Specialty Conference

Adult Still's Disease—Recognition of a Clinical Syndrome and Recent Experience

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This discussion was selected from the weekly Grand Rounds in the Department of Medicine, University of Washington School of Medicine, Seattle. Taken from a transcription, it has been edited by Drs Paul G. Ramsey, Assistant Professor of Medicine, and Philip J. Fialkow, Professor and Chair of the Department of Medicine.

ERIC B. LARSON, MD, MPH:* Adult Still's disease has been described in the medical literature for years but has been recognized widely by its current name only in the past decade. Interestingly, a case of an *adult* patient with signs and symptoms of Still's disease was reported in *The Lancet* in 1896, one year before George Still published his classic monograph describing a special form of arthritis in children.[1]

From a clinician's perspective, the major problem has been recognizing that the syndrome of adult Still's disease is a nosologic entity that is diagnostically puzzling and, in some patients, disabling. This problem is well illustrated by the fact that in 1975, the last and only time this topic was presented previously at the University of Washington Medicine Grand Rounds, the presenter realized during the preparation of his talk that adult Still's disease was the correct diagnosis of one puzzling case that he had followed for more than ten years. Because recognizing adult Still's disease has been and continues to be a problem, an appropriate beginning is to review the historical evolution of this disease. This review will take us up to the past decade when the disorder gained wider recognition in the literature. The clinical features of adult Still's disease will be shown by reviewing all papers published in English describing two or more patients.[2-9]

Finally, I shall present details of a series of patients with adult Still's disease[10] seen and followed by physicians associated with the University of Washington to illustrate the nature of this puzzling ailment and its outcome.

History

George Still published his monograph, "On a Form of Chronic Joint Disease in Children," in 1897[11] to describe a disease that he felt deserved special recognition. What is today called Still's disease was based on findings in 12 of the 22 cases reported in that article. Of the 22 cases, Still had seen 19 during a brief two-year residency at Great Ormand Street Infirmary, London.

In Still's original description, he attempted to distinguish a form of chronic joint disease in children from rheumatoid arthritis of adults.[11] Areas of distinction included "affection" of the lymphatic glands, splenic enlargement and pyrexia: "In some cases was sudden hyperpyrexia, lasting an hour or two and then subsiding rapidly. . . . The pyrexial periods are not usually associated with any clinically demonstrable exacerbation of the joint trouble, nor indeed is it possible to usually find any definite cause of the fever." He also described pericardial and pleural effusions and a sex ratio of 1.5 female patients to 1 male patient, compared with the 5:1 ratio described by Garrod[12] in adults with rheumatoid arthritis. Still also argued that the disease is different from other diseases affecting joints in childhood, specifically a form of arthritis that he felt was indistinguishable from adult rheumatoid arthritis (six cases) and a form of post-rheumatic fever arthritis consisting of capsular fibrosis of small joints in the hands and feet—so-called Jaccoud's syndrome. Perhaps one of the most striking features of Still's initial description[11] was an omission. Still did not describe the presence of rash, a key feature in the diagnosis of Still's disease today.

Although adults probably had illnesses similar to some of the cases Still described, the subsequent medical literature does not contain descriptions of cases that clinicians for 70 years considered to be adult Still's disease. However, patients with findings of adult Still's disease were included in cases of undiagnosed fever reported by Reimann and de Bardinis in 1949 in a paper on periodic fever.[13] One patient in this series had transient rash, recurrent fever of short duration to 40°C (104°F), mild leukocytosis, lymphadenitis and intense arthralgia and myalgia. These findings suggest the diagnosis of Still's disease. In addition, reports of cases of fever of unknown origin[14-16] include patients who today might be diagnosed as having adult Still's disease, as do some of the classic series describing patients with rheumatoid arthritis.[17] At the

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same time, in the French and German literature there were occasional reports of an illness called "subsepsis allergica,"[18,19] also called "Wissler's syndrome"[20] and later the Wissler-Fanconi syndrome.[21] This syndrome consists of intermittent fever of extreme magnitude, exanthem, leukocytosis and arthritis. Wissler reviewed his experience with the disease in 1916 and described the cases of two patients, aged 44 and 32 years, in a review article of the syndrome bearing his name.[22]

The first use of the term "adult Still's disease" was by Eric Bywaters, the eminent English rheumatologist, in the 1966 Heberden Oration, "What Is Still's Disease?"[23] In his discussion of the features of Still's disease—fever, rash, lymphadenopathy and splenomegaly—he stated that he had rarely seen adults with such features that he would describe as adult Still's disease.

