Sonography as a replacement for sialography for the diagnosis of salivary glands affected by Sjögren's syndrome

Recently, it has been suggested that sonographic evaluation of the salivary glands is useful in the diagnosis of Sjögren’s syndrome. Kawamura et al and, more recently, Ariji et al, showed that descriptive and quantitative assessment of the salivary glands by sonography efficiently differentiated between diseased and normal glands in patients with Sjögren’s syndrome. They showed that the proposed sonographic gradings correlated well with the sialographic gradings. These findings suggest that sonography might be an alternative diagnostic tool for Sjögren’s syndrome.

Here, we attempted to determine whether sonography can take the place of sialography as an alternative technique for the assessment of salivary gland involvement in Sjögren’s syndrome. Sialography and sonography were performed on 294 patients who presented with sicca syndrome (171 positive and 123 negative for Sjögren’s syndrome). We diagnosed patients with Sjögren’s syndrome on the basis of the criteria of the European Community Study Group. Sonographic features characteristic of Sjögren’s syndrome are heterogeneous echogenicity with hypo- and hyperechoic signals throughout the affected gland (fig 1).

Table 1 shows the performance of each of the diagnostic criteria. Sialography performed best among the five diagnostic criteria—that is, sialography, functional tests (Saxon and Schirmer), and serological tests (SS-A and SS-B). Interestingly, when used instead of sialography, sonography provided a good performance, comparable with that of sialography (McNemar test, p=0.067). In contrast, the other diagnostic criteria did not perform as well as the two imaging criteria.

Logistic regression analysis was performed to identify diagnostic criteria that might be used as predictive indicators for differentiating between patients with and without Sjögren’s syndrome. Univariate logistic regression analysis showed that the six diagnostic criteria assessed (sialography, sonography, Saxon’s test, Schirmer test, SS-A, and SS-B) did correlate with a positive diagnosis of Sjögren’s syndrome, indicating that these six criteria, if used alone, could effectively predict the presence of Sjögren’s syndrome (table 1).

On multivariate analysis, however, only sialography and sonography showed significant correlations with a positive diagnosis of Sjögren’s syndrome (table 1); when sialography was used together with the functional and serological criteria, only sialography showed a significant correlation. If sonography was used instead of sialography, only sonography displayed a significant correlation with a positive diagnosis of Sjögren’s syndrome (table 1). Collectively, these findings suggest that the sonography performs as well as sialography in differentiating between parotid glands affected by Sjögren’s syndrome and normal glands. In contrast, the other diagnostic criteria did not perform as well as the two imaging criteria.

Some discrepancies were found between the diagnostic performance in the present study and that in previous studies. For example, Schirmer’s test in our study performed poorly compared with the performance reported by Vitali et al. SS-A and SS-B displayed high sensitivity and low specificity in our study, whereas low sensitivity and high specificity were found in the previous study. These inconsistencies may be due to the differences in patient groups or in techniques, or both. Despite these differences, the performance by sialography was similar, consistent with the notion that the imaging techniques, including sialography, provide reliable results in the diagnosis of Sjögren’s syndrome.

In conclusion, a diagnosis of Sjögren’s syndrome can be made on the basis of a wide range of diagnostic tests, and not merely on fixed combinations of these tests. Evaluation of salivary gland involvement contributes significantly to the performance of the criteria. Thus the availability of different imaging techniques, such as Doppler sonography and magnetic resonance imaging, to assess salivary gland involvement allows clinicians to classify patients with sicca syndrome correctly.

Figure 1 Sialography (A and B) and sonography (C and D) of the parotid glands in patients who presented with sicca syndrome (dry eyes and dry mouth). Normal glands (A and C), and glands affected by Sjögren’s syndrome (B and D) are shown for comparison. Sialography of the parotid glands with Sjögren’s syndrome shows characteristic globular (B) staining patterns. Sonography of the parotid glands with Sjögren’s syndrome shows irregular echogenicity and multiple hyperechoic bands and hypoechoic areas in the gland (D).

Table 1 Performance and logistic regression analysis of diagnostic criteria for Sjögren’s syndrome

<table>
<thead>
<tr>
<th>Diagnostic Test</th>
<th>Sensitivity [%]</th>
<th>Specificity [%]</th>
<th>Accuracy [%]</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sialography</td>
<td>87</td>
<td>90</td>
<td>92</td>
<td>Coefficient 6.02 SE 0.75 p Value &lt;0.00001</td>
<td>Coefficient 4.87 SE 1.06 p Value &lt;0.00001</td>
</tr>
<tr>
<td>Sonography</td>
<td>76</td>
<td>91</td>
<td>92</td>
<td>Coefficient 3.69 SE 0.39 p Value &lt;0.00001</td>
<td>Coefficient 3.97 SE 1.07 p Value &lt;0.00001</td>
</tr>
<tr>
<td>Saxon test</td>
<td>72</td>
<td>90</td>
<td>84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schirmer test</td>
<td>70</td>
<td>83</td>
<td>80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SS-A</td>
<td>59</td>
<td>71</td>
<td>66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SS-B</td>
<td>60</td>
<td>67</td>
<td>56</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS, not significant.
Radiographs of the hands and feet were normal. There were slight erosions of the sacroiliac joints and of the symphysis pubis.

The patient was treated with non-steroidal anti-inflammatory drugs (NSAIDs) and on several occasions with local injections of corticosteroids into the interphalangeal joints. For the psoriatic nails he took acitretin (Neotigason) at a daily dose of 20 mg, for 12 months, but the nail lesions did not improve. In view of the persistence of the DIP joint involvement the patient was treated since January 2000 with sulfasalazine (the dose being progressively increased from 0.3 g daily to 2 g daily), in addition to NSAIDs. Three months later, the nail lesions started to regrade and they disappeared progressively (fig. 1b); the improvement has persisted until now. Concomitantly, there was a marked improvement of the arthritis.

