Rheumatic Manifestations of Hematological Diseases

Essay

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Internal Medicine

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المظاهر الروماتيزمية لأمراض الدم

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الملخص العربي

إن المظاهر الروماتيزمية وبخاصة في أمراض الدم الخبثية ليست نادرة الحدوث ومن الممكن أن تكون نتيجة لعدة آليات مثل اضطراب أو انتشار الخلايا السرطانية ومهاجمتها للمفاصل وكذلك نتيجة للتأثيرات الجانبية للأدوية الكيماوية.

إن التهابات المفاصل، التهابات الأعصاب، مرض التهابات العضلات والجلد، أمراض المشابهة للذئبة الحمراء وكذلك مرض التهاب المفاصل المتماثل والمصاحب بالورم هي أكثر الأمراض الروماتيزمية اصطحاباً لأمراض الدم الخبيثة.

وجود أعراض أخرى مصاحبة لهذه الأمراض الروماتيزمية مثل الحمى والشحوب والفرفرة والتهاب الغدد الليمفاوية، وكذلك تضخم الكبد والطحال قد يؤدي إلي تشخيص الأمراض الدموية الخبيثة.

بالنسبة لمرض سرطان الدم اللوكيما فإن 5.8 من المرضى قد يظهرون للمرة الأولى بشكوى من التهابات المفاصل. أما بالنسبة لأمراض الأوعية الليفاوية فإن نسبة حدوث أمراض المناعة الذاتية قد تزيد من 2: 3 عن نسبة حدوثها في الناس الطبيعيين.

في حالات مرضى سيولة الدم فإن نسبة حدوث تضخم بالمفاصل وتجمعات دموية قد تصل إلي 50% من الحالات بينما في مرض خلايا الدم المنجلية فإن التهابات العظام والمفاصل وكذلك جلطات العظام قد تحدث بكثرة.

وقد لوحظ وجود علاقة بين مرض أنيميا البحر المتوسط وروماتيزم المفاصل في بعض الدراسات مما نتج عنه استنتاج علاقة بين جينات انيما البحر المتوسط وروماتيزم العظام.

إن وجود تغيرات في الأشعة السينية لبعض المرضى قد يؤدي إلي التشخيص المبكر لمرض ترسيب الحديد الوراثي مما قد يجنبهم حدوث المزيد من المضاعفات.

ولذلك كان من الضروري أن يكون الأطباء علي دارية كافية بالمظاهر الروماتيزمية لأمراض الدم.

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List eviations

ABVD : Adriamycin, Bleomycin, Vinblastine, Dacarbazine
AIDS : Acute immunodeficiency syndrome
ALL : Acute Lymphoblastic Leukemia
AML : Acute Myelogenous Leukemia
ANA : Antinuclear antibodies
ANCA : Anti-neutrophil cytoplasmic antibodies
ANF : Anti-nuclear factor
APS : Antiphospholipid syndrome
BD : Behcet Disease
CBC : Complete Blood Count
CLL : Chronic Lymphoid Leukemia
CML : Chronic Myelogenous Leukemia
CMML : Chronic Myelomonocytic Leukemia
CPK : Creatine phosphokinase
CPPD : Calcium pyrophosphate dehydrate deposition disease
CT : Computerized tomography
dcSSc : diffuse cutaneous systemic sclerosis
DM : Dermatomyositis
DMARDs : Disease modifying antirheumatic drugs
EF : Eosinophilic fasciitis
EN : Erythema nodosum
ET : Essential thrombocytosis
FAB : French - American - British Classification
Fc : Fragment crystallisable
GCA : Giant Cell Arteritis
Hb : Hemoglobin
HCL : Hairy Cell Leukemia
HCV : Hepatitis C Virus
HH : Hereditary Hemochromatosis
HIV : Human Immunodeficiency Virus
HLA : Human Leucocytic antigen
HTLV-1 : Human T-Lymphotropic virus type I

List of Abbreviations (Cont.)

