Thesis of Ph.D. studies

Characteristics of different subsets and long-term outcome in patients with idiopathic inflammatory myositis

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1. Introduction

The heterogeneous group of idiopathic inflammatory myositis (IIM) consists of rare systemic autoimmune diseases. The hallmark of these disorders is a progressive weakness of the proximal muscles mediated by an autoimmune process. In the case of dermatomyositis, typical cutaneous symptoms are present. In majority of the patients, systemic involvement also occurs. Clinicopathological subsets of IIMs differ in their pathomechanism, symptoms, clinical course and prognosis. The most common forms are a polymyositis (PM) and dermatomyositis (DM). Overlap myositis (OM) is accompanied by symptoms of another autoimmune disease. The cancer-associated myositis (CAM) has the worst prognosis. Myositis occurs in childhood as well (juvenile IIM).

The Dermatomyositis/Polymyositis Outpatient Clinic has been started in 1985 at the 3rd Department of Internal Medicine, University of Debrecen. Since then, more than 300 patients has been diagnosed and followed up. Our aim was the critical analysis of clinical aspects of IIMs in these patients, focusing on the clinical course, survival, medium- and long-term functional outcome and quality of life, and to evaluate patients with uncommon forms of IIMs, such as juvenile and cancer-associated myositis.

2. Aims of the study

1. Evaluation of clinical course in patients with IIMs
    a. Which clinical course types are common?
    b. In what frequency relapses develop? Which factors contribute to relapses?
    c. Are there prognostic factors for special?
2. Outcome in patients with IIMs: survival and prognostic factors
    a. What is the survival probability in patients with IIMs?
    b. Are there any differences between clinicopathological subgroups?
    c. How do systemic manifestations affect survival?
    d. What are the most common causes of death? What are the prognostic factors for death?
3. Evaluation of functional outcome and quality of life
    a. How does the myositis affects physical abilities and function?
    b. How does the myositis affects the quality of life?
4. What are the differences between juvenile and adult patients with IIMs concerning on the clinical course?
5. Evaluation of clinical and immunological characteristics of cancer-associated dermatomyositis

3. Patients and Methods

Our patients has been diagnosed and followed up by the 3rd Department of Internal Medicine, University of Debrecen. We analyzed the medical records recording the following data: age, sex, the time of diagnosis, duration of symptoms before the diagnosis was made, extraskeletal and extramuscular manifestations at any time during the clinical course, laboratory alterations, therapy, response to treatment, complications of treatment and the date of death or the end of follow-up.

I. Diagnosis of IIMs and patient evaluation

Diagnosis was made based on Bohan and Peter criteria. We evaluated our patients as follows: I. muscle strength (MMT), II. laboratory tests, III. evaluation of systemic manifestations, IV. evaluation of functional abilities, V. evaluation of quality of life. In the study of functional outcome and quality of life, written informed consent was obtained for participation in all cases.

II. Methods

1. Muscle power, MMT

   To evaluate muscle power, the 0-5 point British Medical Research Council System scale was used to test muscle strength of the following maneuvers on each side: shoulder abduction, elbow flexion, elbow extension, finger strength, hip flexion, hip abduction, knee extension, foot dorsiflexion and neck flexion /manual muscle strength testing (MMT)/. 0 is the lowest and 5 is the highest score indicating the level of muscle power the maximum score is 85 points, which refers to normal muscle power.

2. HAQ

   Functional ability was assessed using a translated Hungarian version of the Stanford HAQ disability index (HAQDI). The HAQ was self-administered. HAQ examines disability in 24 sub-category items in 8 categories: dressing and grooming, arising, eating, walking, hygiene, reach, grip and activities. There are four possible responses ranging from 0 to 3 for each sub-category item (0=able to perform without any difficulty, 1=able to perform with some difficulty, 2=able to perform with much difficulty, 3=unable to perform). When devices (cane, walker, wheelchair, tube chair, etc.) or aids (help from another person) are taken into account, then plus 1 score is added, but the maximum score is 3. Category scores are obtained by taking the highest score of the sub-category items in each category. The HAQDI score is calculated as the mean of the category scores. Therefore the range of the HAQ score is 0.0-3.0. Patients were classified as mildly disabled with a score of 0.1-

1.0, moderately disabled with a score of 1.01-2.0 and severely disabled with a score of 2.0-3.0. 87 questionnaires were completed from a possible 90 and 80 were assessable. (A minimum of 6 from the 8 categories must be completed in order to compute the HAQDI score.)