Discussion

Nail disease is significantly associated with PsA. It is particularly common in cases with DIP joint involvement and tends to indicate more severe PsA. In view of the close chronological relationship between the administration of sulfasalazine and the improvement of the nail lesions, it can be considered that sulfasalazine played a beneficial part in the pathological condition of our patient. Dermatological assessment of patients treated with sulfasalazine for PsA has been reported in two series; according to the report published in the series of Gupta et al, patients treated with sulfasalazine for PsA showed signs of cutaneous improvement compared with those receiving placebo. The series of Farr et al reports improved cutaneous lesions in as few as 3/15 patients treated with sulfasalazine and 1/15 patients receiving placebo. However, we could not find any indication of the evolution of possible simultaneous psoriatic nail lesions.

Treatment of PsA with cyclosporin or etanercept is effective for both joint and skin lesions of PsA; again no data about the outcome of psoriatic nail lesions were provided in these clinical studies. Our case report might be the occasion to draw the attention of rheumatologists to the possible beneficial effects of basic treatment such as sulfasalazine not only for PsA but also for treating psoriatic nails.

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References


Home sequential high dose intravenous immunoglobulins in systemic autoimmune disease

The high cost of IV immunoglobulins is often considered to be a disadvantage of this treatment. However, this does not take into account the benefits gained—for example, the savings achieved in the costs of corticosteroids and immunosuppressive drugs and, above all, the improvement in quality of life achieved through functional improvement, as noticed in inflammatory myopathies and Still’s disease. It is precisely to minimise the costs of IV immunoglobulin treatments and to enable patients to remain at home that we have developed the administration of IV immunoglobulins at home when sequential treatments are necessary.

Between January 1995 and March 2000 30 patients (18 women, 12 men) were enrolled, with a mean (SD) age of 44.0 (9.9) for the women and 51 (0.9) years for the men (range 21–74). All the patients had received the first two treatments in hospital to ascertain their tolerance. Patients mostly received Tégéline (314 treatments), Endotubine (81 treatments), and Gammagard (three treatments). All the patients had a corticoid-dependent or refractory autoimmune disease (mostly polyarthritis, dermatomyositis, and adult onset Still’s disease).

The doses prescribed for each treatment were generally 2 g/kg. Treatments were carried out monthly and consisted of two days when performed in hospital and five days when performed at home. The average flow rate of the IV immunoglobulin perfusions performed at home was 10 g/2 h (extreme value: 30 min–4 h). The secondary effects of the treatments at home remained conventional and minor.

The efficacy of the IV immunoglobulin was determined by the patients as very good in 17%, good 33%, modest 3%, nil 47%. The efficacy of the IV immunoglobulin was described by the senior doctor as very good 33%, good 30%, nil 17%. Evaluation of the efficacy described by the patients themselves was based on purely functional criteria (general condition, pain,
muscular deficit, etc), which explains the difference between the two evaluations. Cases where the IV immunoglobulin resulted in a reduced use of corticosteroids, or cases where IV immunoglobulins made it possible to avoid using immunosuppressive drugs were regarded as a success by the senior doctor, whereas patients did not necessarily have the same impression. The 23 patients (77%) who said they had benefited from the IV immunoglobulin treatments at home gave the following reasons: better comfort (n=12), presence of next of kin (n=10), more occupation (n=6), maintaining activities (n=3), avoiding repeated trips to the hospital (n=3), better quality of sleep (n=2), better mood (n=5), time gain (n=3), and per fusion in the pharmacy and at home).

The mean cost of a treatment in hospital was $2701 against $2471 for a treatment at home.

Cost for one treatment in hospital : $2701

Cost for one treatment at home: $2471

Table 1: Evaluation of the cost of at home IV immunoglobulin treatments (n=277) and comparison with the theoretical cost in hospital

<table>
<thead>
<tr>
<th>IV Immunoglobulin</th>
<th>24 h hospital stay with hospital lump sum</th>
<th>Small equipment</th>
<th>Nursing</th>
<th>Total cost for 277 treatments</th>
<th>Savings achieved for 277 treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theoretical cost in hospital</td>
<td>$2055</td>
<td>$605</td>
<td>$41</td>
<td>$748274</td>
<td>$580556 (representing the virtual economy made by the hospital department (drug budget + small equipment))</td>
</tr>
<tr>
<td>Effective cost at home</td>
<td>$2363</td>
<td>(15% of retrocession overcost*)</td>
<td>0</td>
<td>$684588</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>*In France when a drug is retroceded by a hospital pharmacy, it is invoiced 15% higher, the difference being paid to the hospital administration to cover the management and traceability costs.</td>
</tr>
</tbody>
</table>

Table 2: Home IV immunoglobulin infusion guidelines for patients with autoimmune disease

1. Need for a defined diagnosis
2. Presence of rational physiopathological basis that could “legitimise” the use of IV immunoglobulin
3. Senior hospital prescription
4. Respect of the contraindication of home IV immunoglobulin programme: coronaryopathy, insufficient or ischaemic cardiopathy, recent stroke, nephropathy, uncontrolled hypertension, thrombosis of the perfused vein, hypersensitivity reaction after the first or second hospital infusion
5. More than one hospital based infusion before infusion at home to assess the tolerance
6. Average flow rate of IV immunoglobulin no quicker than 10 g per two hours
7. Collaboration with a home care organisation for visiting nurses and for collection of tubing and used bottles

Elastofibroma dorsi

Elastofibroma is a rarely diagnosed benign fibroproliferative lesion which occurs most commonly in the periscapular region of middle aged to elderly women. Recognition of the lesion is important as the differential diagnosis includes other benign and also...
malignant tumours. We report a case of elastofibroma in a patient who presented with shoulder pain to a rheumatology clinic, and review previous publications. Although elastofibroma is uncommon, it has received attention in radiological and orthopaedic publications but not in rheumatology published reports.

