent	80	90	0,889	-1,2
11. Location of pathology:				
Upper limb	14	39	0,359	-11,2
Lower limb	81	55	1,473	3,9
Others	5	6	0,833	-1,8
12. Type of bones affected:				
Long tubular bones	78	55	1,418	3,5
Cancellous bones	15	32	0,469	-7,9
Spine	3	7	0,429	-7,4
Others	4	6	0,667	-4,2
13. Blood type				
0	32	32	1,000	0
A	27	36	0,750	-2,9
B	22	13	1,692	5,3
AB	7	10	0,700	-3,6
14. History of fistula				
yes	82	13	6,308	18,4
no	18	87	0,207	-15,8

Table 2: *The structure of the weight coefficients of the criteria for the differential diagnosis of hematogenous osteomyelitis and malignant bone tumors.*

In 2017 (a prospective study) at clinic 63 patients who required differential diagnosis between HO and MNB approached. All of them tested the differential diagnosis model. The accuracy of the method was 88.9% (56 patients), which was confirmed during subsequent hospitalization of patients.

Discussion

Difficulties in the differential diagnosis between bone pathology of inflammatory and tumor genesis arise not only in outpatient facilities, but also in hospitals. Most often, a preliminary diagnosis is formed on the basis of the clinical picture and radiological methods. We give some clinical observations.

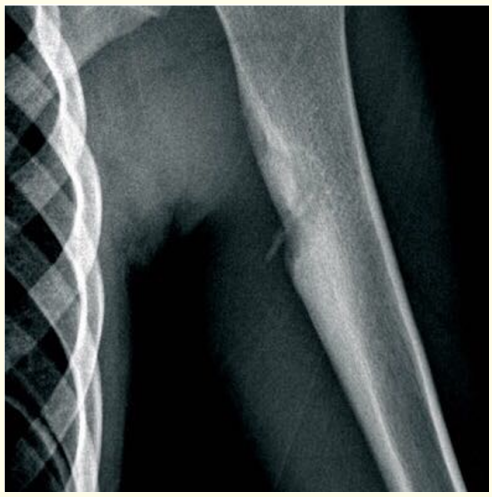

Figure 1: *Radiograph of patient K., 20 years old. Primary chronic hematogenous osteomyelitis (corticolitis). Local hyperostosis, osteosclerosis. The cavity of osteolytic destruction with fuzzy contours. A linear shadow (at an angle to the axis of the bone) is a sequestration resembling a "visor" in osteogenic osteoblastic sarcoma of diaphysis.*

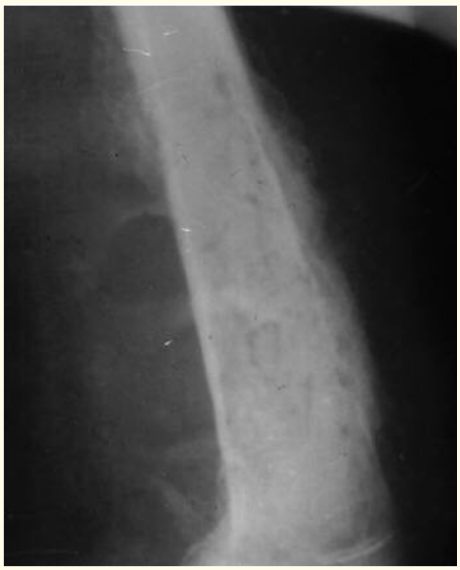

Figure 2: *Radiograph of patient C., 18 years old. HO of the femur in acute phase. The heterogeneous structure of the femur due to destruction and areas of sclerosis with fuzzy contours, periosteal overlays in the diaphysis, and pronounced osteoporosis are visualized. Differential diagnosis with osteogenic osteoblastic sarcoma.*

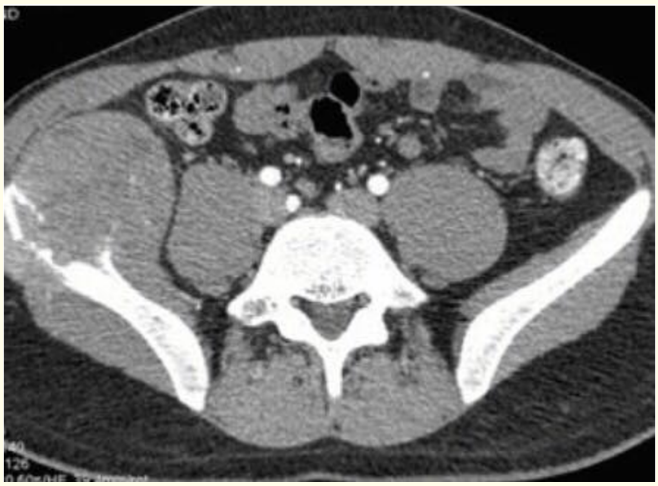

Figure 3: *CT of patient R., 20 years old. Osteogenic sarcoma of the ilium. Osteolytic destruction with a fuzzy uneven contour, at the level of which there is a soft-tissue component of the tumor with a "visor".*

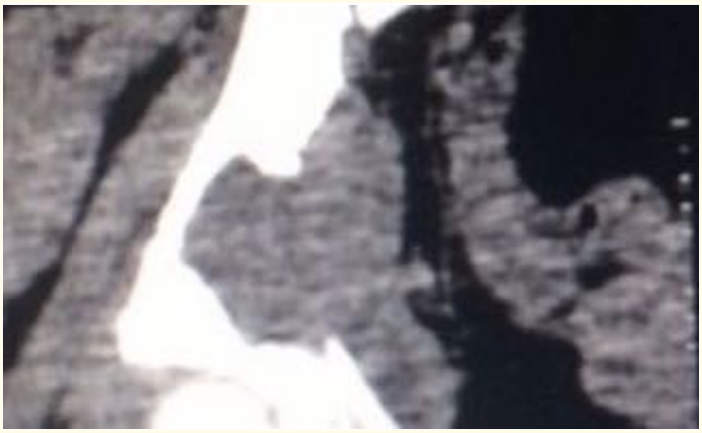

Figure 4: *CT of patient B., 25 years old. Osteomyelitis of the ilium. A site of osteolytic destruction with fuzzy uneven contours, a small soft-tissue component.*

Other diagnostic modalities such as radioisotope, morphological, etc are not always informative. Moreover, not in all cases such studies are available. Also, far from all hospitals have osteomorphologists with sufficient experience. Often, both patients with osteomyelitis and oncological pathology are hospitalized in non-core medical institutions. Thus, the establishment of a final diagnosis and transfer to a specialized hospital requires significantly more time.

Conclusion

Thus, with the use of our modal in practice the differential diagnosis of HO and MNB and the accuracy of the preliminary diagnosis has been improved from 59.8% to 88.9%. Moreover, doctors in a shorter time formulated the concept of patient management. Patient examination time in these cases was reduced. Clinical testing of the differential diagnosis program of HO and MNB in patients of the prospective group confirms the correct selection of criteria.

The most significant in terms of making a preliminary diagnosis: HO included criteria that had the maximum range between a positive and negative value of the prognosis coefficient: male gender, age over 30 years, history of trauma and history of fistula.

The frequency of HO and MNB is not reduced. In recent years, the atypical clinical picture of these diseases has been increasingly verified. In this regard, it is obvious that early diagnosis, on an outpatient basis, shortens the examination time and allows patient to get specialized medical care on time. The data obtained demonstrate that the use of modern organizational approaches in patients with atypical clinical picture for diseases of the bones of infectious and tumor genesis can improve the results of their treatment due to early diagnosis and timely provision of specialized medical care.

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