The paper that most convincingly established Still's disease in adults as a distinct syndrome was published by Bywaters in 1971.[4] It describes 14 cases of which 4 had been presented earlier in a descriptive study of the rash in Still's disease. One important point was that Still's disease in children was a distinct disorder sui generis and not merely an age-related form of adult polyarthritis. Therefore, just as nodular, seropositive, erosive rheumatoid arthritis rarely occurs in children, Still's disease or juvenile rheumatoid arthritis rarely occurs in adults. In 1897 Still stated that Still's disease "is an arthritis in children that is distinct from rheumatoid arthritis,"[11] and Eric Bywaters in 1971 declared that Still's disease is a rare occurrence in adults.[4] It is noteworthy that Still reported 12 cases seen during a two-year residency in a single infirmary, whereas Bywaters collected 14 cases of adult patients over 20 years from referral centers at Taplow and Hammersmith in England. Following Bywaters's papers, adult Still's disease has been recognized widely as a clinical disorder. In fact, series of patients with adult Still's disease have been reported with increasing frequency in North American journals since Bujak and co-workers[3] and Fabricant and colleagues[6] reported series in 1973 and a group of French physicians concluded that the cases of adult patients previously diagnosed as having the Wissler-Fanconi syndrome (subsepsis allergica) had the same disease that Bywaters and others called adult Still's disease.[24,25] From the available literature, a reasonable appreciation of adult Still's disease based on extensive clinical descriptions of patients with this disease can now be obtained.

Literature Review of Adult Still's Disease

Eight papers published in English since 1971 containing two or more cases of adult-onset juvenile rheumatoid arthritis or Still's disease[2-9] provide information about the nature of this syndrome. The clinical features of 59 patients are shown in Table 1. There is a slight female predominance (59%), although one series reports only male patients,[3] another all female patients.[4] It is a disease primarily affecting young adults. The mean age of onset was 24.0 years; median age, 22 years.

Fever, especially high fever, was common, as were rash and arthritis. Less common features included sore throat, adenopathy, splenomegaly, serositis and abdominal pain. However, the frequency with which these findings were reported is variable. The key diagnostic findings were the almost invariable presence of fever, rash and arthritis/arthralgia (the "classical" triad), plus additional but nonspecific and nonlocalizing abnormalities that occurred with variable frequencies. Therefore, the literature shows that adult Still's disease resembles the systemic-onset-type of juvenile rheumatoid arthritis or what has been called Still's-type onset.[26]

TABLE 1.—*Clinical Features of Adult Still's Disease**
(N=59 Patients Except as Noted)

Sex	
Male (%)	41.0
Age	
Mean age at onset (years)	24
Onset at 18-35 yr (%)	86.0
Fever	
≥40°C, N=32 (%)	87.5
>39°C, N=18 (%)	94.4
"Fever," N=9 (%)	77.8
Rash	
Still's, N=49 (%)	93.9
JRA, N=10 (%)	60.0
Arthritis (%)	88.1
Sore throat (%)	49.2
Adenopathy (%)	37.3
Splenomegaly (%)	50.8
Pleuritis/pericarditis (%)	32.2
Abdominal pain (%)	28.6
Hepatic abnormalities, N=45 (%)	33.3

JRA=juvenile rheumatoid arthritis

*From Larson.[10]

Recognition of the seminal clinical features of adult Still's disease is necessary to make the diagnosis. The fever is typically high and spiking, usually quotidian and occasionally double quotidian.[27] The spike occurs in the late afternoon or evening. The duration of fever is typically brief, and the temperature subsides rapidly. Temperature swings of 4°C have been reported to occur in four hours or less.[27]

The rash is perhaps the most helpful feature in the diagnosis of Still's disease, especially when present in association with high fever and arthralgias.[24] It occurs with fever, usually in the evening, and is described as evanescent. It is predominantly a truncal rash, but can spread to the arms and legs including the palms and soles, but usually does not involve the face. The typical eruption is a salmon-pink macular or maculopapular rash beginning as small macules that may coalesce. It usually is not pruritic and may be missed, especially since it occurs in the evening and is evanescent. Patients may not notice it. Koebner's phenomenon is usually present and the rash is more prominent in areas subjected to pressure. The major histologic finding is a polymorphonuclear leukocytic infiltrate in the dermis and perivascular spaces.[4,24]

