(median 18.5) years it is obvious that the
group studied represented patients with JIA
onset before 16 years of age and therefore
involving paediatric cases and adults with
a long duration of the disease. We focused on
the JIA group as a whole since paediatric
patients treated at the Outpatient Depart-
ment of Rheumatology in the University
Hospital Motol in Prague remain our pa-
tients even after they reach the age of 18.
When we re-analyzed the data for paedi-
atric cases only (aged 0-18 years), the per-
centage of AKA positivity was still high;
5/15 of the patients (35%) with RF negative
polyarthritis; 9/12 (75%) of those with RF
positive polyarthritis; and 2/7 of those
(28.6%) with systemic disease.
In accordance with what Dr. Foeldvari (2)
has pointed out, we absolutely agree that
oligoarticular JIA normally represents the
largest subset of JIA and was nearly miss-
ing in the first part of our study. The expla-
nation of that is very simple. As a spe-
cialised rheumatological department we
treat the more severe forms of JIA, which
are sent to our specialised department from
family practitioners. This could be one rea-
son why RF-negative and RF-positive pol-
yarthritides and systemic arthritis dominated
the patient’s cohort that we focused on at
first.
Concerning the definition of disease activ-
ity, our patients were divided into two
groups depending on their disease activity:
i) complete or near remission with or with-
out on-going treatment, and ii) active dis-
ease on the basis of the preliminary criteria
for clinical remission in rheumatoid arth-
ritis (3) and the American College of Rheu-
matology preliminary core set of disease
activity measures for rheumatoid arthritis
clinical trials (4).
Palosuo et al. studied the presence of an-
ti-filaggrin antibody (AF) of the IgG class in
paediatric patients (range 0.9 – 15.2 years)
with juvenile idiopathic arthritis using an
enzyme-linked immunosorbent assay (ELI-
SA),and found that AF are rare in patients
with juvenile oligoarthritides and RF-negative
polyarthritides (5). In a previous study Palo-
suo et al. reported a good correlation be-
tween AFA (ELISA) and AKA (IF assay)
in a cohort of patients with rheumatoid arth-
ritis (6). In the present Letter they com-
pare data on the presence of anti-filaggrin
antibody (AF) of the IgG class in paedi-
atriic patients (range 0.9 – 15.2 years) with
data from our study (1) concerning anti-ker-
atin antibodies measured using indirect
immunofluorescence on rat oesophagus
epithelium in patients with juvenile idi-
opathic arthritis (age range 4 – 44 years) . On
the basis of the previous and present studies
Palosuo et al. conclude that there is a signif-
icant difference between their findings and
those we reported (50% AKA positivity). At
first glance it is obvious that the data of
these two studies cannot be compared, since
no AKA data for patients with juvenile idi-
opathic arthritis (except those 17 patients
with psoriatic arthritis) in Palosuo’s study
(5) and no data on AFA in our study (1) are
available; furthermore, the structure of the
studied cohorts differs significantly. There
is just speculation and no real comparison
between AFA and AKA in differing cohorts
of JIA patients.
Since we used a commercial kit for the
detection and quantification of KAs in
human serum, we automatically avoid prob-
lems with an inadequate standardisation of
the substrates and interpretation difficulties,
as within each test run both positive and
negative controls were included. The AKA
immunofluorescence pattern was easily
readable as negative or positive in most of
the analysed samples. On the other hand,
there is no doubt that ELISA is much easier
to interpret, without an element of arbitrary
interpretation. Several explanations might arise if one
enters into the details of the procedure and
literature. In their study Palosuo et al. (6)
monitored AKA serum samples diluted 1: 10
and 1:50 only and interpreted laminar
staining of the stratum corneum at a serum
dilution of 1:10 as positive. We kept in mind
the manufacturer’s instructions (7) that in
some cases sera positive for AKA may
either be very weak or negative at the initial
screening dilution (prozone phenomenon).
In such cases the sera should be screened at
the next higher dilutions and, if positive, the
antibody titres determined.
Moreover, testing only 1:10 and 1:50 serum
samples may result in missing positive
results at titres of 1:20 and 1:40. If we take
a look at our data, 25 out of 30 patients
(83%) had sera positive for AKA (1) at
these critical dilutions, which were omitted
in the study of Palosuo et al. (6). Only 5 out
of 30 patients had sera positive at the high
levels of 1:80 and 1:160.
If we examine the data of Noqueira et al.
(8) we can see also that significantly higher
diagnostic sensitivities of AKA (0.40) diag-
nosed by IIF on rat oesophagus epithelium
were found in comparison to ELISA results
with purified human epidermal (0.22) or
human recombinant filaggrins (0.31) at
0.99 specificity in a cohort of rheumatoid
arthritis patients.