A 43 year old Turkish woman, previously fit and healthy, was referred to our outpatient clinic with a two year history of right shoulder pain. The pain was described as a dull ache of gradual onset, around the posterior aspect of the shoulder over the scapula, which was worse on movement of the arm. There was no weakness. Over the preceding four months the patient had noticed a swelling below the inferior angle of the right scapula which would appear and disappear with movement of the arm. The patient had no other medical history or relevant family history.

On examination there was a full range of movement of both shoulders and neck with no wasting or neurological signs. Pain was reproduced around the right shoulder when the arm was circumducted. In this position a firm, poorly circumscribed, and minimally mobile mass of 5 x 5 cm was apparent underlying the inferior angle of the scapula. The rest of the examination was normal.

Initial investigations showed a normal full blood count, bone profile, and inflammatory markers, and a normal radiograph of the right shoulder and scapula. Subsequent magnetic resonance imaging (MRI) showed a poorly circumscribed heterogeneous soft tissue mass between the chest wall and the scapula (fig 1). The signal intensity was similar to that of skeletal muscle but interspersed with low signal intensity areas representing adipose tissue. The mass lies between the serratus anterior (short arrow) and the thoracic cage (C). L, latissimus dorsi.

Figure 1 Magnetic resonance image (T. weighted axial) of the right infraspinacular region showing a poorly defined mass (long arrow) with areas of high signal within. The mass lies between the serratus anterior (short arrow) and the thoracic cage (C). L, latissimus dorsi.

Elastofibroma dorsi, first described in 1961, is a benign, slow growing, mesenchymal soft tissue lesion. Most (99%) occur in the subscapular region, usually on the right side. The lesions have occasionally been found in the extremities, head, abdominal and thoracic cavities. Of those in the subcapsular region approximately 10% are bilateral. The cause and pathogenesis are unclear, but it is suspected that subclinical microtrauma may lead to reactive hyperplasia of elastic fibres with consequently increased production of fibrous tissue. Clinically, over 50% of subjects are asymptomatic and may present with a painless swelling; approximately 25% present with a clicking sensation when the arm is moved, while fewer than 10% present with pain.

Plain radiographs may be normal or may show soft tissue density in the periscapular region when the scapula is raised. Computed tomography usually shows a heterogeneous soft tissue mass with poorly defined margins. MRI is the best non-invasive technique and most useful for diagnosis. Elastofibromas appear as poorly circumscribed soft tissue lesions with similar signal intensity to that of skeletal muscle but interspersed with high signal intensity areas representing adipose strands. The differential diagnosis includes desmoid tumours, neurofibroma, and liposarcoma. However, these tumours usually show strong enhancement after gadolinium injection. Usually faint enhancement is seen with elastofibromas, although marked enhancement, mimicking malignant tumour, has been occasionally reported. Biopsy should therefore be undertaken as the confirmatory procedure and to exclude sarcoma.

In cases where the patient is asymptomatic excision is unnecessary. Malignant transformation is unknown. In symptomatic cases local excision is the best treatment. Recurrence has not been reported.

We conclude that elastofibroma should be considered in the differential diagnosis of subscapular pain. Although an uncommon lesion with a variable clinical presentation, the site and MRI appearances are characteristic. Awareness of the benign nature avoids unnecessary surgery and reassures a symptomatic patient.

References


Olecranon bursitis due to Candida parapsilosis in an immunocompetent adult

Septic bursitis (SB) mainly affects the olecranon and patellar bursa. Subcutaneous localisation predisposes to trauma and may subsequently lead to infection. Most cases of SB are related to the subject’s occupation (roofing, gardening, plumbing), but surgical interventions (aspiration, intrabursal injection) are among other probable causes.1 Bacteria account for most cases, Staphylococcus aureus being the most commonly found (80%).1,2 Fungal isolation is quite rare and always associated with immunosuppression or debilitating conditions,3 but some species of Candida, Cryptococcus, Penicillium, and Sporothrix schenckii have been described.4 These atypical organisms usually develop in a late indolent pattern, and a delay in diagnosis and treatment may lead to considerable difficulties in eradication of infection. We report a case of SB caused by Candida parapsilosis in a previously healthy man, with no underlying disease or any risk factors, including HIV infection, who probably acquired joint infection at the hospital secondary to local steroid injection.

Case report

A 32 year old man with a one month history of mild inflammation of the right elbow presented to our hospital on 19 May 2000. He had
an unremarkable past medical history, which did not include any toxic habits or recent trauma. Bursal aspiration showed that the synovial fluid had inflammatory characteristics (leucocyte count 4.9×10^3 cells/l (54% neutrophils), and a glucose level of 3.8 mmol/l), but there were no crystals and a fluid culture was negative. A diagnosis of olecranon bursitis was established, and conservative management (bursa aspiration and rest) was decided on. Bursal effusion was repeated over the next four days, so a further aspiration was carried out and local injection with triamcinolone acetate (20 mg) was given. However 24 days later the pain persisted and swelling of the elbow joint was noted. Laboratory synovial findings showed a leucocyte count of 15.7×10^3 cells/l (60% neutrophils) and a glucose level of 0.8 mmol/l. Culture yielded a few colonies of Candida sp, but antifungal treatment was not started because it was considered that this might be caused by contamination. One month later (28 July), the patient presented to the emergency room owing to development of a new extremely painful episode of bursitis. After joint aspiration, a steroid injection was again given, but this time a fluid culture was not carried out.

