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THE DIFFERENTIAL ALGORITHM BETWEEN RHEUMATOLOGIC AND MALIGN DISEASES

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ABSTRACT

Objective: The aim of this study is to determine the differential algorithm between rheumatism and malignant diseases. For every pediatrician, to be warned when attending joint pain and child arthralgia and prevent and treat within time malignant diseases. **Methods:** Our case presented in Pediatric Clinic, was referred by Regional Hospital of Ferizaj with suspected diagnose of Febris Rheumatica and Arthralgia. The main complaint was joint pain. Initially the patient was admitted at Cardiology and Rheumatology department. Then after examinations was referred to Hemato-Oncology department. Hospitalized during the period from 12.12.2014 to 18.01.2015. **Results:** Bone marrow biopsy as terminal diagnostic tool reviled severe malignant hematologic disease, which was masked by clinical and lab findings as Febris Rheumatica. **Conclusion:** Arthralgia as one of child's often complain, should have a special attention paid to, as it might be a warning sign for a lot of diseases. Steroid treatment should not be used before final diagnose of the disease and before rolling out hematologic etiology with peripheral blood smear.

Key words: algorithm, rheumatism, malign disease, arthralgia, febris rheumatic, joint pain.

1. INTRODUCTION

Pediatric rheumatism diseases are a group of child disorders with common presentation of inflammatory symptoms (1). Although, a great progress has been made in terms of pathofisiology of these disorders, their etiology still remains unknown. Despite major advances in laboratory investigations, main diagnosis algorithm remains: anamnesis and physical examination. Most of this group of diseases are classified as inflammatory arthritis, enthesitis syndroma and vasculitis. There are also subgroups among them. Non inflammatory disorders, that cause musculoskeletal pain, belong to articular hypermobility and other syndromes (2, 3).

Malignant diseases have the highest mortality rates among child diseases. What's encouraging is that, they treatment has improved lately. For a basic diagnosis we have to take a careful history and good physical examination, considering child's complaints (2, 3, 4). Patient's age is first that draws attention, for the etiology. Joints pain is present and differentiation between mechanical or inflammatory etiology is crucial. If besides pain there are also swollen ankles, rigidity, warmness and redness which improves with movement and activity, than we should think of inflammatory etiology (5, 6, 7). Pain which deteriorates with activity by the end of the day and with deteriorating swollenness, then we should think of mechanical etiology. As the joint pain might be common complain of children, special attention should take duration and time of presentation (7). Acute migratory arthritis, which attacks small and large ankles, is associating sign of Rheumatic fever. Arthritis which improves for a few weeks might be Reactive (Streptococcus, Epstein Barr parvovirus B19). Chronic swollen ankles are sign of a juvenile rheumatoid arthritis.

The manifestation of signs between rheumatic diseases differs by the pain character, which in LES is very severe but with less swollenness, and in juvenile arthritis is more rigor and swollenness but less pain (8).

The aim of this study is to determine the differential algorithm between rheumatism and malignant diseases. For every pediatrician, to be warned when attending joint pain and child arthralgia and prevent and treat within time malignant diseases.

2. METHODS AND MATERIALS

Diagnosis is based on presentation history, physical examination, laboratory, ultrasound and radiology examination. Our case presented in Pediatric Clinic and first hospitalized at Cardiology and Rheumatology department. After

examinations referred to Hemato-Oncology department. Hospitalized during the period from 12.12.2014 to 18.01.2015.

Case presentation: Our case was referred by Regional Hospital of Ferizaj, with suspected diagnosis of Febris Rheumatica and Arthralgia. The main complaint was joint pain. The pediatrician has prescribed Acetylsalicylic Acid and Ibuprofen. In the family history there is no inherited diseases or other chronic diseases.

Physical examination: The patient was male, age 11 years old, weight 36kg, height 149 cm, conscious and oriented, and pallid, eutrophic, afebrile, eupneic, eucardic. With impression of not very severely ill patient. Physical examination of the organs and systems were within normal findings. Upper and lower extremities had pain with edemas and deformities (Figure 1 and 2).