3. SF-36

   The SF-36 is a self-administered questionnaire containing 36 items, which represent 8 domains: physical functioning, role functioning, bodily pain, general health, vitality, social functioning, role emotional and mental health. The physical functioning domain gives information about the extent of limitation while performing physical activities. Physical role refers the extent to which physical health interferes with work or other daily activities. The bodily pain domain measures the intensity of pain and its effect on normal work. General health domain is a summary of the current evaluation of health status. Vitality domain shows whether the patient feels energetic or tired. Social functioning indicates problems interfering with normal social activities. Emotional role domain corresponds to the extent to which emotional problems interfere with work or other daily activities. Finally, the mental health domain refers to general mental health (depression, anxiety, behavioral-emotional control). The SF-36 scores are calculated on a 0-100 worst to best scale. SF-36 is translated and validated for Hungarian conditions. 87 questionnaires were completed from the possible 90.

III. Statistical analysis

All data were analyzed using the SPSS for Windows 10.0 statistics software (SPSS Inc., Chicago, IL, USA). Student's test, ANOVA, Mann-Whitney or Fisher's exact test was applied to verify statistical significance between patient groups. Correlational analyses were performed to assess the correlational structure of the variables (Pearson's correlation or Spearman's rank correlation, as appropriate). The survival curves were drawn using the Kaplan-Meier method. The log-rank test was used to determine the statistical significance of the observed difference in survival rates between patient groups. Stratified Cox regression analysis with forward stepwise variable selection method was used to assess the variables predicting death. Z-test was used to determine the statistical significance of the observed differences in SF-36 scores between patient groups and the normal population. Multiple linear regression models were applied to try to find variables that best predict the value of the HAQ or SF-36 scores. P values less than 0.05 was considered significant.

4. Results

I. Characteristics of clinical course

In this study 111 patients with primary IIMs, (62 with PM, 29 with DM and 20 OM) participated. The duration of follow-up was 24-274 months (median 98 months). In all clinicopathological subgroup, the myositis was diagnosed in autumn (P=0,032). The clinical course was acute-fulminant in 5 patients (4%), monophasic in 51 patients (46%), polyphasic in 42 patients (38%) and chronic in 13 patients (12%). The type of clinical clinical course was not different among the clinicopathological subgroups. In patients with chronic and polyphasic disease course, the delay of diagnosis was longer than in monophasic patients (P=0,008). Initial elevation of CK and LDH did not differ according to the subsequent clinical course, however, the decrease in muscle strength was greater in patients with acute course (P<0,001). Type of clinical course did correlate with presence of clinical symptoms and anti-Jo-1 autoantibodies. The time interval between the diagnosis and achievement of remission was 1-13 months (median 5 months) in monophasic patients, and 1-12 months (median 4 months) in polyphasic patients. In all clinicopathological subset, the relapses occurred within the first 24 months of the disease. In patients with polyphasic course, annual relapse rate did not differ among the clinicopathological subsets. The majority of relapses occurred during the maintenance treatment or during the withdrawal of maintenance treatment.