On 1 August clinical symptoms persisted. Physical examination showed an increase in the size of the olecranon bursa. The patient had never presented with fever, arthralgias, or any general complaints. Laboratory studies, including a test for antibodies to HIV, were normal or negative. Magnetic resonance imaging was performed showing multiseptate bursitis; the adjacent structures were normal. A removal of 10 ml bursa fluid again yielded a positive culture for Candida that was later identified as C. parapsilosis (Madrid, National Centre for Microbiology). Antifungal sensitivity testing showed a minimal inhibitory concentration for amphotericin B of 1 mg/l, 5-fluorocytosine 0.25 mg/l, fluconazole 0.23 mg/l, itraconazole 0.03 mg/l, and ketoconazole 0.015 mg/l. By the end of August, oral fluconazole was started at a dose of 400 mg/day for seven days, and then 200 mg daily. Recovery was slow and the patient needed repeated drainage. As follow up cultures were still positive, on 27 September it was decided to carry out surgical debridement with complete excision of the olecranon bursa. This material was not cultured, but histopathological analysis was performed demonstrating pseudohyphae structures, without granulomatous reaction or foreign bodies. After bурсectomy, the patient continued fluconazole treatment (same maintenance dose) for six weeks more. Six months later he is completely asymptomatic.

Infection of superficial bursae (olecranon, prepatellar, and infrapatellar) is generally associated with different occupations or physical activities. Local trauma may predispose micro-organisms to penetrate by the transcutaneous route. Similarly, intrabursal steroid injection, a habitual therapeutic procedure, may lead to infection. Weinstein et al noted that development of infection after this procedure occurred in 12% of a series of cases. Most frequently bacteria cause infections, but unusual pathogens like fungi have also been reported. Candida septic bursitis is extremely rare. After a thorough review of the Medline database (from 1966 to January 2001) using medical subject headings, and keyword searches that included “septic bursitis” and “Candida bursitis”, we found only five reports. Two caused by C. albicans, two by C. tropicalis, and another one by C. lusitaniae (table 1). Characteristically, in all the cases, and in the present report, different risk factors or underlying diseases were found. Four cases were caused by haematogenous spread and two induced by direct penetration, including our case. The olecranon bursa was affected in three cases, including the present report. C. parapsilosis is a well known cause of arthropathies that has been described secondary to systemic dissemination in intravenous drug users, and also by direct inoculation secondary to trauma. It is not strongly associated with immunocompromised hosts, but rather with invasive procedures or prosthetic devices. More recently C. parapsilosis has emerged as an important nosocomial pathogen. This is the Candida species that is most commonly isolated from the hands of healthcare workers. In contrast with other Candida species, colonisation with C. parapsilosis rarely occurs before the onset of invasive infection, suggesting an exogenous source of infection.

Appropriate antifungal drugs to treat Candida infections are available, but appropriate drug levels in osteoarticular structures are difficult to achieve. So for successful treatment of this infection, surgery is sometimes required. Half of the patients with Candida SB reviewed needed surgery for complete resolution (table 1). We would like to summarise several aspects of the present report: Firstly, steroid injection must never be omitted, as it is very difficult to achieve a higher degree of awareness is necessary to achieve prompt diagnosis and successful treatment. Nevertheless, special care must be taken to avoid complicating side effects in iatrogenic manipulations, so preventive measures to reduce the incidence of infection must never be omitted.

### References

Prevalence of allergic respiratory diseases in patients with RA

The balance between Th1 and Th2 cell activity is crucial in many autoimmune disorders. It has been suggested that rheumatoid arthritis (RA) is Th1 cell predominated, whereas atopic diseases are Th2 cell directed. Some recent observations of a decreased presence of atopy in patients with RA have received a lot of attention. It has been suggested that a Th2 cell related disorder such as atopy might have a protective role against the onset of a Th1 cell mediated disease such as RA, and the biological importance of the Th1/Th2 paradigm has been emphasised.

We evaluated the prevalence of atopic respiratory diseases in 126 consecutively observed outpatients from the American College of Rheumatology (ACR) criteria. The prevalence of allergic respiratory diseases was investigated in all patients by an exhaustive interview and the administration of a diagnostic questionnaire. Skin prick tests were made according to the EAACI guidelines, with a panel including the most common airborne allergens of our area. A diagnosis of allergic rhinitis was made in 21 patients (16.8%). The diagnosis was based on a suggestive clinical picture associated with the positivity of skin prick tests. Seven of 21 patients also had symptoms of asthma and 3/21 had undergone specific immunotherapy before the onset of RA symptoms. In 20/21 patients allergic respiratory symptoms had started before the onset of RA symptoms. In 5/21 patients atopic symptoms had totally disappeared by the time of this study. Patients with RA with associated atopic disease did not differ from other patients with RA in the following characteristics: (a) sex (76.2% female v 75.2%); (b) positivity of rheumatoid factor (71.4% v 63.8%); (c) presence of subcutaneous noduli and/or other extraarticular manifestations (14.3% v 21.9%); (d) functional class according to the ACR revised criteria (class I-II: 64% v 60%); (e) current treatment with two or more disease modifying antirheumatic drugs in combination (57.1% v 60.9%); (f) current steroid treatment (57.1% v 54.3%). Notably, most patients from both groups (90.9% v 76.8%) were taking steroids at a low dose—namely, not more than 5 mg daily of prednisone, when they were evaluated for this study.

Patients with atopic diseases were younger (mean age 53.8 v 57.5) and had a shorter average duration of RA (4.5 v 9.7 years) than those without. We found a rather high prevalence of allergic respiratory diseases in our patients with RA (16.8%), comparable with that expected in the general population. Moreover, the presence of atopic disease did not seem to influence the severity of RA.

The difference between our data and other reports could be due to the methods used to determine the presence of atopic diseases. Those other studies started from the administration of standardised questionnaires to patients with RA and this method might have caused an underestimation of atopic symptoms. Conceivably, prolonged steroid treatment, as well as the systemic symptoms and disability associated with RA, may often cause occult symptoms of rhinitis and asthma that only emerge at deeper analysis.