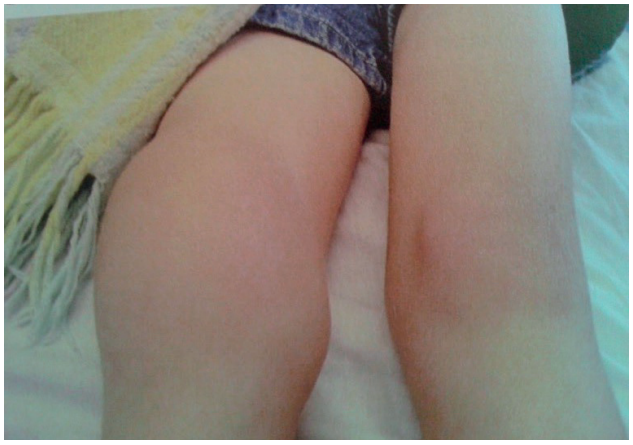

Figure 1. Clinical appearance of the right knee during hospital admission

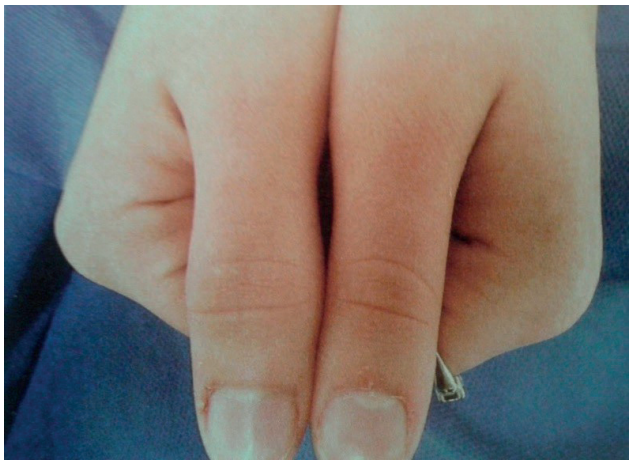

Figure 2. Right thumb joint edema during hospital admission

Ethical clearance: The study had been approved by the Regional Ethical Board at the Institute of Occupational Medicine and by the Research Ethics Committee, University of Prishtina, Kosovo.

3. RESULTS

Laboratory findings: ESR: 45.....60; RBC 4.78 .4.75..3.96; Hgb 131..127..98; Htc 34.9..26.5..29; MCV 74..72. 73; MCHC 37.5.36.5.35.6. WBC: Leukocytes 15.0; Monocytes 2.5..2.4...2.5...1.8; Basofyles 1.7...1.5...1.5...1.8; Euz 3.6...3.8...3.1...3.8; PLT 333...369...357...403; Glicaemia 4.66...4.41...3.59; BUN 2.31...1.62; Creatinina 55.3...43.4; Bil 7.07...5.62...3.41; Bil. direct 1.4; Tot. prot. 77.4.. 62.3...55.9; Cholesteroli 3.64...3.67; Triglic: 0.82...2.23; ALP 277...94; AST 11; ALT 27; LDH 1089; CRP 137.9; ASTO 200; Fe 8.38; Albumines 32.3; Alfa feto protein 0.7; Lipazis 31.8; Fybrinogen 2.36; Ionized calcium 1.17; Ferritin 283.4; PCT 182.0. SAB: Ph 7.57...7.42; PCO2 22...44; PO2 171...34; Na 131...132; K 4.1...3.8; Ca 0.93...1.19; Protrombine time 80%; Trombin Time 12%.