Rheumatic manifestations as
presenting signs of infective
endocarditis

Sirs,
We have read with interest the article by
Slobodin et al. "Sacroiliitis as a presenting
manifestation of infective endocarditis" (1).
We fully support their conclusions and
would like to underline the importance of
considering rheumatic manifestations as
presenting signs of infective endocarditis
(IE).
With respect to this, we have recently re-
ported a large series of non-drug addict
patients with rheumatic manifestations in
the setting of IE (2). We examined the fea-
tures of patients diagnosed with clinically
definite IE according to Duke’s classifica-
tion criteria at a single reference hospital
for a defined population in Lugo (North-
western Spain) during a 12-year period.
Between 1987 and 1998, 100 consecutive
patients had 110 episodes of clinically de-
finite IE. In this study we found that the inci-
dence of rheumatic manifestations was
41.8%. Rheumatic manifestations occurred

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more commonly among men in their 50s. Back pain (19.1%) was the most common rheumatic manifestation. Myalgia (15.5%) was also frequently observed, as was arthralgia without arthritis (10%). Peripheral arthritis (13.6%) was also present, but generally as monoarthritids. In contrast, sarcoidosis was only observed in a single patient. This patient was a man in his early twenties, who had positive blood cultures for *Enterococcus faecalis*, and experienced a progressive improvement of his sacroiliac pain following antibiotic therapy with ampicillin and gentamicin (2).

It is worth noting that in our series of patients with IE and rheumatic manifestations microhematuria was observed in almost 60% of the patients, versus 27% in IE patients without rheumatic manifestations (2).

In summary, unexplained peripheral synovitis, arthralgia or low back pain along with unexplained microhematuria may be possible warning signs for the presence of IE. Awareness of these complications may be useful to avoid inappropriate delay in the diagnosis of this severe disease.

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References

Macrophage activation syndrome as the initial manifestation of systemic onset juvenile idiopathic arthritis

Sirs,

The macrophage activation syndrome (MAS), a clinical syndrome caused by excessive proliferation and activation of well-differentiated macrophages, has been associated with a heterogeneous group of conditions that include drugs, infections, and neoplastic and rheumatologic diseases. MAS has been described in association with systemic onset juvenile idiopathic arthritis (soJIA), with various triggering events such as bacterial or viral illness or the use of nonsteroidal antiinflammatory drugs (NSAIDs), gold salts, sulfasalazine or methotrexate (MTX) (1). Because of the life-threatening nature of this syndrome, prompt recognition is mandatory and treatment with high doses of corticosteroids and cyclosporine A in MAS associated with soJIA has been advocated (2). We present the case of a 2-year-old boy who developed MAS syndrome shortly after the start of a febrile arthritis retrospectively diagnosed as soJIA and only 4 days after treatment with salicylates was initiated.

The patient was admitted to our hospital after 8 days of high spiking daily fever reaching 39.5°C and monoarthritis of the right wrist. On admittance, physical examination showed a slight swelling over the ulnar area of the right wrist with normal general, neurologic and ophthalmologic examinations. An evanescent erythematous maculopapular rash over the trunk and upper extremities was evidenced. Laboratory data showed a white blood cell count of 17.4 x 10^9/l (72% granulocytes), Hb 10.6 g/dl, hematocrit 31%, and platelet count 486 x 10^9/l. Serum urate, creatinine, calcium, phosphorus, alkaline phosphatase, transaminases, and -glutamyltranspeptidase were within the normal range. The prothrombin time (PT) and partial thromboplastine time (PTT) were normal. Rheumatoid factor and antinuclear antibodies were negative. C-reactive protein was elevated to 216 mg/l. Ferritin was elevated to 56,807 g/l with normal serum iron level and binding. Serologic tests for the usual bacterial or viral diseases were negative. An abdominal echography showed hepatomegaly with normal kidneys and spleen. A thorax radiograph was normal. Bone radiographs showed soft tissue swelling. The electrocardiogram was normal. On day 3 after admission acetylsalicylic acid was initiated (100 mg/kg/day). Melena appeared on day 6 together with maintained fever, 77 x 10^9/platelets, Hb 8.70 g/dl, and 8.2 x 10^9 leukocytes. PT and PTT were prolonged at 23.3 seconds (normal 11-15) and 57 seconds (normal 25-40), respectively, with low fibrinogen 1.09 g/l. GPT was elevated to 83 U/L, GOT to 77 U/L and LDH to 9,570 U/L. Hypoalbuminemia 30 g/L was noted. Triglycerides were 2.27 g/l. Platelets reached 26 x 10^9/so that platelets and fresh plasma were necessary. A gastroscopy disclosed 4 erosions over the antrum and a haemeraemic fundus suggesting NSAID gastropathy. Salyclates were stopped. Bone marrow aspiration showed the presence of abundant macrophages with phagocytesis (Fig. 1).

MAS was diagnosed and glucocorticoids 1 mg/kg/day were initiated. The corticosteroid dose was gradually increased up to 3.5 mg/kg/day to control the systemic disease and fever. After 10 days of corticosteroid therapy, platelets and a coagulation test were normal and the patient was discharged. Two months later, because of tenosynovitis of both shoulders and malaise, oral MTX up to 0.6 mg/kg/day was administered with resolution of the joint symptoms. Presently corticosteroids have been stopped. No MAS recurrence was found after MTX introduction.

MAS is a clinical syndrome characterised by persistent unremitting fever, lymphadenopathy, hepatosplenomegaly, mental status changes, easy bleeding, depression of the three blood cell lines, low erythrocyte sedimentation rate (ESR), and elevated serum liver enzyme values (1). The pathologic finding on bone marrow aspiration is the presence of numerous well-differentiated macrophages actively phagocyting hema-topoietic elements (3). SoJIA is a multisystemic disease in which extra-articular features are prominent and include fever, rash, lymphadenopathy, hepatosplenomegaly, carditis and laboratory abnormalities such as anemia, leukocytosis, thrombocytosis and hyperferritinemia. MAS has been de-