MEDICAL GRAND ROUNDS
Parkland Memorial Hospital
December 15, 1966

ANKYLOSING SPONDYLITIS

AND ITS SO-CALLED VARIANTS

*"Having lately seen part of an Human Skeleton, all the bones whereof were so united as to make but one continued Bone without Articulation, I thought it might be acceptable to the Curious to be presented with some Account thereof."**

**Bernard O'Connor, M.D., 1691*

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Case #1: ([redacted] [redacted]

This 44-year old [redacted] male was admitted on [redacted]/58 with a history of back pain which had begun at age 17. This was accompanied by stiffness in the low back with sciatic radiation. At age 20, he had tuberculosis of the right upper lobe which healed. At 27, he was rejected from military service because of his back trouble.

At 29, the patient developed a urethral discharge. This was followed by a four-month episode of acute polyarthritis involving knees, ankles, feet, and hands. The attack subsided, leaving the peripheral joints inactive, and they remained so until the patient's death. Although there was no eye involvement at this time, the patient subsequently had a number of attacks of iritis and the root joints, hips, and shoulders, were painful from time to time. Following the episode of peripheral polyarthritis, the digits of the right hand and the toes of the right foot retained hyperextension deformities. There was also a hallux valgus on this side.

In 1954, the patient developed symptoms of diminished myocardial reserve. Investigation revealed an enlarged heart and evidence of aortic insufficiency. EKG showed occasional episodes of incomplete heart block and Wenckebach phenomenon.

On admission, numerous examinations of the blood pressure showed wide pulse pressure. The patient was stiff but erect. Pupils reacted poorly and there were synechiae bilaterally. Chest wall was completely restricted. The heart was enlarged and a loud diastolic murmur was heard at the base. Hyperextension deformities were present in the right proximal interphalangeal joints and the toes were retracted on the right. There was limitation of abduction of both shoulders and hips. A hallux valgus was present on the right.

Chest x-ray showed cardiomegaly. Erythrocyte sedimentation rate was 65 mm/hr (Westergren). STS, non-reactive. Left heart catheterization showed findings consistent with chronic left ventricular failure.

The patient was considered for surgery to insert a Hufnagel aortic valvular prosthesis, but when Dr. Hufnagel was consulted, he advised against proceeding with the surgery. The patient was discharged on digitalis and diuretics.

The patient was again admitted on [redacted]/59 with complaints of shortness of breath and distension of the abdomen. Blood pressure was 150/50-0. Physical findings were as previously described with markedly enlarged heart and loud diastolic murmur. X-rays of the spine showed typical changes of ankylosing spondylitis. There was also narrowing of the carpal joint spaces on the right. The patient was again discharged without surgery.

On [redacted], 1959, the patient was admitted to [redacted] [redacted] with symptoms of digitalis intoxication. He became semi-comatose. Subsequent course was marked by pneumonitis, urinary tract infection, and finally anuria. Patient died on [redacted]. Autopsy was performed.

At autopsy, the heart was enlarged. The valves appeared to be structurally within normal limits with the exception of the aortic valve which had a rolled, free edge. The main bodies of the cusps were still thin and pliable. There was a small amount of scar tissue at the base of the valves and the junctions were somewhat thickened, although the picture did not suggest severe aortic insufficiency. The left ventricle was somewhat dilated, the coronary vessels were large and showed no evidence of atheroma.

Most of the bone was markedly sclerotic. Sternoclavicular joints on both sides were large, firm, and bony. Cartilages of other joints were described as calcified. The spinal column was considerably more sclerotic than normal. The marrow was gray and showed heavy, bony trabeculation.

Microscopic: Cardiac hypertrophy and perivascular lymphocytic cuffing of blood vessels in the epicardium. Microscopic picture of the valves or of the aorta not described. Liver and spleen were congested. Kidneys showed focal healed pyelonephritis in the cortex, the prostate nodular hyperplasia, and the testicles some atrophy and fibrosis.

Comment: A case of atypical ankylosing spondylitis,with aortic insufficiency, illustrating the tendency of the atypical disease to develop complications.