Ig : Immunoglol

LA : Leukemic Arthritis
LCV : Leukocytoclastic Vasculitis
LDH : Lactate dehydrogenase
MC : Mixed Cryoglobulinemia
MCP : Metacarpophalangeal
MDS : Myelodysplastic Syndrome
MGUS : Monoclonal gammopathy of undetermined significance
MM : Multiple myeloma
MPD : Myeloproliferative diseases
MRI : Magnetic Resonance Imaging
NHL : Non-Hodgkin's lymphoma
NSAIDs : Non-steroidal anti-inflammatory drugs
OA : Osteoarthritis
PAN : Polyarteritis nodosa
PCV : Polycythemia vera
PMR : Polymyalgia rheumatica
PTs : Pseudotumours
RA : Rheumatoid arthritis
RAEB : Refractory anemia with excess blasts
RD : Rheumatic disease
REAL : Revised European American Lymphoma
RF : Rheumatoid factor
RNP : U1 Ribonucleoprotein
RP : Raynaud's phenomenon
RPR : Rapid plasma regain
RS3PE : Remitting seranegative symmetric synovitis with pitting edema
SCD : Sickle cell disease
SLE : Systemic lupus erythematosis
SS : Sjogren syndrome
TNF : Tumor necrosis factor
VAD : Vincristine, Adriamycin, Dexamethasone
WHO : World Health Organisation

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Introduction

The musculoskeletal system is the mirror of other body systems and it is affected in many systemic non rheumatic diseases ***(Pinheiro et al., 2006).***

The musculoskeletal hemopoietic system interrelationship is well established, patients with hematological disorder especially those with hematological malignancies have many complaints, in some instance it could dominate the clinical picture and many of these patients were 1st seen in rheumatology clinic with many rheumatological manifestations ***(Senel et al., 2006).***

Lymphomas especially non Hodgkin's lymphoma (NHL), leukemias specially acute lymphoblastic leukemias, myelodysplastic syndromes are the most common hematological illnesses associated with affection of the musculoskeletal system (arthritis / arthralgias) with picture similar to juvenile RA in children with acute lymphoblastic leukemias ***(Jardin et al., 2005).***

NHL patients may present with arthritis of both knees and this might delay the correct diagnosis ***(Doukkali, 2004).*** In all patients presenting with musculoskeletal complaints with or without purpuric eruptions unless hematological malignancies in mind, the diagnosis will be delayed or missed due to the unusual presentation to rheumatologist in rheumatology clinic ***(Farmakis et al., 2005).***

The prevalence of leukemic arthritis varies from 12 to 16 % in childhood leukemias. Interestingly, diagnosis of arthritis may be associated with or after the diagnosis of the hematological disease ***(King and Costenbader, 2007).***

Arthritis develops earlier in acute leukemias and later in chronic leukemias, the knees are the most frequently involved, but the small joints of the hands might be also affected ***(Giaggounidis et al., 2005).***

Thalassemias, sickle cell anemia and myelodysplasias are associated with variable skeletal and articlar manifestations. Many autoimmune phenomena could associate patients with myelodysplastic syndromes and chronic myelomonocytic leukemia, the most important of which are: one of the classical vasculitic syndromes, arthritis, fever, polyneuropathy, autoimmune hemolytic anemia and pulmonary infiltrates ***(Saif et al., 2002; Pinheiro et al., 2006).***

Acute systemic vasculitis (medium – large) vessels may associate lymphoproliferative disorders especially NHL and hairy cell leukemia, it doesn't fit with any of the classical vasculitis e.g.: polyarteritis nodosa ***(LaBerge and Kerlan, 2002).***

Aim of the study

The aim of this study is to review the most recent literatures and researches concerning the rheumatological manifestations of hematological diseases.