II. Outcome in patients with IIMs: survival and prognostic signs

A survival analysis was performed using data for 162 patients diagnosed between 1976 and 1997 according to Bohan and Peter's criteria. Patients were followed up for a minimum of 5 years (median 101.5 months) for surviving patients or to the date of death. Cumulative survival probability was calculated by Kaplan-Meier method. The influence of extraskeletal and extramuscular involvement was analyzed as prognostic factors for death by Cox proportional hazards survival model. Eighteen disease-specific deaths had been observed and pulmonary and cardiac complications were the most frequent causes of death. Global survival rates were 95%, 92% and 89% for 1, 5 and 10 years, respectively. Analysis for clinicopathological subgroups revealed that cancer-associated myositis had the worst, while juvenile and overlap myositis had the best prognosis. 5- and 10-year survival rates were 94.2% and 89.4% for patients with primary polymyositis and 90.1% and 86.4% for primary dermatomyositis patients, respectively. In the whole group of patients with idiopathic inflammatory myopathy cardiac (P<0.01) and respiratory muscle involvement (P=0.045) was

significant prognostic factors for death. In the group of primary polymyositis/dermatomyositis cardiac involvement was the main prognostic factor for death (P<0.01).

III. Functional outcome and quality of life in patients with IIMs

87 adult, definitive IIM patient participated in the evaluation of functional outcome (52 with PM, 21 with DM, and 14 with OM). The duration of follow-up was 36 months at least. Functional ability after a median follow-up of 107.1 months (36.4–273.3) was heterogeneous. The median HAQDI score was 0.875 (range: 0-2.875). As measured by the HAQ, 14 patients (17.5%) had no disability (HAQDI=0), 31 patients (38.8%) were mildly disabled, 25 (31.2%) were moderately disabled and 10 (12.5%) were severely disabled. There were no significant differences in HAQDI scores among PM, DM and OM patients, while the disease course had a significant effect on functional ability. Patients with relapsing-remitting and chronic-progressive disease course had significantly higher HAQDI scores than monophasic patients (P=0.029 and P=0.013). Disease activity and muscle power measured by MMT were correlated with HAQDI (r=0.28, P=0.009 and r=-0.61, P<0.001). Polyphasic or chronic-progressive disease course, osteoporosis, and long-term follow-up were predictive factors of higher HAQDI scores. In terms of quality of life, significant differences from population norms were shown in all domains of SF-36. There were no significant differences among PM, DM and OM patients within the scores of SF-36 domains. Interestingly, there was also no difference according to the disease course. Considering that the measured indices may evaluate some similar aspects of functional outcome, we examined possible relationships among them. Some domains of the SF-36 were correlated with HAQDI. Significant relationships were revealed between HAQDI and (i) physical functioning domain (r=-0.71, P<0.001), (ii) HAQDI and role functioning domain (r=-0.52, P<0.001), (iii) HAQDI and bodily pain domain (r=-0.52, P<0.001), (iv) HAQDI and role emotional domain (r=-0.42, P<0.001). Work status was also examined. We evaluated the ability to work regarding past and current employment in our cohort of patients. 37/87 patients (42%) were not able to work at any point in her/his life due to IIM. The proportion of disabled patients was not different among PM, DM and OM subsets. Interestingly, there was no significant relationship between the work status and quality of life.

IV. Characteristics of clinical course in juvenile patients with myositis

The disease course of 23/38 patients (60%) with JDM was classified as monophasic. 12/38 patients (31.6%) had polycyclic clinical course and 3/38 patients (7.9%) had chronic disease.

37 juvenile DM patients were treated with glucocorticoids initially. 20/37 (54.1%) patients were responsive to glucocorticoids, while 17/37 (45.9%) children required second-line immunosuppressive agents. 18/35 (51.4%) adult patients had monophasic, 13/35 (37.1%) had polycyclic, 1/35 (2.9%) had chronic disease and 3/35 (8.6%) had acute fulminant myositis. 20/35 (57.1%) adult DM patients achieved remission receiving only glucocorticoids. 15/35 patients (48.9%) required additional immune suppressive agents as initial therapy to achieve remission.

V. Characteristics of cancer-associated myositis

There were no malignancies among polymyositis, overlap or juvenile myositis patients. Twenty-four of 90 dermatomyositis patients also had a malignant disease. The exact time limit of the association of a malignant disease with myositis is controversial. Therefore, we evaluated our patients as having CAM based upon evidence came from population-based cohort studies. Patients with malignancy that occurred more than 2 years before or more than 5 years after the diagnosis of myositis were discharged from further evaluation (there were 16 patients with CAM). Patients with cancer-associated dermatomyositis were significantly older than primary myositis patients and had more severe cutaneous and muscle symptoms. Dysphagia and diaphragmatic involvement were more frequent among cancer-associated patients, while extramuscular features were less frequent. After successful treatment of the malignancy, we were able to manage myositis symptoms. One-year survival rate was significantly better in primary dermatomyositis patients.