Case #2: ([redacted] [redacted])

This 27-year old [redacted] male was first seen in [redacted], 1962 with polyarthritis, and a diffuse, psoriatic rash. Illness began in [redacted] 1961, with a penile discharge, mild conjunctivitis, and arthritis in the right knee and hip. After two months, the urethritis and conjunctivitis subsided and he developed a diffuse psoriatic eruption involving trunk, extremities, scalp,

and face, and the lesions of keratodermia blenorrhagica on the soles of the feet. All the nails were involved. With the onset of the rash, he developed multiple small joint (DIP, PIP, and MCP) involvement plus bilateral arthritis of the wrists, elbows, knees, and ankles. The arthritis and psoriasis became progressively more severe resulting in marked deformities and confining the patient to a wheelchair. The course of the disease was unaffected by aspirin or steroid therapy.

ESR was 69 mm/hr (Westergren); slide latex fixation test, negative; subsequently sensitized sheep cell agglutination, LE and antinuclear fluorescence tests also negative.

In [redacted], 1963, the patient was given a course of I.V. methotrexate therapy with moderate improvement in skin lesions and joint pain, but he relapsed within a month and further treatment with methotrexate in two courses over the next year improved the skin lesions slightly, but did not significantly decrease the inflammation in the joints. Throughout this time, he maintained an anemia of 7.0 to 8.0 gms%, unresponsive to iron, folic acid, or vitamin B_{12}. Sedimentation rates ranged between 94 and 146 mm. Latex fixation, sensitized sheep cell agglutination, antinuclear fluorescence, and LE tests were repeatedly negative.

On [redacted] 1964, the patient exhibited a diffuse, psoriatic eruption about the face, trunk, hands, and feet. All nail beds were prominently yellowed and pitted. There was severe polyarthritis involving the ankles, knees, wrists, and elbows with prominent involvement of the distal joints of the hands and feet. Severe flexion deformities of the fingers, elbows, and knees.

Hemoglobin was 7.2 gms; white blood count, 9,750 with 78 per cent polys, 20 per cent lymphocytes, and 2 per cent monocytes; serum iron, 56 mcg%; and total iron binding capacity, 188 mcg. ESR ranged between 82 and 134 mm/hr.

Treatment with 6-mercaptopurine (6-MP) was begun at this time in a dosage of 75 mg/day. Two weeks after onset of therapy, the skin eruption looked less erythematous and the inflammation about the joints began to subside. When seen on [redacted], 1964, some nine weeks after the onset of 6-MP therapy, marked clearing of skin lesions was noted with the beginning of new nail growth. The joints were cool, there were no effusions, and he had gained approximately 10 to 15 degrees of additional extension of the elbows and knees. The dosage of 6-MP was gradually decreased to 50 mg/day. When seen on [redacted] 1965, approximately a year after the onset of therapy, the patient showed no active arthritis or skin lesions. He had gained considerable range of motion in the knees and elbows, and

walked with the aid of crutches. ESR was between 96 and 118 mm/hr.

During the next several months, the patient regained full ambulation and discarded his crutches. Complaints of intermittent epigastric pains, which had been present prior to institution of 6-MP therapy, were investigated and shown to be associated with deformity of duodenal bulb.

About [redacted] 1966, the patient voluntarily stopped taking 6-MP. One month later, he developed an anterior uveitis. This responded to symptomatic therapy. Alkaline phosphatase on [redacted]/66 was 10.2 Bodansky units, and on [redacted]/66, 16.0 Bodansky units. On [redacted]/66, i.e., 8½ months after stopping 6-MP, he complained of a urethral discharge and an erythematous eruption of the groin and perirectal region, with recurrence of psoriatic patches between the fingers. ESR was 39 mm/hr. 6-MP was reinstituted on [redacted]/66 at 75 mg/day. The patient began to improve within a day, and the skin lesions appeared to be resolving when he was seen in the clinic one week after the start of therapy.

Comment: A case of psoriatic arthropathy with features of Reiter's disease, which responded to 6-mercaptopurine therapy.