In conclusion, our data question the hypothesis of a mutual antagonism of RA and atopy, suggesting caution in interpreting previous data and confirming that things are often not as simple as they can seem at first glance.

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Henoch-Schönlein purpura: a possible complication of hepatitis C related liver cirrhosis

Henoch-Schönlein purpura (HSP) is a systemic small vessel vasculitis predominantly affecting children and, less commonly, adults. Classical HSP includes a tetrads of palpable purpura, arthritis, abdominal pain, and nephropathy. The diagnosis of HSP is based on the presence of any two of the four criteria in the tetrads (87% sensitivity and specificity). Gastrointestinal disease has been recorded in up to 82% of adult patients in one series and is usually self limiting with colicky abdominal pain, but may progress to ischaemic bowel perforation. We present the case of a 63 year old man with HSP, who was admitted to hospital with severe abdominal pain and a skin biopsy demonstrating IgA complexes (fig 1). However, the possibility of hepatitis C associated IgA/C3 mixed cryoglobulinaemia cannot be ruled out despite a negative cryoglobulin screen on two occasions. In this patient an IgA mediated vasculitis may have been the nidus for thrombus formation and abdominal catastrophe. The role of liver cirrhosis in the development of HSP is intriguing. Patients with cirrhosis may develop HSP as a consequence of defective liver metabolism of IgA circulating immune complexes (CICs), resulting in tissue deposition, although this is known to occur without overt vasculitis. Aetiology and paediatric HSP differ in the incidence and severity of renal involvement, with nephropathy and progression to renal insufficiency being greater in adult HSP which is associated with a poor outcome. Gastrointestinal manifestations vary widely and include abdominal pain, nausea/vomiting, intestinal haemorrhage and, rarely, perforation. There have been no large clinical trials in adults with complicated HSP. Corticosteroids used in a series of children have been shown to relieve symptoms, but fail to deal prospectively with the prevention of HSP in complicated cases. Adults respond favourably to corticosteroids and may be managed with short courses of treatment, but corticosteroid may also mask severe abdominal catastrophe.

Several important points can be learnt from this case report:
• Although nephritis is the most important long term prognostic factor in HSP in the short term, gastrointestinal disease can lead to death despite early therapeutic intervention.
• Liver cirrhosis secondary to hepatitis C may precipitate development of HSP or mixed cryoglobulinaemic vasculitis through the defective metabolism of CICs.
• Given the increasing incidence of hepatitis C related liver disease worldwide, the association of these diagnoses and the clinical implications should be considered more often.

Acknowledgement
We thank Drs Karen Stout, Brett Sheppard, Amy Howard, and Sandhya Venugopal for their participation in, and discussions about, this case.
immunofluorescence study showing granular skin biopsy from a purpuric lesion. Direct

Table 1 Significant laboratory values on the day of admission

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient's values</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/l)</td>
<td>114</td>
<td>135–175</td>
</tr>
<tr>
<td>White blood cell count (&lt;×10⁹/l)</td>
<td>14000</td>
<td>3.4–10</td>
</tr>
<tr>
<td>Platelet count (&lt;×10⁹/l)</td>
<td>130</td>
<td>0.15–420</td>
</tr>
<tr>
<td>Complement C3 (mg/l)</td>
<td>400</td>
<td>880–2030</td>
</tr>
<tr>
<td>Complement C4 (mg/l)</td>
<td>&lt;100</td>
<td>160–470</td>
</tr>
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<td>Serum creatinine (µmol/l)</td>
<td>88</td>
<td>70–110</td>
</tr>
<tr>
<td>Alkaline phosphatase (U/l)</td>
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<td>35–105</td>
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<td>Aspartate aminotransferase (U/l)</td>
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<tr>
<td>Alanine aminotransferase (U/l)</td>
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<tr>
<td>Lactate dehydrogenase (U/l)</td>
<td>176</td>
<td>110–205</td>
</tr>
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<td>Total bilirubin (µmol/l)</td>
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<td>4–20</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>13</td>
<td>36–52</td>
</tr>
<tr>
<td>Urine analysis (RBC/HPF)</td>
<td>20</td>
<td>0–3</td>
</tr>
<tr>
<td>ANA titre</td>
<td>2/40</td>
<td>&lt;1/40</td>
</tr>
</tbody>
</table>

RBC/HPF, red blood cells/high power field; ANA, antinuclear antibody.

Figure 1 Immunofluorescence staining of a skin biopsy from a purpuric lesion. Direct immunofluorescence study showing granular deposition of IgA in the walls of superficial dermal blood vessels, a characteristic finding in Henoch-Schönlein purpura.

Severe aortic regurgitation in RF positive polyarticular JIA

An 18 year old girl of Moroccan origin with a clear medical history was transferred to the Netherlands in February 1989 because of a two year history of untreated polyarthritis. The disease had pursed a rapidly destructive course, resulting in contractures and ankylosis of hips, knees, shoulders, and elbows and small joint deformation. A diagnosis of juvenile idiopathic arthritis (JIA) polyarticular type, functional class IV was made. No nodules were present. Laboratory analysis at that time showed borderline positive serum rheumatoid factor (RF) 30 IE/ml. Tests for antinuclear antibodies and HLA-B27 were negative. Treatment was started with intensive physiotherapy and intramuscular gold, the latter being replaced by sulphasalazine because of proteinuria. In 1990 she was treated for a unilateral uveitis. In 1992 her right eye was replaced. Until 1993 cardiac examination showed no murmurs and chest roentgenogram was normal.

In November 1995 she was admitted to our clinic in Portland Oregon with a complaint of dyspnea, syncope, and fever. She had a 10 year history of untreated polyarthritis. In 1992 her right eye was replaced.

She underwent surgical replacement of her aortic valve with a Medtronic Hall prosthetic valve. The postoperative course was uneventful. Pathological evaluation of the excised strongly thickened and fibrotic trileaflet aortic valve was performed.