5. Discussion

The development of myositis showed a seasonal pattern in our patients, while the relapses did not relate to seasons. In most of the previous studies, DM and JDM appeared to begin in spring and summer, while PM did not show seasonal pattern. Seasonal occurrence of DM supposed to be due to sun light exposure in spring and summer months. According to the clinical course, monophasic and polyphasic types occurred frequently. Among clinicopathological subsets, the type of clinical course did not differ. Our patients had a greater relapse rate than previously described. All PM, DM and OM patients had similar relapse rate. Most of the patients had multiple relapses. Long-term follow-up of patients with IIMs is very important, because relapses can occur frequently.

Present work indicates that myositis patients described in this study have higher survival rates than reported previously worldwide. We performed a long-term survival study on patients with myositis who were diagnosed, treated and followed up in a single clinical immunology department in Hungary. Our study indicates that myositis patients had higher survival rates than previously reported worldwide. This can be attributable to (i) these large series based upon patients who were diagnosed 2-3 decades before (ii) distribution of clinicopathological subgroups were not similar, mainly the frequency of cancer associated cases (iii) an improvement in diagnostic tools and therapeutic modalities resulting in an increase of survival rates. Our survival curve was heterogeneous with an accelerated mortality during the first year after diagnosis, and a slower mortality during the following 10 years, except for those who had cardiac complications later on the clinical course. We found no significant difference between groups of primary PM and primary DM, although most of the studies report better survival rates for PM patients. Deaths due to pulmonary complications were observed early in the course in our cohort of patients and cardiovascular complications occurred late on the course. Myositis patients may have severe extraskeletal and extramuscular manifestations - pulmonary, gastrointestinal and cardiac involvement - which often affect the prognosis unfavorably. In patients with primary PM, the presence of dysphagia and the presence of cardiac involvement were associated with a significantly worse survival probability. In the cases of primary DM survival rates were worsened significantly by male gender, older age (above 45 years) at the time of diagnosis, presence of ILD and presence of cardiac involvement. Effect of pulmonary involvement, especially ILD on the survival may be controversial, however, most authors found higher mortality rates compared to patients without ILD.

Classic factors of poor prognosis are older age, male sex, African-American race, ILD, presence of anti-Jo-1 and anti-SRP autoantibodies, associated malignancy, delayed or inadequate treatment, dysphagia, dysphonia, cardiac and pulmonary involvement. In our study unfavorable prognostic signs were respiratory muscle and cardiac involvement.

Myositis continues to have a great impact on life both in medium- and long-term. Present work indicates that myositis patients have a significantly poorer quality of life compared to that of the normal population, but there was no difference among the patients according to the clinicopathological subsets. The distribution of HAQDI scores revealed that only 17.5% of the patients had no disability and 12.5% were severely disabled. The majority of patients (70%) were mildly to moderately disabled. Therefore, there was an unfavorable functional outcome, taking into consideration that only 13% of the patients had an active disease at the time of the study. As clinicopathological and serological subsets differ from each other in prognosis, we compared the functional outcome of PM, DM, OM and anti-Jo-1 patients. There were no difference among them, however, our cohort presented relatively few OM and anti-Jo-1 positive patients. Patients, who had polyphasic or chronic-progressive disease course, or had a longer duration of the disease, tended to have higher HAQDI scores. Our patients had a marked impairment of quality of life, as significant differences from Hungarian population norms were shown in all domains of SF-36. We found no difference among clinicopathological subsets as also found by Sultan et al. There was no difference according to disease course in SF-36 scores. We also tried to analyze broader aspects of impaired Quality of life in myositis patients. The multivariate regression analysis showed that the most important predictors were gender, the duration of follow-up, and the presence of polyarthritis or osteoporosis.

