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Differential Diagnosis of Systemic-Onset Juvenile Arthritis and Rheumatic Masks of Oncohematological Diseases: Results of a Retrospective Cohort Study

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Background. *Patients with malignant oncohematological diseases (OHD) may have such symptoms as fever, lymphadenopathy, hepatosplenomegaly, joint pain, arthritis, elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) concentration, anemia that require differentiation from clinical implications of systemic juvenile idiopathic arthritis (sJIA).* ***Objective.*** *Our aim was to determine diagnostic criteria that can differentiate rheumatic masks of OHD from sJIA.* ***Methods.*** *The retrospective study included 86 children with sJIA and 21 children with OHD who had rheumatic masks and were hospitalized in rheumatological departments with an initial diagnosis of sJIA. OHD were represented by acute lymphoblastic leukemia (n = 17), neuroblastoma (n = 1), and lymphomas (n = 3).* ***Results.*** *Blast cells in the peripheral blood test were detected in 9/17 (53%) patients with acute leukemia at different times from the appearance of complaints and hospitalization. Diagnostic criteria for differentiating OHD from sJIA were the number of active joints ≤ 3 (diagnostic odds ratio, OR, 4.4, 95% confidence interval, CI, 1.5-13.2), CRP concentration < 15 mg/L (OR 5.6, 95% CI 1.7-18.4), platelets ≤ $307x10^9$/L (OR 22.9, 95% CI 4.9-107.0), white blood cells ≤ $8.9x10^9$/L (OR 50.2, 95% CI 6.3-401.3), albumin > 43.3% (OR 28.8, 95% CI 5.6-149.2), absence of exanthema (OR 39.8, 95% CI 8.4-188.5). The most frequent symptoms with the greatest specificity were night pain (sensitivity 0.57, specificity 1.0), bone pain (sensitivity 0.95, specificity 1.0), pathological fractures (sensitivity 0.14, specificity 1.0).* ***Conclusion.*** *The identified diagnostic criteria can be used for differential diagnosis of OHD with rheumatic masks and sJIA.*
Key words: *systemic juvenile idiopathic arthritis, leukemia, malignant neoplasms, differential diagnosis.*

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RESULTS

Table 1. Diseases requiring differential diagnosis with systemic juvenile idiopathic arthritis

Non-rheumatic diseases	Rheumatic diseases
Septicemia	Acute rheumatic fever
Bacterial endocarditis	Systemic lupus erythematosus
Bacterial infections: brucellosis, typhoid, tuberculosis	Systemic vasculitis: Kawasaki disease, ANCA-associated vasculitis*
Leishmaniasis	Juvenile dermatomyositis
Viral infections	Inflammatory bowel disease
Solid tumors, leukemia	Auto-inflammatory syndromes
Immunodeficiencies	Reiter's syndrome

Note. * — vasculitis associated with antineutrophil cytoplasmic antibodies.

Table 2. Comparative analysis of patients with sJIA and OHD (data at the time of inpatient hospitalization)