Musculoskeletal symptoms are the other distinctive features of adult Still's disease. Systemic-onset juvenile rheumatoid arthritis has been called "systemic without arthritis"[26,28] because of the frequent absence of arthritis, as described by Still,[11] during the early phase. All patients, however, do have prominent myalgias (especially involving lumbar, cervical and thigh regions) and polyarthralgias about large joints. These are worse with spiking fevers but may persist between spikes. The arthritis, when present, is usually mild, fleeting

and affects only a few joints. The most commonly affected joints are knees, fingers and wrists.[28] Erosions are uncommon during systemic-type disease and most authors report that there is no consistent relationship between articular manifestations and extraarticular, systemic manifestations. The characteristic features of arthritis in adult Still's disease have been described by Elkon and co-workers (descendant from Bywaters's original report)[29] and Medsger and Christy.[9] The most characteristic feature is the development of carpal ankylosis (Figure 1).[9] Typically, patients have evidence of arthritis in the wrist during acute phases of the disease, but this is usually easily controlled with anti-inflammatory agents. Over a 1½- to 4-year period, the condition progresses to nonerosive ankylosis of the carpal bones, especially those bones bordering the capitate. This occurred in 7 of 13 patients in the Medsger series[9] and 10 of 11 patients observed for 7 to 36 years in England (mean age, 20.2 years).[29] Similar ankylosis has been described in the tarsal bones.[30] The British have also described erosive ankylosis at the interphalangeal joints (sparing the metacarpophalangeal joints and with somewhat unusual ankylosis in the distal interphalangeal joints) and ankylosis of the cervical spine.[29] Once ankylosis occurs, at-