In the study of characteristics of clinical course in juvenile patients, we have not observed correlation between relapse free survival and initial therapeutic regimens. The hazard of the relapse was found higher during the first year after the remission than later on the disease course in both of juvenile and adult patients. We have not found significant difference between juvenile DM and adult DM survival curves.

The subset of cancer-associated myositis differs from primary myositis in many aspects of clinical and immunological features. Prognosis and life-expectancy in cancer associated myositis patients is determined by the underlying malignant disease. Therefore age- and sex-specific examinations for detection of an underlying malignancy are important in the management of patients with dermatomyositis.

6. Summary of new results

The heterogeneous group of idiopathic inflammatory myositis consists of systemic autoimmune diseases, which are characterized by the progressive weakness of the proximal muscles. As these are rare disorders, it is very important to manage patients in specialized centers. The 3rd Department of Internal Medicine, University of Debrecen is the largest center for patients with idiopathic inflammatory myositis in Hungary. Until now, more than 300 patients has been diagnosed and followed up regularly.

We evaluated our long-term clinical experience. Concerning on the clinical course, we found that myositis followed a seasonal pattern in our patients, as myositis tended to occur in autumn. The monophasic and the polyphasic course affected the same proportion of patients. Relapses occurred mostly in the first 24 months of the disease. The survival probability was quite favorable compared to the literature data. On the other hand, the systemic manifestations, mainly pulmonary and cardiac involvement influenced the prognosis. Juvenile patients have similar disease course to the adult patients. Cancer-associated myositis occurred in the one fifth of the dermatomyositis patients. It is very important to screen for malignancy in them, mainly when the clinical picture seems atypical.

In patients with musculoskeletal diseases, the management should include not only the appropriate treatment of the disease, but also the prevention of decrease in functional disability and worsening the quality of life. Considering on the long-term functional outcome, majority of myositis patients have limitations in some extent in performing activities of everyday life, even if they are in remission. Functional outcome of patients with polyphasic and chronic disease course is considerably worse than patients with the monophasic form of the disease. In terms of quality of life, significant differences from population norms were shown in many aspects of quality of life. There were no differences in the quality of life among patients according to clinicopathological subset or disease course. Although mortality of our cohort was favorable, myositis continues to have a great impact on life both in medium- and long-term.

7. Publication

Articles related to Ph.D. studies

1. András C, Ponyi A, Constantin T, Csiki Z, Illés Á, Szegedi G, Dankó K. Myositisek tumorral történő társulása. Magyar Onkológia. 2002, 46: 253-259.

2. Ponyi A, Constantin T, Dankó K. Az anti-szintetáz szindróma. Magyar Immunológia. 2002, 1: 13-19.

3. Constantin T, Ponyi A, Garami M, Gergely L, Fekete G, Dankó K. A juvenilis dermatomyositis klinikai jellemzői. Orvosi Hetilap. 2003, 144: 1245-1250.

4. Dankó K, Ponyi A, Constantin T, Zeher M, Szegedi G. Tumorral asszociált myositis. Allergológia és Klinikai Immunológia. 2003, 6: 64-70.

5. Dankó K, Ponyi A, Constantin T, Borgulya G, Szegedi G. Long-term prognosis and survival of patients with idiopathic inflammatory myopathies. Medicine (Baltimore). 2004, 83: 35-42.
IF: 4.500 (2003)

6. Constantin T, Ponyi A, Bense T, Sallai Á, Gergely L, Garami M, Fekete G, Dankó K. A juvenilis dermatomyositis klinikai sokszínűsége – esetismertetés és klinikai összefoglaló. Gyermekgyógyászat. 2004, 55: 65-73.

7. Tállai B, Morshed AS, Flaskó T, Ponyi A, Dankó K, Tóth Cs. Prostatacarcinomával társult akut dermatomyositis. Lege Artis Medicinae. 2004, 14: 139-142.

