The role of HLA B27 in the diagnosis and management of low-back pain and sciatica

WILLIAM F. BINGHAM, M.D.

Department of Neurosurgery, Gundersen Clinic, Limited, and La Crosse Lutheran Hospital, La Crosse, Wisconsin

Present diagnostic criteria for ankylosing spondylitis (AS) lean heavily on the x-ray examination, but there is much dispute as to its efficacy, especially in mild or early cases. Determinations of the HLA B27 histocompatibility antigen appear to define the population at risk far better than any other means. Of 31 patients who had the HLA B27 antigen, all had negative latex fixation tests and axial polyarthritis complaints (seronegative spondyloarthropathy or rheumatoid variant). Three had Reiter's syndrome and one had ulcerative colitis. Of the remaining 27 patients, nine had definite AS, 11 had probable AS, and seven had possible AS. Eleven of the 27 underwent at least one invasive spinal procedure (myelogram, laminectomy, fusion, facet denervation) before a diagnosis of AS was made.

Key Words • backache • histocompatibility antigen • histocompatibility testing • myelography • spinal fusion • spondylitis • spondylitis, ankylosing

For many years ankylosing spondylitis (AS) was felt to be a rare, stereotyped, and debilitating disease. It is now appreciated that AS is relatively common, protein in symptomatology, and generally mild. Since the initial complaint is usually diffuse low-back pain with or without radiation into the buttocks and lower limbs, accurate and early diagnosis is especially important for the neurological and orthopedic surgeon.

The diagnosis of AS is often missed, or at best delayed, despite a meticulous history, physical examination, and laboratory and radiological work-up. Sciatica is not an uncommon presenting complaint. Some individuals with AS even report an alternating phenomenon in which the pain shifts from side to side with weight bearing. Sciatic paresthesias are typically absent. When the onset is acute and episodic, lumbar disc disease is frequently blamed. When symptoms are precipitated by trauma, the diagnosis is even more obscured. The "classic" physical findings are of little help. A critical analysis of chest expansion, for example, found considerable overlap between AS patients and the normal population. There may also be a disturbing contradiction between symptomatology and physical findings. One patient known to the author, but not included in the present study, has advanced AS with complete obliteration of both sacroiliac joints and an ankylosed lumbar spine. He has been gainfully employed as a carpenter for many years. His only complaint has been occasional, mild, diffuse backache. His underlying condition was discovered accidentally when he was injured at work and was subjected to diagnostic x-ray examination. Various laboratory tests, such as the erythrocyte sedimentation rate (ESR), lack specificity. Even the radiological
examination has many sources of error (see below).

In 1973, two teams researching in tissue transplantation independently reported that 88% to 96% of AS patients were found to have the HLA B27 (formerly W27) histocompatibility antigen compared to 4.8% of persons in a normal population. Two subsequent prospective studies of normal, healthy B27-positive volunteers revealed an increased prevalence of the disease in a subclinical, low-grade, or atypical form. Both studies supported the notion that AS was far more prevalent than previously thought. In view of the diagnostic and therapeutic problems posed by early AS, especially when low-back pain and sciatica are the presenting complaints, a retrospective analysis of our B27 positive population was performed.

**Clinical Materials and Methods**

The study includes the first 145 HLA B27 tests ordered at the Gundersen Clinic/La Crosse Lutheran Hospital complex during the period from April 18, 1975, to September 30, 1976. The first 18 determinations were made by the Tissue Typing Laboratory of the Department of Surgery at UCLA. Most testing was performed with the microdroplet lymphocyte cytotoxicity method; however, a few determinations were made with the newly developed platelet antigen inhibition technique. All subsequent testing was performed by the Immunobiology Research Center in Madison, Wisconsin, using only the former method.

All charts were reviewed by the author. Multiple factors (presenting complaint, sex, occupation, and other historical items; physical examination, especially objective neurological, orthopedic, and rheumatological findings; laboratory and radiographic studies) were analyzed to determine the efficacy of the test compared to traditional means of diagnosis. A diagnosis of definite AS was made when the patient fully satisfied Ogryzlo’s modification of the Rome criteria. A diagnosis of probable AS was made when the disease was strongly suspected but these criteria could not be met fully. In keeping with the epidemiological tenets of the American Rheumatism Association, a diagnosis of possible AS was made when none of the diagnostic criteria could be met aside from a history of low-back pain with associated equivocal physical and radiological findings. Traditionally, the first two categories have been used for clinical investigation and statistical reporting. The third category necessarily includes subjects who may never develop AS.

**Summary of Cases**

Thirty-one of the 145 patients screened had the HLA B27 antigen (Table 1). All had negative latex fixation tests and axial polyarthritic complaints (seronegative spondyloarthropathy or rheumatoid variant). Three of the positive patients had Reiter’s syndrome; an additional patient with this disease did not have B27. This incidence of 75% corresponds roughly to the 63% to 96% positivity reported in the literature.

One B27-positive patient had ulcerative colitis; one B27-negative patient had Crohn’s disease. In 60% to 75% of patients with enteroplastic spondylitis B27 is present.

No patients were encountered with psoriatic spondylitis, Yer- sina arthritis, or juvenile rheumatoid arthritis. All of these diseases are associated with significant B27 positivity.

Several patients had uveitis, another entity with increased B27 positivity, but this was always in association with definite AS or Reiter’s syndrome. No patients with uveitis were encountered who did not have the B27 antigen.