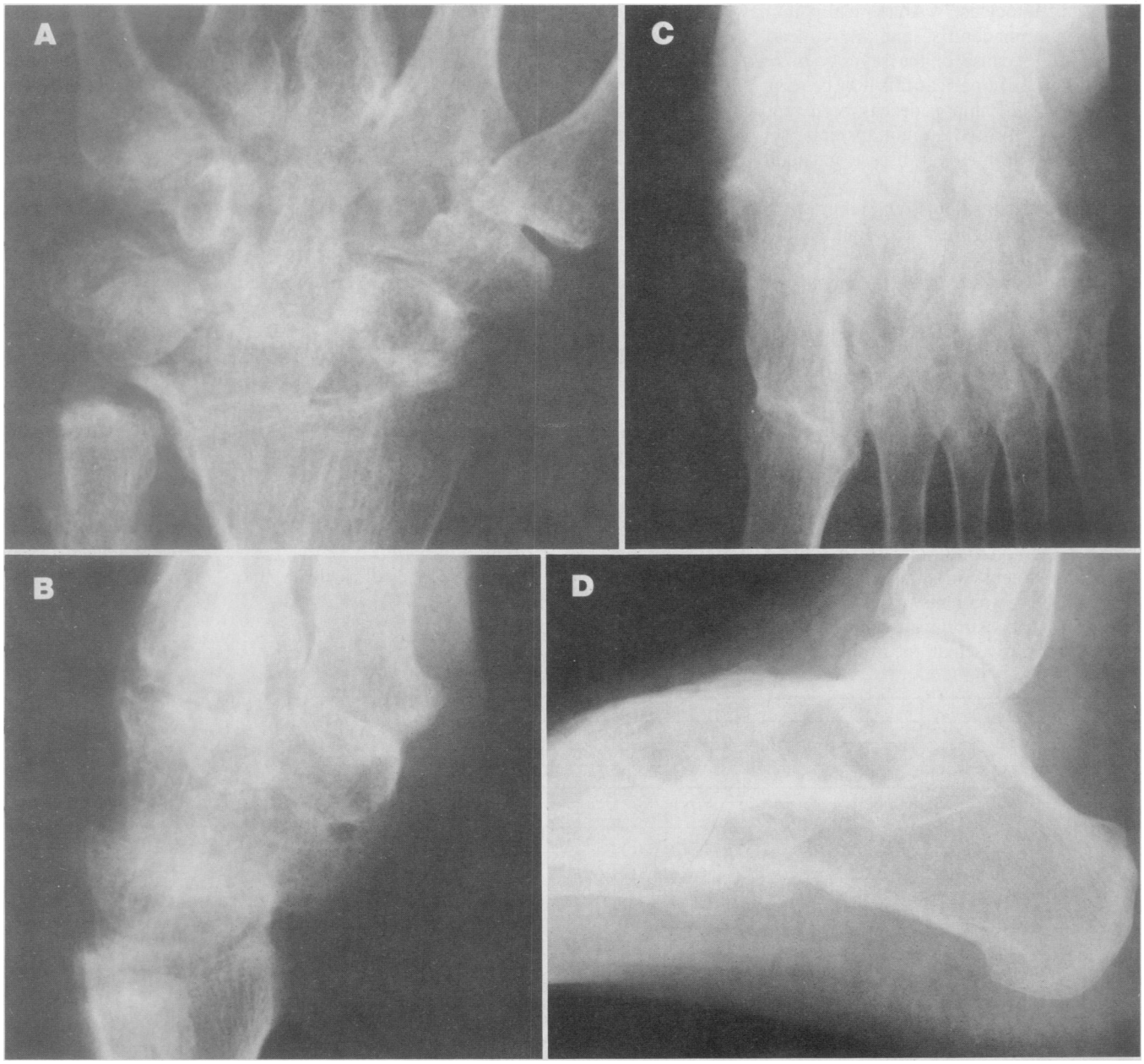

Figure 1.—X-ray films from case 16 with typical changes of adult Still's disease. A, Posteroanterior view of the right wrist shows ankylosis of the radial carpal joint and the capitate-lunate joint. The other joints are narrowed and there are areas of erosion. **B,** Lateral view of the right wrist shows the areas of ankylosis. **C,** Anteroposterior view of the tarsal region of the right foot shows complete bony fusion of all of the visualized joints, including the metatarsal-tarsal area. No remaining joint surfaces are identified, other than a small area between the middle and medial cuneiforms. **D,** Lateral view of the right ankle shows bony ankylosis of the subtalar joint. There is also fusion in the area of the midtarsal joints. There is generalized demineralization of the bony structures, with coarsening of the trabecular pattern. (Courtesy of R. F. Kilcoyne, MD, Department of Radiology, University of Washington.)

tacks of arthritis in that region tend to resolve or be minimal and the patient is usually left with painless decreased range of motion.

The other features of adult Still's disease are not as characteristic as the fever, rash and musculoskeletal findings. Sore throat has been described by many authors and is probably related to the disease, since no pathogens have been identified and antistreptolysin O titers do not rise.[4] The lymphadenopathy, hepatomegaly and splenomegaly are nonspecific. At times, these findings have raised suspicion of lymphoma; biopsy specimens, however, have shown only reactive lymphadenitis and, in the liver, focal aggregation of lymphocytes and leukocytes.[3,4] Abdominal pain may be due to mesenteric lymphadenitis and may lead to exploratory laparotomy because of the severity of pain and peritoneal signs. Pleuritis or pericarditis may be recurrent and disabling and pericardial tamponade has been reported.[31,32] Hepatic abnormalities (raised aminotransferase levels) also occur.[33] One case of chronic liver disease and adult Still's disease has been reported.[34] Acute hepatic and renal failure has been described in two patients with adult Still's disease. Both patients were on a regimen of salicylates and indomethacin; one patient died.[33,35]

Laboratory evaluation of patients with suspected adult Still's disease has focused on excluding other diagnostic possibilities. The most common abnormalities in patients with Still's disease are hematologic: leukocytosis (greater than 15,000 per μl in 80% to 90% of patients); normochromic, normocytic anemia (80% to 90%), and an increased erythrocyte sedimentation rate. Tests for rheumatoid factor and antinuclear antibody are consistently negative. Some patients have elevated immunoglobulin levels. All laboratory findings, however, are nonspecific.