8. Ponyi A, Constantin T, Dankó K. Antiphospholipid and antisynthetase syndrome in a patient with polymyositis-rheumatoid arthritis overlap. Clin Rheumatol. 2004, 23: 371-372.
IF: 0.850 (2003)

9. Váncsa A, Ponyi A, Constantin T, Gergely L, Dankó K. Dermatomyositishez társuló, késői megjelenésű extranodalis follicularis lymphoma. Lege Artis Medicinae. 2004, 14: 489-493.

10. Ponyi A, Borgulya G, Constantin T, Váncsa A, Gergely L, Dankó K. Functional outcome and quality of life in adult patients with idiopathic inflammatory myositis. Rheumatology. 2005, 44: 83-88.
IF: 3.760 (2003)

11. Ponyi A, Constantin T, Balogh Z, Szalai Z, Borgulya G, Molnar K, Teffner I, Garami M, Fekete G, Dankó K. Disease course, frequency of relapses and survival of 73 patients with juvenile or adult dermatomyositis. Clin Exp Rheumatol. 2005, 23: 65-71.
IF: 1.919 (2003)

12. Ponyi A, Constantin T, Müller J, Borgulya G, Zeher M, Fekete G, Dankó K. A juvenilis dermato/polymyositis szerológiája. Allergológia és Klinikai Immunológia. 2005, közlésre elfogadva.

13. Tállai B, Flaskó T, Salah MA, Ponyi A, Tóth Cs, Dankó K. Prostate cancer in the background of acute, definitive dermatomyositis: successful treatment with radical perineal prostatectomy. Clin Rheumatol. 2005, közlésre elfogadva.
IF: 0.850 (2003)

14. Ponyi A, Garami M, Constantin T, András C, Tállai B, Váncsa A, Gergely L, Dankó K. Cancer-associated myositis: clinical features and prognostic signs. Ann NY Acad Sci. 2005, közlésre elfogadva.
IF: 1.892 (2003)

Abstracts related to the Ph.D. studies

1. Dankó K, Ponyi A, Constantin T, Borgulya G, Szegedi G. Long-term prognosis and survival of patients with idiopathic inflammatory myopathies in Hungary. Ann Rheum Dis. 2003, 62(S1): 303.
IF: 3.827

2. Ponyi A, Borgulya G, Constantin T, Váncsa A, Gergely L, Dankó K. Functional outcome and quality of life in patients with idiopathic inflammatory myositis. Ann Rheum Dis. 2004, 63(S1): 241.
IF: 3.827 (2003)

3. Constantin T, Ponyi A, Balogh Z, Szalai Z, Fekete G, Dankó K. Disease course of 72 patients with juvenile and adult dermatomyositis. Ann Rheum Dis. 2004, 63(S1): 241.
IF: 3.827 (2003)

4. Ponyi A, András C, Váncsa A, Gergely L, Constantin T, Dankó K. Cancer-associated myositis: clinical features and prognostic signs. Autoimmunity Reviews. 2004, 3(S2): 76.

5. Constantin T, Ponyi A, Teffner I, Molnár K, Balogh Z, Szalai Z, Fekete G, Dankó K. Initial treatment and subsequent relapse rate of patients with juvenile and adult dermatomyositis. Autoimmunity Reviews. 2004, 3(S2): 145.

Other articles

1. Dankó K, Constantin T, Ponyi A, Szegedi G. Emelkedett szérum neopterin szintek polymyositises/dermatomyositises betegeinkben. Focus Medicinae. 2001, 3: 12-16.

2. Constantin T, Varga E, Kovács V, Ponyi A, Koós R, Kovács G. Antifoszfolipid-szindróma ritka klinikai manifesztációja gyermekkori szisztémás lupus erythematodesben. Gyermekgyógyászat. 2004, 55: 221-228.

3. Gergely L, Aleksza M, Váróczy L, Ponyi A, Sipka S, Illés Á, Szegedi G. Intracellular IL-4/IFN-gamma producing peripheral T lymphocyte subsets in B cell non-Hodgkin's lymphoma patients. Eur J Haematol. 2004, 72: 336-341.
IF: 1.714 (2003)

4. Constantin T, Ponyi A, Balázs G, Sallai Á, Dankó K, Fekete G, Karádi Z. Az MR vizsgálatok szerepe és helye a juvenilis dermatomyositis diagnosztikájában. Magyar Immunológia. 2004, 3: 33-39.