Microscopic findings in one of the rheumatoid leaflets showed granulomatous tissue with lymphoplasmocellular infiltration and some polymorphonuclear cells around two areas of fibrinoid necrosis surrounded by a palisade of histiocytes (figs 1 and 2). These findings are similar to the description of a developed typical rheumatoid nodule.

At follow up after four years the aortic valve prosthesis still functions well and the patient has no cardiac signs and symptoms.

To our knowledge, this case is the first illustrated report of typical rheumatoid nodules found in an aortic valve removed owing to aortic valve insufficiency in a patient with polyarticular JIA. Our patient never had any nodules on other locations. Valvular disease is rare in patients with JIA and consists of valvulitis with a substrate with non-specific respiratory distress and increasingly frequent attacks of angina pectoris. Her heart rate was 84 beats/min with a blood pressure of 160/0 mm Hg. A grade 3/6 systolic ejection murmur that radiated into the ascending aorta was heard over the cardiac apex as well as a grade 3/6 early diastolic decrescendo murmur over the left sternal border. A pericardial friction rub was not present. Examination of the carotid arteries disclosed a murmur and palpable thrill on both sides. An electrocardiogram showed left ventricular hypertrophy and the chest radiograph slightly cardiomegaly. An echocardiogram demonstrated left ventricular dilatation (65 mm; normally <55 mm) and an abnormally thickened aortic valve. Colour Doppler echocardiography showed severe aortic regurgitation, a pressure gradient over the aortic valve (maximum pressure gradient 38 mm Hg, mean gradient 24 mm Hg), and diastolic back flow in the abdominal aorta. The diagnosis aortic valve insufficiency and secondary angina pectoris was made.

The disease had pursued a rapidly destructive course, resulting in contractures and ankylosis of hips, knees, shoulders, and elbows and small joint deformation. A diagnosis of juvenile idiopathic arthritis (JIA) polyarticular type, functional class IV was made. No nodules were present. Laboratory analysis at that time showed borderline positive serum rheumatoid factor (RF) 30 IE/ml. Tests for antinuclear antibodies and HLA-B27 were negative. Treatment was started with intensive physiotherapy and intramuscular gold, the latter being replaced by sulphasalazine because of proteinuria. In 1990 she was treated for a unilateral uveitis. In 1992 her right eye was replaced. Until 1993 cardiac examination showed no murmurs and chest roentgenogram was normal.

In November 1995 she was admitted to our clinic in Portland Oregon with a complaint of dyspnea, syncope, and fever. She had a 10 year history of untreated polyarthritis. In 1992 her right eye was replaced.
changes of fibrosis and necrosis. Valvular involvement has been described in patients with all types of JIA; the aortic valve being most commonly affected. Valvular disease is associated with severe destructive articular disease.

Furthermore, our case report confirms the possibility of successful mechanical aortic valve replacement in a case of severe progressive aortic valve insufficiency and secondary angina pectoris in a patient with polyarticular JIA.

We recommend regular cardiac appraisal as part of the routine assessment of every patient with JIA. Whenever cardiac murmurs are detected in these patients, echocardiographic assessment should be considered, because if there is valve insufficiency the cardiac function may deteriorate and cardiac surgery may be needed.

Acknowledgments

We are grateful to Dr J van der Meulen, cardiothoracic surgeon, for the surgical description and to Dr AC van der Wal, pathologist, for his pathology specimen evaluation. We thank Dr FM Westerweel, rheumatologist, for allowing us to report on her patient.

References


The presenting symptoms (girdles bilateral and symmetrical stiffness and pain) are accompanied by systemic features (fatigue, weight loss, raised ESR) and the marked improvement after prednisone confirm the diagnosis of polymyalgia rheumatica.

As far as we know this is the first report of pericardial tamponade requiring pericardial drainage in this disease.

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Remission of Behçet's syndrome with TNFα blocking treatment

Goossens et al reported on a patient in whom a remission of Behçet's syndrome was induced with tumour necrosis factor (TNF) blocking treatment. We would like to add our experience in a patient with Behçet's disease associated with rheumatoid arthritis (RA), treated with infliximab (Remicade).

A 47 year old male patient, born in Morocco, living in Israel, was diagnosed 14 years ago with Behçet's disease; he had severe pain in knees, feet, hands, and wrists of hands, feet, and knees. Radiography showed articular bone erosions; rheumatoid factor was positive, with a high erythrocyte sedimentation rate and C reactive protein. In parallel, the patient reported recurrent buccal and genital ulcers two to three times a month with papulopustular skin lesions on the feet. HLA-B5 (51) was positive. There was no eye involvement. A diagnosis of Behçet's disease associated with erosive, seropositive RA was suggested. The patient was treated with sulfasalazine and colchicine without improvement; steroid treatment with auranofin was added. The disease was poorly controlled with progressive erosions in hands, knees, and feet. Later, pulse steroids, methotrexate, azathioprine, and cyclosporin were added serially, either singly or in combination.

In subsequent years he became dependent on steroids and never achieved complete remission. In December 2000 the patient was admitted to hospital with severe active polyarthritis, flexion contractures of the elbows, and an especially swollen left knee with Baker's cyst and severe erosive disease. The patient additionally had buccal and penile ulcers. Because of the lack of response to conventional treatment we decided to treat him with infliximab (Remicade; Schering), a chimeric IgG monoclonal antibody directed against TNF. He received 300 mg intravenously (3 mg/kg) at intervals of two weeks, six weeks, and then every eight weeks. Two weeks after the first infusion the ulcers of mouth, penis, and other skin lesions were already considerably smaller and later disappeared. The polyarthritis improved considerably, except for the left knee, which required total replacement. Infliximab was given with continued colchicine and azathioprine. Our case, as in Goossens' report, suggests that infliximab may have a beneficial therapeutic effect in microscoros and cutaneous lesions as well as...
Fatigue and immune activity in Sjögren’s syndrome

Despite major desiccation of mucous membranes in Sjögren’s syndrome (SS), fatigue is often experienced by patients as the most disabling complaint. Unfortunately, there is no proper treatment available to combat the fatigue in SS. Besides a variety of somatic and non-somatic conditions, increased immune activity has been implicated as a cause of fatigue in autoimmune diseases. If responsible for fatigue in SS, it could serve as a treatment target. The purpose of this study was, therefore, to examine the relation between fatigue and immune variables in SS.