Rheumatic Syndromes Associated with Hematological Malignancies

Musculoskeletal manifestations of primary disorders of blood as hemophilia, sickle cell disease, B-thalassemia or hemochromatosis are well recognized. Also leukemia, lymphoma, myelodysplastic syndrome and myeloproliferative disorders may have rheumatic manifestations. Rheumatic manifestations may follow, come concurrently with or precede the diagnosis of hematological malignancies ***(Vital and Emery, 2007).***

Rheumatic disorders associated with hematological malignancies have been attributed to different mechanisms: paraneoplastic syndromes (induced by the malignancy through hormones, peptides, autocrine and paracrine mediators, antibodies and cytotoxic lymphocytes), direct invasion by malignant cells, disturbed immunity and adverse reactions to chemotherapy ***(Andras et al., 2006).***

Rheumatic disorders could be similar to premalignant lesions taking several years to develop to full malignancy. In cases of paraneoplastic rheumatic syndromes, the diagnosis of the associated malignancy appears shortly after the onset of these syndromes. Clinically, rheumatic disorders due to direct invasion of articular and periarticular tissue by malignant cells

are difficult to differentiate from paraneoplastic rheumatic syndromes. That is why rheumatic manifestations of malignancy are described together ***(Marmur and Kagen, 2002).***

Table (1): A review of rheumatic manifestations commonly associated with hematological malignancies:

Rheumatic Manifestations	Commonly associated hematological malignancies
Arthritis/Arthralgias	Most of the hematologic malignancies; lymphoma specially NHL and acute leukemia specially in children
Vasculitis	Leukemias especially hairy cell leukemia, Lymphomas
Dermatomyositis-Polymyositis	Lymphomas
Lupus-like syndromes	Leukemia, Hodgkin's disease, myeloma
Atypical polymyalgia rheumatica	Multiple myeloma, Myeloproliferative diseases
Remitting seronegative symmetric synovitis with pitting edema (RS3PE)	Myelodysplastic syndrome, Lymphomas, Leukemias
Vasculitis with digital necrosis / Late Rayaund	Angiocentric lymphoma, Chronic myeloid leukemia, Myeloma
Eosinophilic fasciitis	Several hematologic malignancies
Erythromyelalgia	Myeloproliferative disorders
Relapsing polychondritis	Myelodysplastic syndrome, Leukemia, Lymphoma, Myeloproliferative disorders

Inspite of the rheumatological problems in patients with hematological malignancies, still it is not practical or cost-effective to search for malignancy in all patients with

rheumatic conditions, unless there are additional findings suggestive of malignancy.

Findings in rheumatic diseases suggestive of malignancy are:

1)Long standing premalignant rheumatic disorders:

Some rheumatic syndromes could be considered premalignant conditions as in cases of rheumatoid arthritis (RA) and Sjogren's syndrome (SS) with lymphoproliferative disorders ***(Naschitz, 2001).***

2) Exposure to carcinogens or drugs that may induce malignancy:

Exposure to carcinogens as inhaled tobacco, radioactive substances and certain non ionic industrial pollutants or drugs especially immunosuppressive drugs raise the suspicion of malignancy in patients with rheumatic disorders ***(Naschitz, 2001).***

3)Presence of another paraneoplastic syndrome, presence of associated risk signs:

Petechiae, bleeding gums or severe pallor with asymmetrical synovitis in one or two joints ***(Naschitz, 2001).***

4)Specific rheumatic syndromes:

- Asymmetric polyarthritis presenting in the elderly with an explosive onset.
- Rheumatoid arthritis with monoclonal gammopathy.
- Presentation of cutaneous leukocytoclastic vasculitis

after age of 50 years.

- Dermatomyositis: if presenting after the age of 45 years, usually it is associated with malignancy or premalignant condition.
- Sjogren syndrome with monoclonality.
- Polymyalgia rheumatica with atypical features.
- Presentation of Raynaud's phenomenon after age of 50 years.
- Eosinophilic fasciitis unresponsive to corticosteroid therapy.
- Erythema nodosum lasting more than 6 months.

(Naschitz, 2001)

5)Autoantibodies as tumor markers:

Several connective-tissue specific antibodies were detected in sera of patients with preclinical stages of malignancy ***(Naschitz, 2001)***

1)Arthritis:

Arthritis means joint inflammation. It is not a disease, but it is a symptom of more than hundred rheumatic diseases. It presents with pain, stiffness and swelling in the joints. Any joint could be affected, axial or peripheral. Some rheumatic conditions can result in debilitating, even life threatening complications or may affect other parts of the body including muscles, bones and internal organs ***(Eustice et al., 2007).***

Arthritis can affect anyone at any age, including children. The incidence of arthritis increases with age, but