5. Constantin T, Ponyi A, Fekete G. Clinical relevance of anti-phospholipid antibody tests in childhood. Eur J Pediatr, 2004, 163(8): 507.

   IF: 1.157 (2003)

6. Dankó K, Constantin T, Ponyi A. A polymyositis és dermatomyositis korszerű kezelése. Focus Medicinae. 2005, 6: 17-22.

7. Constantin T, Ponyi A, Karádi Z, Kovács G. A gyermekkori szisztémás lupus erythematosus új, innovatív terápiás lehetőségei. Focus Medicinae. 2005, 6: 26-32.

8. Gergely P, Blazsek A, Dankó K, Ponyi A, Sallai K, Nagy E, Poór G. Detection of TT virus in patients with idiopathic inflammatory myopathies. Ann NY Acad Sci. 2005, közlésre elfogadva.

   IF: 1.892 (2003)

Other abstracts

1. Constantin T, Ponyi A, Garami M, Sallai Á, Dankó K. Juvenilis dermatomyositis. Allergológia és Klinikai Immunológia. 2002, 5: 46.

2. Ponyi A, Constantin T, Dankó K. Polymyositis-rheumatoid arthritis overlap szindróma. Magyar Reumatológia. 2002, 43: 151.

3. Constantin T, Ponyi A, Garami M, Gergely L, Dankó K. Juvenilis dermatomyositis. Magyar Reumatológia. 2002, 43: 138.

4. Ponyi A, Constantin T, Dankó K. Cyclosporin A treatment of idiopathic inflammatory myopathies. Ann Rheum Dis. 2003, 62(S1): 304.

   IF: 3.827

5. Ponyi A, Constantin T, Borgulya G, Dankó K. Idiopathias inflammatoricus myopathiákban szenvedő betegek túlélésének vizsgálata. Allergológia és Klinikai Immunológia. 2003, 6: 116-117.

6. Constantin T, Ponyi A, Molnár K, Tefner I, Szalai Z, Balogh Z, Fekete G, Dankó K. Juvenilis idiopathias inflammatoricus myopathiák kezelése során szerzett tapasztalataink. Allergológia és Klinikai Immunológia. 2003, 6: 102-103.

7. Constantin T, Karádi Z, Balázs G, Sallai Á, Ponyi A, Fekete G. Modern képalkotó vizsgálatok szerepe és helye a juvenilis idiopathiás inflammatoricus myopathiák diagnosztikájában. Gyermekgyógyászat. 2003, 54(1S): 101.

8. Ponyi A, Constantin T, Borgulya G, Dankó K. Idiopathias inflammatoricus myopathiákban szenvedő betegek túlélésének vizsgálata. Magyar Reumatológia. 2003, 44: 171. (legjobb poszter)

9. Constantin T, Ponyi A, Karádi Z, Balázs G, Sallai Á, Dankó K, Fekete G. Az MRI vizsgálat szerepe és helye a juvenilis dermatomyositis diagnosztikájában. Magyar Reumatológia. 2003, 44: 172.

10. Constantin T, Ponyi A, Teffner I, Molnár K, Balogh Z, Szalai Z, Müller J, Dankó K, Fekete G. Hungarian registry of children with juvenile dermatomyositis – first steps and preliminary results. Magyar Reumatológia. 2004, 45S: 71-72.

11. Karádi Z, Constantin T, Ponyi A, Varga E, Jókúti L, Balázs G, Fekete G. Diagnostic value of magnetic resonance imaging on the detection of muscle improvement in patients with juvenile dermatomyositis. Magyar Reumatológia. 2004, 45S: 72.

12. Ponyi A, András C, Váncsa A, Gergely L, Constantin T, Dankó K. Cancer-associated myositis: clinical features and prognostic signs. Magyar Reumatológia, 2004, 45S.