Thirty-six consecutive patients with primary SS visiting our outpatient departments participated in this study. Two control groups were used: a group of 18 patients diagnosed with secondary SS, and a group of 34 non-medicated healthy controls. Diagnoses were used: a group of 18 patients diagnosed with primary SS visiting our outpatient departments

Fatigue was equally raised in patients with both primary and secondary SS, and differed significantly from that of healthy controls. Twenty-one (58%) patients with primary SS scored “high” or “very high” out of the six categories for depression according to the SCL-90 criteria. These depression scores did not significantly differ from the scores in secondary SS patients. Further analysis showed that 79% of the fatigue in patients with primary SS could be explained by depression, total level of immunoglobulins, and thromboocyte counts (p<0.001). Both depression and thromboocyte counts showed a significant positive correlation, whereas levels of immunoglobulins showed a negative correlation.

Though tempting as a treatment target, the immune and inflammatory variables failed to predict fatigue satisfactorily in primary SS. Levels of immunoglobulins showed, surprisingly, a significant negative correlation. Thromboocyte counts showed a significant positive correlation. Although increases in thromboocytes follow the acute phase reaction, no significant correlation between thromboocyte counts and CRP levels were found. A chance association between fatigue and thromboocyte counts as well as immunoglobulin levels seems thus possible. Therefore, the intriguing question whether immune or inflammatory activity is a causative factor of chronic fatigue in SS remains unexplored.

Because no difference in fatigue was found between patients with primary and secondary SS, the presence of another autoimmune disease appears to have no additional effect on the amount of fatigue in SS. In agreement with findings of previous studies, a significant relation was found between the degree of fatigue and the level of depression in patients with primary SS. It is concluded that none of the laboratory variables reflecting immune activity predict fatigue satisfactorily in primary SS. Signs of depression, as present in most of the patients with primary SS, proved to be the most relevant cause of their exhausting fatigue. Therefore we recommend including a psychosomatic approach in the treatment of fatigue in primary SS.

Table 1 Dutch Fatigue Scale. Each item is scored on a 1 to 4 point scale

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Listlessness</td>
<td>1-4</td>
</tr>
<tr>
<td>2. Perceived need for additional energy to finish required tasks</td>
<td>1-4</td>
</tr>
<tr>
<td>3. Verbalisation of an unmitting and overwhelming lack of energy</td>
<td>1-4</td>
</tr>
<tr>
<td>4. Inability to restore energy, even after sleeping</td>
<td>1-4</td>
</tr>
<tr>
<td>5. Increase in rest requirements</td>
<td>1-4</td>
</tr>
<tr>
<td>6. Decreased libido</td>
<td>1-4</td>
</tr>
<tr>
<td>7. Inability to maintain usual routine</td>
<td>1-4</td>
</tr>
<tr>
<td>8. Impaired ability to concentrate</td>
<td>1-4</td>
</tr>
<tr>
<td>9. Decreased performance</td>
<td>1-4</td>
</tr>
</tbody>
</table>

References

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wise men of steroid research, describes the history of the glucocorticoids graphically and in detail. He has enriched research in this field with significant contributions since the beginning of the 1960s and now looks back amusingly and expressively on the past decades. Luca Parente's contribution ranges from naturally occurring to synthetic glucocorticoids and their effects in the organism. The sections that deal with the desired anti-inflammatory/immunomodulatory effects and adverse reactions give a valuable overview.

A few chapters should be highlighted that are of particular interest for both rheumatologists and clinical immunologists. That on molecular and cellular aspects of cytokine regulation by glucocorticoids has been prepared very carefully from a didactic point of view. It not only describes T cell activation and the effect of glucocorticoids thereon, but also provides useful information for an understanding of the function and regulation of cytokines. It is recapitulated that the central therapeutic effects of glucocorticoids are ultimately the inhibition of the synthesis of interleukin 2 and interleukin 6; glucocorticoids influence the transcription of around 1% of all genes! However, they also have an influence on the translational and post-translational mechanisms by which proteins are synthesised, processed, and exported from cells. This fact applies, in particular, to the influence on cytokine metabolism. Just to mention a few key concepts: post-transcriptional, translational, and post-translational mechanisms; modulation of cytokine receptors; indirect effects that occur as a result of the extensive interactions among various cytokines.

The chapter written by John Kirwan is worth reading for the rheumatologist, as it deals with the clinical aspect of the systemic administration of glucocorticoids in chronic inflammatory arthritis (typified by rheumatoid arthritis (RA)), in vasculitis episodes typified by those in systemic lupus erythematosus, and in polymyalgia rheumatica and temporal arthritis. It is clearly written, because it questions apparently known facts, especially taking the example of RA. The important very short term anti-inflammatory effects are accepted and are broadly exploited. But is the risk/benefit potential also positive for medium and long term treatment? Do the glucocorticoids perhaps have a much more fundamental influence on the development and progression of RA than previously thought? Is there a differentiated and even treatment-time-dependent influence on synovitis, on the one hand, and on radiological progression, on the other? Possible answers to these exciting questions will not be anticipated here. However, this chapter, in particular, can be recommended, broadening as it does our picture of reality that is sometimes restricted to standard viewpoints.