Echocardiographic examination: Echocardiographic examination was within normal ranges. On abdominal ultrasound examination, liver had some changes on shape and echogenity. Hypo genic oval suspected shape (3.2cmx1.88cm) was detected close to Vena portae. Splint was 12 cm large. Also suspected formation within the left upper pole of the kidney was detected. Rapid agglutination test on Brucellosis was negative. Lang Rtg had just some Broncho vascular highlighting, but no pathologic findings. Urine and urinculture no pathologic findings. On Peripheral blood smear, dominate Granulocytes. Hypocromia was detected and Platletes were present. Bone marrow function findings were: the series of RBC were slightly suppressed. There were infiltration of vacuolated cells and no megakaryocytic cells were found. Hematologists proposed to do flu cytometry analyses. Ophthalmologist consultation resulted with no pathologic findings. Thoraxes CT resulted with no pathologic findings. Abdominal MRI findings: liver slightly enlarged, bile ducts and blood vessels were normal. Normal cholecyst. Kidneys were with no pathologic findings. Spleen slightly enlarged. Pancreas enlarged, with suspection on Pancreatitis or Lymphoma. Brain CT: On the left hemisphere a hypo dens zone was detected, with borderline 42x17mm, suspected epidural hematoma. That time the boy was transferred to Neurosurgery Clinic for intervention, and after patohystologic examination.

Biopsy findings: Dg: Burkitt lymphoma, high grade infiltration character. Its recommended, imuno-feno-typization. The boy is transferred now to hematooncology department, and Guideline based treatment was started. But the condition deteriorated resulting in death.

4. DISCUSSION

Our aim is to highlight the arthritic presentation of lymphoproliferative diseases in children. The majority (75%) of children with ALL did not have blasts in the peripheral blood at the time of evaluation by pediatric rheumatologists (9). In our Institution this was the first case which is diagnosed with Burkitt lymphoma after his presentation with arthritis complaints. Relation with ALL has been described in a several research works, but relation to Burkitt Lymphoma, still has not been described. A center in India during the period from January 2005 – October 2008, has compared the clinical profile of 11 children, which has presented with musculoskeletal complaints, and who were diagnosed to have ALL. They found that pain without physical findings is important issue. Also the hematological parameters were not significant, except lymphocytosis, leukopenia (10, 11) case presentation, similar to our case, has been described to a patient treated for juvenile idiopathic arthritis for six months, without success. That time the hematological features appeared and the diagnosis was settled (12).

Multicenter case-control study has explained the pos-

sibility to distinguish childhood leukemia from juvenile rheumatoid arthritis. They have compared several findings in order to identify the predictive factors for leukemia using basic clinical and laboratory information. They found that the 3 most important factors that predicted a diagnosis of ALL were low white blood cell count (< 4 x 10(9)/L), low-normal platelet count (150-250 x 10(9)/L), and history of nighttime pain. Other findings, including antinuclear antibody, rash, and objective signs of arthritis, were not helpful in differentiating between these diagnoses because they occurred at similar rates in both groups.

Cases of Lymphoma after immunosuppressive treatment are explained, as it is more common finding. There was a doubling risk of lymphoma in new onset cases of inflammatory polyarthritis. In one large recent study from Sweden there was also a doubling of lymphoma risk in a cohort of 3000 incident cases. It has been suggested that the increased occurrence of lymphoma is primarily driven either by the inflammatory process of the rheumatoid arthritis itself or by the use of immunosuppressive treatment (13,14). There were some hypothetical theories regarding presence of Epstein-Barr virus and lymphomas. But as analyzed with EBER in situ hybridization, it appears to be uncommon in RA related lymphomas. It`s supposed that there is an increased proliferative drive caused by self or non-self-antigens, which may play a role in lymphoma development in RA patients, but this has to be further studied (15).

There are cases when the arthritic symptoms are present and there are also hematological findings present albeit rare. In one case a 7-month-old girl, presented with left acute mastoiditis and a white blood cell count of 79,000/mm. This finding shows that even in atypical presentation and ages we should consider Burkitt lymphoma.

Based on our case and the other inflammatory and arthritic cases in which the final diagnosis was neoplastic disease, especially when isolated, the finding is unlikely to be child arthritis (16). So we suggest to think of alternate diagnoses including neoplastic disease.

5. CONCLUSION

- Arthralgia is a quite often child's complain, and should have a special attention paid to, as it might be a warning sign for a lot of diseases.
- In these cases relevant or adequate anamnesis and physical examination with a careful prescription of analgesic medications must be carried out, before the final diagnose is made.
- Steroid treatment should not be used before final diagnose of the diseases and before rolling out hematologic etiology, with peripheral blood smear.

- Author's contribution: all authors contributed equally in the preparation of the manuscript.
- Conflict of interest: none declared.

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