13. Constantin T, Ponyi A, Varga E, Kiss E, Fekete G, Kovács G. Antifoszfolipid szindróma juvenilis szisztémás lupus erythematodesban. Allergológia és Klinikai Immunológia. 2004, 7: 73-74.

14. Ponyi A, Constantin T, Dankó K. Idiopathiás inflammatoricus myopathiák intravénás immunglobulin kezelésével szerzett tapasztalataink. Allergológia és Klinikai Immunológia. 2004, 7: 92.

15. Constantin T, Ponyi A, Pállinger É, Dankó K, Tomsits E, Müller J, Fekete G, Kovács G. Cytokine expression changes and altered distribution of T helper and T cytotoxic lymphocytes in a patient suffering from autoimmune hepatitis. Tissue Antigens. 2004, 64: 367.

IF: 1.737 (2003)

16. Müller J, Constantin T, Hauser P, Ponyi A, Csóka M, Szendrői M, Garami M. Rare coincidence of chronic monoarthritis and Ewing sarcoma in a seventeen years old female (case report). Tissue Antigens, 2004, 64: 387.

IF: 1.737 (2003)

17. Constantin T, Ponyi A, Karádi Z, Fekete G. Peditop – online gyermekgyógyászati kurzusok. Gyermekgyógyászat. 2004, 55(S2): 14.

18. Constantin T, Ponyi A, Varga E, Koós R, Kovács V, Fekete G, Kovács G. Juvenilis antifoszfolipid-szindróma. Gyermekgyógyászat. 2004, 55(S2): 14-7.

19. Müller J, Constantin T, Erlaky H, Hauser P, Ponyi A, Szendrői M, Garami M. Ewing-sarcoma kialakulása hat évvel krónikus monoarthritist követően. Gyermekgyógyászat. 2004, 55(S2): 70.

20. Müller J, Schuler D, Hauser P, Ponyi A, Szendrői M, a Magyar Gyermekonkológiai Hálózat, Garami M. A magyar és a német eredmények összehasonlítása a gyermekkori Ewing-sarcoma kezelésében. Gyermekgyógyászat. 2004, 55(S2): 71-2.

21. Ponyi A, Constantin T, Molnár K, Tefner I, Szalai Z, Balogh Z, Dankó K, Fekete G. Juvenilis dermatomyositisben szenvedő betegeink kórlefolyásának jellemzése. Gyermekgyógyászat, 2004, 55 (S2): 87.

22. Constantin T, Ponyi A, Pállinger É, Dankó K, Tomsits E, Müller J, Fekete G, Kovács G. Immunophenotyping of T lymphocytes in a patient with autoimmune hepatitis. Autoimmunity Reviews. 2004, 3(S2): 129.

23. Müller J, Constantin T, Hauser P, Ponyi A, Csóka M, Szendrői M, Garami M. Chronic monoarthritis followed by Ewing sarcoma in a seventeen year old girl. Autoimmunity Reviews. 2004, 3(S2): 130-131.

24. Constantin T, Ponyi A, Varga E, Müller J, Kovács V, Fekete G, Kovács G. Antiphospholipid syndrome accompanied by a silent splenic infarct in a patient with juvenile systemic lupus erythematodes. Autoimmunity Reviews. 2004, 3(S2): 140.

25. Karádi Z, Constantin T, Ponyi A, Dankó K, Varga E, Jókúti L, Balázs G, Fekete G. Diagnostic value of MRI on the detection of myositis relapses in patients with juvenile dermatomyositis. Autoimmunity Reviews. 2004, 3(S2): 144-145.

26. Sümegi A, Dankó K, Kiss E, Szegedi A, Tar T, Ponyi A, Szegedi G, Antal-Szalmás P. A CD14, TLR2 és TLR4 gének polimorfizmusainak vizsgálata autoimmun és immunpatomechanizmusú betegségekben. Magyar Immunológia. 2004, 3: 69.

27. Müller J, Schuler D, Hauser P, Ponyi A, Szendrői M, a Magyar Gyermekonkológiai Hálózat, Garami M. Ewing sarcomas gyermekek kezelésével elért hazai eredményeink. Magyar Onkológia. 2004, 48(S1): 17.