The remaining 27 B27-positive patients thus constituted a population of special interest, namely those persons without evidence of other obvious disease who presented with various combinations of pain in the low back, hips, and lower limbs. These patients are graphically depicted in Figure 1 according to the decades in which they were found to be B27 positive. Multiple data (sex, age at time of B27 diagnosis, occupation, trauma history, presenting complaints, highest ESR, history
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Illustrative Cases

Case 9

This 26-year-old man sustained an anterior wedge compression fracture of the first lumbar vertebral body in an industrial accident in 1970. Over the ensuing 6 years, he had a total of seven plain films taken of the lumbar spine, pelvis, and abdomen for recurrent low-back pain and other medical problems. On the seventh examination, the fifth radiologist to view his films commented upon erosion and widening of the inferior portion of the right sacroiliac joint (Fig. 2 upper right). In retrospect, these changes were present on his initial films (Fig. 2 upper left). Tomograms of the sacroiliac joints showed unequivocal bilateral inflammatory changes (Fig. 2 lower left). His HLA B27 test was positive, and a diagnosis of definite AS was made on the basis of his clinical and radiographic findings.

Case 14

This 34-year-old man first developed low-back pain while working on a construction project in 1964. He underwent a lumbar myelogram and an anterior lumbar discectomy and fusion in 1967. Because of recurrent low-back pain he underwent a repeat myelogram in 1973, followed by an L3–4 and L4–5 laminectomy and bilateral L4–5 discectomy. Six months later he underwent a repeat laminectomy for “removal of scar tissue between L-4,5.” One of the L-5 roots was inadvertently partially severed. A bilateral posterolateral L4–5 fusion was then performed.

In 1976, the patient presented at the Gundersen Clinic with chief complaints of “leg aching, neck pain and stiffness, and back pain . . . usually the back pain is simply a nuisance.” There were no objective neurological findings. Chest expansion was 4 cm; ESR was 1 mm/hr. The Minnesota Multiphasic Personality Inventory was diagnostic of depression. X-ray films of the lumbar spine showed a pseudoarthrosis at L4–5, with erosion of the midportion of the left sacroiliac joint. The HLA B27 test was positive, and a diagnosis of probable AS was made.

Discussion

Present diagnostic criteria lean heavily on the radiological examination.7,8,10–12,14,23 This
is unfortunate since the sacroiliac joints are probably the most difficult ones to interpret radiologically, particularly in adolescent and mild cases. There is no single view which shows all parts of the joint to advantage. There is no commonly accepted system of interpretation of grading. A tendency may also exist on the part of radiologists to underdiagnose AS because of its presumed rarity.

When the radiological criteria for the diagnosis of ankylosing spondylitis are applied in a critical fashion, multiple abnormalities are noted that were previously missed. Calin and Fries found no normal sacroiliac joints in their retrospective study of pelvic x-ray films in 19 "healthy" persons who were B27-positive. This contrasted significantly with only nine of 36 controls with radiographic abnormalities. Cohen, et al., also found a statistically significant increase in sacroiliac abnormalities in their study of 24 B27-positive patients and their matched controls. Of the 23 patients who allowed pelvic x-ray films to be taken, only
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Fig. 2. Case 9. Upper Left: Anteroposterior film of lumbosacral spine taken in 1970. An anterior wedge compression fracture of L-1 is not evident on this view, but erosion and widening of the inferior portion of the right sacroiliac joint are clearly seen (arrow). The left sacroiliac joint is normal. Upper Right: A similar view taken in 1976. There had been minimal interim changes in either joint, but those on the right were first commented upon at this time. Lower Left: Anteroposterior tomographic cut through both sacroiliac joints taken in 1976 showing unequivocal bilateral inflammatory changes (arrows).

nine were free of any cortical breaks, erosions, and sclerosis involving the sacroiliac joints. There were statistically significant differences between the B27 group and their matched controls for bilateral cortical breaks and unilateral and bilateral erosions. Asymmetrical involvement, sometimes only unilateral abnormality, was commonly encountered.

The most disturbing association of the present study was the high incidence of invasive spinal procedures (myelogram, laminectomy, fusion, facet denervation). Eleven of the 27 patients underwent at least one invasive spinal procedure. Three of the 11 had classic sciatica and symptoms suggesting pain of mechanical origin. Their physical and myelographic findings were consistent with lumbar disc herniations. At laminectomy, two patients had extruded discs, and the third had a modest midline disc protrusion. The former two have done well postoperatively. The third remains symptomatic, but she has improved considerably over her preoperative status. Therapeutic plans for two patients (Cases 9 and 12) were altered radically when they were found to be B27-positive. More critical clinical and x-ray assessment resulted in a diagnosis of definite AS in both. No myelogram or surgery was performed, although these were the principal reasons for admission.

Unlike many of the other screening tests, such as lumbosacral spine films, ESR, white blood count, and rheumatoid factor, the HLA B27 test result will not vary. Like a person's ABO blood group the antigen is genetically determined, a single reliable determination suffices. Grahame, et al., found the HLA B27 test to be of little value as a screening technique in the orthopedic clinic. In their survey, the prevalence of B27-positive patients did not differ greatly from that of AS in the parent population. In the author's experience the test has been more useful for inpatients, particularly those for whom invasive diagnostic and/or therapeutic spinal procedures are considered. Case 14 serves as an excellent example. The literature describes many similar diagnostic and therapeutic dilemmas.

To be sure, the patient may harbor both ankylosing spondylitis and a lumbar disc rupture, and he may require appropriate therapy.

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for each condition (Cases 7, 17, and 18). The patient may be one of the 4% to 8% of the normal population who is B27-positive, and effective surgical treatment may even be postponed or declined because of a false-positive result. Similarly, the clinician should not exclude a diagnosis of AS because the test is falsely negative. Results should be interpreted cautiously with the intent of modifying the diagnostic work-up and therapeutic plans if there is reason to believe the patient has AS in one of its protean forms.

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References


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