Indicator	Patients with OHD	Patients with sJIA	*p*
Age, years (*n* = 21/86)	3.2 (2.5; 8.3)	4.7 (2.4;7.9)	0.823
Girls, abs. (%)	9/21 (43)	45/86 (52)	0.437
Clinical signs			
Number of active joints, abs. (*n* = 21/86)	1 (1; 3)	4 (2; 13)	0.006
Exanthema, abs. (%)	2/21 (10)	67/83 (81)	0.001
Splenomegaly, abs. (%)	9/21 (43)	39/85 (46)	0.803
Lymphadenopathy, abs. (%)	9/21 (43)	52/85 (61)	0.128
Hepatomegaly, abs. (%)	9/21 (43)	56/85 (66)	0.052
Hemorrhagic syndrome, abs. (%)	3/21 (14)	6/85 (71)	0.287
Lung involvement*, abs. (%)	1/21 (5)	18/85 (21)	0.079
Heart disease*, abs. (%)	0/21 (0)	21/85 (25)	0.011
CNS involvement*, abs. (%)	3/21 (14)	6/84 (7)	0.296
Kidney damage*, abs. (%)	1/21 (5)	7/85 (8)	0.590
Night pain, abs. (%)	12/21 (57)	0/86	0.001
Bone pain, abs. (%)	20/21 (95)	0/86 (0)	0.001
Pathological fractures, abs. (%)	3/21 (14)	0/86 (0)	0.001
Laboratory signs			
Hemoglobin, g/L (*n* = 21/85)	108 (95; 126)	103 (83; 113)	0.093
White blood cells, $\times 10^9$/L (*n* = 21/85)	7.4 (5.3; 8.3)	14.6 (9.3; 18.5)	0.002
Platelets, $\times 10^9$/L (*n* = 20/85)	175 (110; 249)	436 (256; 583)	0.001
ESR, mm/h (*n* = 18/85)	32 (20; 50)	43 (25; 55)	0.382
CRP, mg/L (*n* = 15/82)	12 (6; 49)	57 (18; 113)	0.005
ALT, u/L (*n* = 18/84)	16 (13; 30)	35 (21; 70)	0.001
AST, u/L (*n* = 17/82)	33 (28; 44.0)	39 (30; 63)	0.153
GGT, u/L (*n* = 2/38)	86 (70; 102)	40 (21; 86)	0.244
ALP, u/L (*n* = 15/72)	356 (254; 504)	340 (203; 428)	0.512
LDH, u/L (*n* = 12/70)	788 (279; 1,569)	538 (420; 795)	0.621
Ferritin, ng/ml (*n* = 6/61)	263 (88; 458)	446 (143; 1,848)	0.169
Triglycerides, mmol/L (*n* = 6/60)	1.4 (1.0; 1.6)	1.6 (1.1; 2.8)	0.217

Note. * — lung involvement shall mean the presence of dyspnea, cough, pulmonary infiltrates, pleurisy and/or respiratory failure; heart disease — pericarditis, myocardial damage, circulatory insufficiency; CNS involvement — any cerebral, focal or meningeal symptoms; kidney damage — changes in urine tests (proteinuria, hematuria). sJIA — systemic juvenile idiopathic arthritis, OHD — oncohematological diseases, ESR — erythrocyte sedimentation rate, CRP — C-reactive protein, ALT — alanine aminotransferase, AST — aspartate aminotransferase, GGT — gamma glutamyltranspeptidase, ALP — alkaline phosphatase, LDH — lactate dehydrogenase.

Table 3. Diagnostic consideration of the parameters allowing to distinguish between OHD and sJIA

Indicator	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)	PPV, %	NPV, %	OR (95% CI)
Number of active joints ≤ 3	0.76 (0.53; 0.92)	0.58 (0.47; 0.59)	0.69 (0.60; 0.79)	30.7	90.9	4.4 (1.5–13.2)
CRP ≤ 14.9 mg/L	0.67 (0.38; 0.88)	0.74 (0.63; 0.84)	0.76 (0.66; 0.84)	38.8	90.2	5.6 (1.7–18.4)
Platelets ≤ 307×10^9/L	0.90 (0.67; 0.98)	0.73 (0.62; 0.82)	0.81 (0.72; 0.88)	44.6	96.6	22.9 (4.9–107.0)
Albumin > 43.3%	0.86 (0.57; 0.98)	0.83 (0.71; 0.91)	0.85 (0.75; 0.93)	54.9	96.0	28.8 (5.6–149.2)
White blood cells ≤ 8.9×10^9/L	0.94 (0.73; 0.90)	0.76 (0.66; 0.85)	0.83 (0.75; 0.9)	49.2	98.2	50.2 (6.3–401.3)

Note. CRP — C-reactive protein, OR — odds ratio, CI — confidence interval, AUC — area under the curve, PPV/NPV — positive/negative predictive value.

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CONFLICT OF INTERESTS

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