Table 1
FAMILIAL OCCURRENCE OF ANKYLOSING SPONDYLITIS

Group	*Number*	*No. Cases Ankylosing Spondylitis*	*%*
Relatives	2478	45	1.8
Controls	2486	2	0.08

DeBlecourt, 1963

Table 2
COMPARISON OF RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

	Rheumatoid Arthritis	*Ankylosing Spondylitis*
Male/female ratio	1:3	5:1 to 10:1
Age onset	Variable	15-25
Subcutaneous nodules	25%	None
Valvular lesions	Very rare	Common
X-ray	Osteoporosis	Ossification
Rheumatoid factor	Usually +	Absent
Vascular lesions	+	-
Overlap with connective tissue disease	+	-
Hand involvement	Very common	3%
LE test	11-25%	0%
Different response to radiation, butazolidin and gold salt therapy		

Table 3
AORTITIS IN ANKYLOSING SPONDYLITIS

1. Dilatation of aortic valve ring.
2. Dilatation of sinuses of valsalva.
3. Thickening, shortening of leaflets and rolling of free margins.
4. Partial fusion of commissures.
5. Aortitis in most proximal portion of aorta.

Table 4
PREVALENCE OF AORTIC INSUFFICIENCY IN PATIENTS WITH ANKYLOSING SPONDYLITIS IN RELATION TO AGE, DURATION OF SPONDYLITIS AND PERIPHERAL JOINT INVOLVEMENT

		Patient's Age (Years)			*Duration of Spondylitis (Years)*			
		30	*40*	*55*	*5*	*10*	*15*	*30*
Percentage of Patients with Aortic Insufficiency	In the total series (519 patients)	1.3	3.8	8.8	1.0	1.6	3.5	10.1
	In those with peripheral joint involvement (183 patients)	4.0	8.5	18.3	2.1	3.9	7.9	18.1

Table 5
AORTIC INSUFFICIENCY OF ANKYLOSING SPONDYLITIS

Frequently associated with:

Peripheral joint involvement

Acute non-migratory polyarthritis

Urethritis

Iritis

Table 6
ISOLATED AORTIC INSUFFICIENCY IN ANKYLOSING SPONDYLITIS

	No. Patients	*No. with AI*
Ankylosing spondylitis	519	21
Rheumatoid arthritis	508	3

Graham & Smythe, 1958

Table 7
CARDIAC CHANGES IN RHEUMATOID ARTHRITIS

1. Healed pericarditis - 40%.
2. Minor changes in valves and chordae tendinae - 12% have rheumatic heart disease.
3. "Subcutaneous" nodules in pericardium, myocardium, and valves: true rheumatoid heart disease. Very rare.

Table 8
CLINICAL FINDINGS IN ANKYLOSING SPONDYLITIS

	%
1. Peripheral joint involvement	25-50
2. Acute anterior uveitis	20-25
3. Aortitis	4-10
4. Prostato-vesiculitis	85-95

Table 9
CLINICAL FINDINGS IN REITER'S SYNDROME

	%
Polyarthritis, urethritis	100
Conjunctivitis, uveitis	32-75
Sacroileitis	30-60
Ankylosing spondylitis	20
Balanitis	25
K. blenorrhagica	10-25
Stomatitis	10

Table 10
ANKYLOSING SPONDYLITIS IN REITER'S SYNDROME
(27 cases over 2 years duration; mean 14.5 years)

	No.	%
Bilateral sacroileitis	13	48
Ankylosing spondylitis	8	30

A. E. Good, 1962

Table 11
ARTHRITIS IN INFLAMMATORY DISEASES OF INTESTINES

Disease	*% Polyarthritis**	*% Sacroileitis*	*% Ankylosing Spondylitis***
Ulcerative colitis	15-22	18	2.5-6.4
Regional ileitis	18	20	3.0-6.6
Whipple's disease	67-100	19	?

* 77-95% females
** 67-87% males } in ulcerative colitis and regional ileitis

Table 12
PSORIASIS AND ARTHRITIS

	No.
Psoriatic arthropathy	32
"Indistinguishable" type	66
Coincidental rheumatoid arthritis	20
	118

Wright, 1959

Table 13
SPINAL INVOLVEMENT IN 33 PATIENTS WITH PSORIATIC ARTHROPATHY

	No.	*%*
Sacroileitis	19	57
Ankylosing spondylitis	8	24

Wright, 1965

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