Special studies have not offered a consistent pathophysiologic explanation for the syndrome. Circulating immune complexes were found by a staphylococcal A binding assay but not the C1q assay in patients with acute disease.[29] The histology of skin lesions is similar to nonnecrotizing immune complex vasculitis—perivascular neutrophilic infiltrates associated with mast cells with minimal endothelial damage.[29] British authors have suggested that these findings are consistent with immune complexes being deposited in vessel walls that are rapidly removed by neutrophils, followed by mast cell degranulation, neutrophil lysis and macrophage clearance of neutrophil granules.[29]

The University of Washington Experience

In the past 13 years, 17 patients at the University of Washington have been diagnosed as having adult Still's disease. This series of patients has been reported recently in a review article.[10] Six were from an ongoing series of patients with fever of undetermined origin. The other 11 cases came from records that were kindly provided by a number of people.* The case definition was that of Medsger and Christy[9]: (1) high spiking fever without known cause; (2) arthralgias or arthritis (or both) at some time during the illness; (3) serologic tests normal for rheumatoid factor and antinuclear antibodies, and, in addition, at least two of the following features: leukocytosis, evanescent macular or maculopapular rash, serositis (pleuritis, pericarditis); hepatomegaly; splenomegaly, and generalized adenopathy.

Of the 17 patients, 7 were women. The age at which a patient presented for evaluation to a physician varied from 21 to 68 years; 13 were in the age range of 21 to 32 years, with an overall mean age of 32.7 years. In 10 patients, the reason for evaluation was fever of undetermined origin. In the others, fever was present with other symptoms or had occurred in the past. All patients in whom fever was carefully documented had temperatures above 39°C; the mean temperature peak was 39.8°C. The fever pattern was typically quotidian or double quotidian, with a spike occurring in the late afternoon or early evening (Figure 2).

A past history of febrile illness of unknown cause was of particular importance for diagnosis. Twelve patients had had previous episodes of a febrile illness. Although detailed rec-

*These include Drs Robert Willkens, L. Andrew Healey, Gordon L. Starkebaum, Dick Newton, Woodruff Emlen, Arthur Resnick, Oliver Press, Harvey Featherstone and Dennis Boulware.

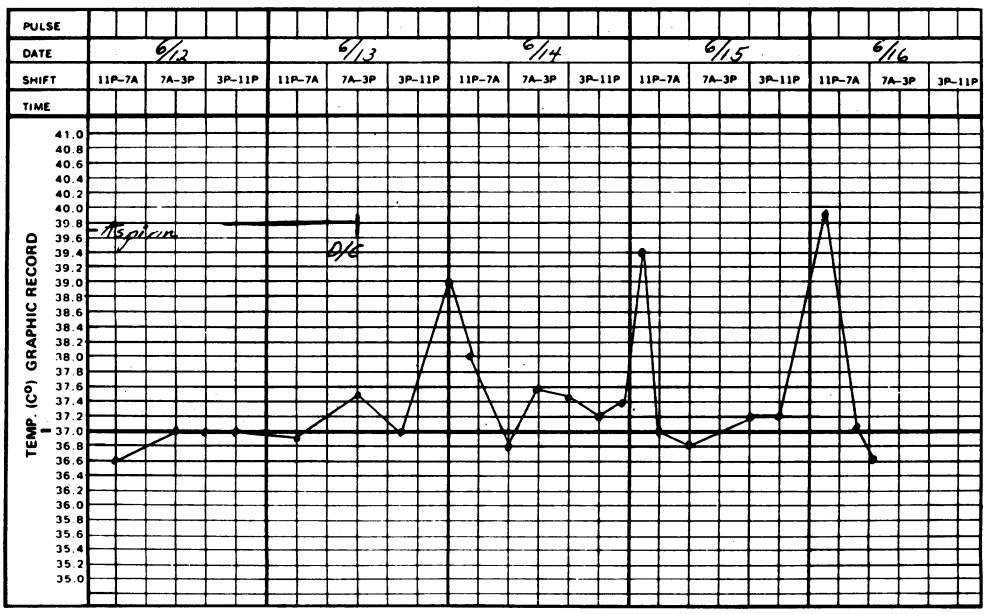

Figure 2.—Fever curve from case 3. After treatment with aspirin (5,280 mg a day) was discontinued, the patient had a spiking fever each evening (quotidian pattern) accompanied by transient rash.