The non-expert in the field might have wished for a little more clarity occasionally in the illustrations. The references to the individual chapters take into account publications up to and including the year 2000. Overall, this is a good example of how knowledge on established drugs such as the glucocorticoids can be clearly updated.

F Buttgerit

FORTHCOMING EVENTS

Tenth Intensive Applied Epidemiology Course for Rheumatologists
11–15 Mar 2002; Manchester, UK
No previous experience in epidemiology is needed. The course is residential and limited to 25 places
Contact: Ms Lisa McClair, ARC Epidemiology Unit, University of Manchester, Oxford Road, Manchester M13 9PT, UK
Tel: +44 (0)161 275 5993
Fax: +44 (0)161 275 5043
Email: Lisa@fs1.scet.man.ac.uk

OMERACT VI
11–14 Apr 2002; Brisbane, Queensland, Australia
Includes two modules: MRI and economics; and five workshops: patients' perceptions, imaging (healing), progressive systemic sclerosis, mean clinical important difference, and osteoarthritis
Contact: Conference Organisers Q2Q, 7 Swan Street, Old Iswoolth, Middlesx TW7 6RJ, UK
Fax: +44 20 8569 9555
Email: q2q@q2q.co.uk

British Society for Rheumatology XIth AGM
23–26 Apr 2002; Brighton, UK
Contact: BSR, 41 Eagle Street, London WC1R 4TL, UK
Website: www.rbmrt.org.uk

4th EULAR Sonography Course
25–28 April 2002; Madrid, Spain
The course is entitled “Practical use of musculoskeletal ultrasonography”
Contact: Esperanza Naredo
Email: enaredo@eresmas.com
Website: www.eular.org/courses and www.saneint.it/eular

10th International Vasculitis and ANCA Workshop
25–28 Apr 2002; Cleveland, Ohio, USA
Contact: Debora J Bork, The Cleveland Clinic Foundation, Desk A50, Center for Vasculitis Care and Research, 9500 Euclid Avenue, Cleveland, OH 44195, USA
Tel: 216 445 8333
Fax: 216 445 7569
Email: borkd@ccf.org
Website for registration and abstract submission: www.clevelandclinicmeded.com/courses/Vasculitis2002.asp

International Congress: New Trends in Osteoarthritis
9–11 May 2002; Milan, Italy
Contact: Organising Secretariat, O.I.C. S.r.l., Via Fatebenefratelli 19, 20121 Milan, Italy
Tel: +39 02 65 71 200
Fax: +39 02 65 71 270
Email: osteoarthritis@oit.it

IOF World Congress on Osteoporosis
10–14 May 2002; Lisbon, Portugal
Contact: IOF Secretariat, 71 cours Albert Thomas, F-69003 Lyon, France
Tel: +33 472 91 41 77
Fax: +33 472 36 90 52
Email: info@ioflyon.org
Website: www.osteofound.org

5th European Conference on Systemic Lupus Erythematosus
26–30 May 2002; Athens, Greece
Chairman Professor HM Moutsopoulos
Contact: Moutsopoulos Congress Organising Bureau
Email: hmoutsp@med.uoa.gr
Email: congress@amphitron.gr

Annual European Congress of Rheumatology
12–15 June 2002; Stockholm, Sweden
Contact: Fred Wyss, Executive Secretary EULAR, Vitikonerasrue 15, CH-8032, Zurich, Switzerland
Tel: +41 1 383 9690
Fax: +41 1 383 9810
Email: eular@bluewin.ch
Website: www.eular.org

10th International Congress on Behçet’s Disease
27–29 June 2002; Berlin, Germany
Contact: Professor Ch C Zouboulis, Department of Dermatology, University Medical Centre Benjamin Franklin, The Free University of Berlin, Fabeckstrasse 60–62, 14195 Berlin, Germany
Fax: 49 30 84456908
Email: zoubbere@zedat.fu-berlin.de
Website: www.usersPages.fu-berlin.de/~zoubbere
15SBD website: www.behcet.ws

Translational Research in Autoimmunity
21–22 Sep 2002; Pavia, Italy
Contact: Organising secretariat: eventi S.R.L., Corso Cavour, 18/20 – 27100 Pavia, Italy
Email: tra@ei20pr.com
Website: www.ei20pr.com
Congress website: www.medicine.ucsd.edu/albani/2001meeting

OsteoArthritis Research Society International (OARSI) World Congress
22–25 Sep 2002; Sydney, Australia
Contact: OsteoArthritis Research Society International (OARSI), 2025 M Street, NW, Suite 800, Washington DC 20036, USA
Tel: +1 202 367 1177
Fax: +1 202 298 3588
Email: osteo@eular.org
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29 Sep–3 Oct 2002; Sicily, Italy
Deadline for abstracts 1 April 2002
Contact: Secretariat, 10th International Congress on Antiphospholipid Antibodies, c/o Kenes International, PO Box 50006, Tel Aviv 61500, Israel
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Fax: 972 3 5140077 or 972 3 5172484
Email: aps@kenes.com
Website: www.kenes.com/aps

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Topics covered will be:
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Website: www.medicongress.com

66th American College of Rheumatology AGM

25–29 Oct 2002; New Orleans, USA
Contact: ACR, Ronald F Olejko, Director of Conferences and Meetings, 1800 Century Place, Suite 250, Atlanta, Georgia 30045–4300, USA
Tel: +1 404 633 3777
Fax: +1 404 633 1870
Email: acr@rheumatology.org
Website: www.rheumatology.org

Third International Meeting on Social and Economic Aspects of Osteoporosis and Osteoarthritis

7–9 November, 2002; Barcelona, Spain
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Fax: 32 4 254 12 90
Email: ypc@compuserve.com

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Severe aortic regurgitation in RF positive polyarticular JIA

I E M Bultink, W F Lems, B A C Dijkmans, R M van Soesbergen and J Lindeman

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