TABLE 2.—*Clinical Features, Treatment and Follow-up of University of Washington Patients**

Case Number	Sex	Duration of Follow-up (yr)	Age at Onset (yr)	Age at Evaluation (yr)	Reason for Evaluation	Initial Clinical Features			Treatment and Response After Evaluation	Subsequent Complications	Treatment and Response
						Musculoskeletal	Rash	Other†			
1 . . .	♀	12	16	26	Fever	Monoarticular hip, arthritis	Present in past	H,S	Afebrile on high-dose ASA	Active, deforming polyarthritis	Corrective operations (hips, knees, hands), ASA, steroids; chronic arthritis
2 . . .	♂	8	17 (FUO)	21	Fever	Pauciarticular	–	L	ASA, steroids caused remission	Sporadic pauciarticular arthritis	ASA, indomethacin controls arthritis
3 . . .	♂	6	20	30	Fever	Pauciarticular arthritis of elbow, wrist	+	L,P	Prednisone 40 mg/d during evaluation; addition of indomethacin controlled attack	Recurrent pauciarticular disease	Indomethacin plus alternate-day steroids for control
4 . . .	♂	3	12 ("Rheumatic fever")	30	Fever	Intense myalgias	+	S,L,P	ASA, prednisone reduced fever	Recurrent pauciarticular disease	High-dose ASA effective; poor compliance
5 . . .	♂	3	49	49	Fever	Intense arthralgias	+	H,S	Initially indomethacin effective, but eventually high-dose prednisone (120 mg/d) required to control fever	Recurrent fever, arthralgias	Does well on alternate-day prednisone, 10-40 mg every other day; ibuprofen controls arthralgias
6 . . .	♂	2.5	28	28	Fever	Arthralgias, shoulder tenderness	+	H,L,P	Indomethacin controlled symptoms	None, illness resolved after 4 mo	No recurrence
7 . . .	♂	2.5	64	68	Fever	Arthralgias of shoulders, wrist	+	S,L,P	Fenoprofen effective transiently; prednisone (40 mg/d) needed for control	Recurrences when prednisone dosage tapered	Alternate-day prednisone most effective; chronic neutropenia without serious infections
8 . . .	♂	1	Uncertain—7, pericarditis; 17, myocarditis	32	Fever, chest pain	Myalgias, muscle tenderness	+	H,S,L,P	Prednisone for pericarditis, fever	None	Alternative-day prednisone currently effective; by history, acute episodes are widely spaced
9 . . .	♀	1.5	44	44	Fever	Intense diffuse myalgia, polyarthralgia	+	S,L	High-dose ASA, indomethacin effective	None	Receiving no treatment
10 . . .	♂	1	24	24	Fever	Pauciarticular arthritis of knee, ankle	+ (Papular)	. . .	High-dose ASA effective	One recurrence 3 mo later	Receiving no treatment
11 . . .	♀	4	42	45	Arthritis	Pauciarticular arthritis of wrist, knee	+	. . .	Outpatient only; NSAID effective	Smoldering polyarthritis	No recurrence of fever after course of gold; requires anti-inflammatory treatment long term
12 . . .	♀	8	Uncertain 12	27	Fever, arthritis	Pauciarticular arthritis of wrist, knees	Present in past	L,P	Indomethacin, prednisone controlled fever	Deforming, erosive polyarticular arthritis	Has had bilateral hip replacements
13 . . .	♂	28	27	29 (in 1955)	Serositis, arthritis, fever	Migratory pauciarticular arthritis	+	L,P	Steroids used in 1955 attack and later	Smoldering polyarthritis, occasionally with fever	Gold effective transiently; taking low-dose prednisone (5-7.5 mg a day) and ASA
14 . . .	♀	4	16	29	Arthritis	Elbow monarthritis	–	L (S age 16)	NSAID effective	Recurrent monarthritis	Various NSAID effective, splenectomy during episode at age 16
15 . . .	♀	3	22	24	Fever, rash	Arthralgias, then polyarthritis	+	H,S,L	Arthritis not helped by anything except steroids	Proliferative polyarthritis	Good response to gold but side effects; taking methotrexate
16 . . .	♂	2	20	27	Arthritis	Pauciarticular arthritis of wrist, MTP joint	?	. . .	NSAID initially effective	Carpal ankylosis, tarsal erosions	Improved with gold therapy; Laotian with scant history
17 . . .	♀	1.5	Uncertain—17, rheumatic fever	24	Arthritis	Monoarticular, then polyarticular arthritis, myalgias	+	L	Sulindac effective; side effects limited to use of ASA	None	Symptoms during 2 episodes controlled with sulindac; decreased ROM in both wrists

ASA=aspirin, acetylsalicylic acid; FUO=fever of undetermined origin; MTP=metatarsophalangeal; NSAID= nonsteroidal anti-inflammatory drugs; ROM=range of motion; –=no, +=yes

*Other details concerning these patients have been published recently.[10]

†H=hepatomegaly, S=splenomegaly, L=lymphadenopathy, P=pleuritis or pericarditis.

ords were typically not available at the time of the evaluation, a patient was usually able to provide enough information to suggest the possibility that the febrile episodes represented earlier attacks of Still's disease. In two patients, the diagnosis was made on the basis of "typical arthritis," without fever or systemic symptoms; both had a history of a Still's-type presentation occurring several years before the diagnostic evaluation.

Arthritis was present at the initial evaluation in 11 of 17 patients. The other six patients had intense arthralgias and myalgias. Other features included rash (14/17), sore throat 6/10), abdominal pain (6/17), hepatomegaly (5/17), splenomegaly (8/17) and adenopathy (11/17). Enlargement of at least one organ of the reticuloendothelial system was present in 13 of the 17 cases. Evidence of serositis was found in seven cases. Common laboratory abnormalities included anemia, leukocytosis, abnormal hepatic enzymes and a rapid sedimentation rate.

The diagnosis of adult Still's disease was eventually made in a *positive* fashion in all cases. Typically, patients received extensive evaluation and often received courses of antibiotics without effect. However, once a diagnosis of Still's disease was considered, it could be made using established criteria, especially when rash was observed or a history of a previous episode was elicited carefully. The consideration that a patient had Still's disease often eliminated the need to consider other illnesses and made the diagnostic workup less tedious. None of the patients had evidence of coexistent bacterial infection; two had positive delayed results on hypersensitivity skin testing for tuberculosis; none had evidence of a reactive arthritis.

Management and Prognosis of Cases of Adult Still's Disease

Evaluating the response to treatment in our patients was complicated by empiric therapeutic trials before diagnosis, dose changes and side effects of anti-inflammatory drugs. The mainstay of therapy was high-dose salicylates. Anecdotes in the pediatric literature describe patients with fever receiving 2.4 grams of aspirin per day who had remission when the dose was increased to 3.0 grams per day.[36] Similarly, in some of our patients a sufficiently high dose seemed to be critical. Salicylate levels should be in the anti-inflammatory range and several authors state that serum concentrations should be at least 25 mg per dl or more before one concludes that giving salicylates is ineffective. Compared with internists, pediatricians seem more likely to use high doses of aspirin and aspirin alternatives like choline or sodium salicylate.

Nonsteroidal anti-inflammatory agents have also been effective. The use of indomethacin, 100 to 200 mg a day given in divided doses, was recommended by Bujak and colleagues in 1973.[3] In the University of Washington patients, one person with fever and systemic symptoms receiving as much as 1 mg per kg per day of prednisone had defervescence and relief of musculoskeletal symptoms only when indomethacin was added to the prednisone regimen. Other newer nonsteroidal anti-inflammatory agents are being used more frequently; fenoprofen, sulindac and naproxen were each effective in relieving fever and systemic symptoms in some patients.

The use of corticosteroids may be necessary to control fever in some patients. Half of our patients were treated with steroids and two required dosages in excess of 100 mg of prednisone per day. These results are comparable to the experience of Bujak and associates[3] in which 60% of patients were eventually treated with steroids, and of Bywaters,[4] who treated 53.8% of his patients with steroids. For most patients, steroids in high daily doses for long periods were not required but side effects including cushingoid habitus, diabetes, infection, acne and osteoporosis have occurred. In our series, several patients experienced possibly avoidable side effects from long-term steroid therapy before the correct diagnosis of adult Still's disease was determined.

A good strategy for minimizing side effects is to administer steroids on alternate days. Bujak and the National Institutes of Health group[3] have recommended a treatment strategy combining high-dose alternate-day prednisone with aspirin or indomethacin coverage in patients whose systemic symptoms are not controlled with nonsteroidal anti-inflammatory drugs. Most patients on alternate-day steroid doses require concomitant treatment with salicylate or another agent for fever. A few patients described in the literature did not have relief of systemic symptoms with high-dose steroids and required cytotoxic therapy.[8] This did not occur in our patients and has been reported by only one other group.[8]

The initial reports of adult Still's disease emphasized the relative benignity of the disease.[3,4,6] The systemic features were controllable and usually lasted for less than six months. Arthritis was said to be mild and less severe than in cases of adult rheumatoid arthritis. However, the disease probably has a more ominous prognosis than originally appreciated.[37] Complications include pericardial tamponade[31,32] and amyloidosis,[38] a well-recognized complication of juvenile rheumatoid arthritis. Interestingly, iridocyclitis is apparently not a problem in adults.[39]

The experience with adult Still's disease in our community is summarized in Table 2. Approximately 20% of patients appear to have self-limited systemic-type disease, although none of these patients has been followed for more than 2½ years. Recurrences or arthritis could still occur in this group. A few patients have systemic recurrence as a major problem. Pauciarticular disease is a recurrent problem with or without sporadic fever in about a third of patients. Salicylates and other nonsteroidal anti-inflammatory drugs are usually effective in this group and steroids are not required or indicated. Finally, in a third of our patients, chronic polyarthritis developed that was asymmetric in 60% of cases; all had negative tests for rheumatoid factor. Some of these patients have received steroids on a long-term basis with the usual side effects, including truncal obesity, susceptibility to infection, osteoporosis and moon facies. Total hip or knee replacement and synovectomies have been required. One patient was recently given a course of methotrexate and acceptable control of symptoms was subsequently achieved with lower doses of prednisone. The follow-up results indicate that in some persons with adult Still's disease, chronic arthritis develops that can be debilitating and resistant to therapy. Similar results have been reported in children with juvenile rheumatoid arthritis.[26,40-43]

Overview

Adult Still's disease has evolved into a well-characterized disease entity. This categorization allows physicians to place

a unifying label on the rare, puzzling case of a patient who presents with a systemic illness characterized by high spiking fever of unknown cause associated with intense arthralgias or arthritis; an evanescent, erythematous macular or maculopapular rash, and other less constant features of systemic illness, including lymphadenopathy, hepatosplenomegaly, sore throat, leukocytosis, anemia and increased concentration of hepatic enzymes. The diagnosis of adult Still's disease is based solely on compatible clinical findings; serologic or other diagnostic tests do not aid in diagnosis. The diagnostic problem presented by these patients with such severe systemic illness and the insecurities inherent in diagnosis based *solely* on clinical features make the availability of the diagnosis, adult Still's disease, useful in patient care.

The cause of adult Still's disease is unknown. Some have speculated that the disease has features of nonnecrotizing immune complex vasculitis.[28] Rubella infection has been associated with adult Still's disease,[44,45] but no definite etiologic relationship has been established. Neither rubella infection nor any other potential antigen has been identified consistently in association with the disease.

Managing patients with the disease depends on establishing the correct diagnosis. The diagnosis should include both recognition of the syndrome and exclusion of other possible diseases. Controlling systemic manifestations may require unusually high doses of aspirin, indomethacin or other nonsteroidal anti-inflammatory drugs, prednisone or combinations of these drugs. Some adults appear to require both high doses of prednisone and indomethacin to control disease manifestations. Fortunately, systemic attacks are usually episodic; steroid toxicity can be minimized by the use of alternate-day dosage and attempts to discontinue steroid use between episodes.

The experience with the University of Washington patients[10] and other reports of long-term follow-up[29,37] indicate that adult Still's disease may be more disabling than was originally reported. At least three patterns of recurrences occur: episodic systemic attacks with or without arthritis, episodic pauciarticular arthritis and disabling, deforming chronic arthritis that may require surgical intervention and long-term anti-inflammatory, gold or cytotoxic therapy.

Progress in adult Still's disease can occur on several fronts. Recognition and diagnosis can be more prompt and efficient; follow-up is often critical for an accurate diagnosis. Understanding the cause of the disease or diseases the syndrome represents is critical because current knowledge is largely descriptive. Finally, therapeutic advances are needed, especially for patients with chronic polyarthritis and its sequelae.

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