INTERVERTEBRAL DISK DISEASE CAUSED BY THE BRUCELLA ORGANISM

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BRUCELLOSIS can produce changes in the spine simulating hypertrophic osteoarthritis and the syndrome of pain in the back and sciatica. The condition has been neglected in the differential diagnosis of disk disease and may have gone unrecognized in many obscure cases of pain in the back. The purpose of this paper is to show that spondylitis caused by Brucella infection in man has its origin in a destructive granulomatosis of the intervertebral disk. This theory opposes the belief that involvement of the disk spreads from the bony matrix. The fact that in most cases the pathology in the vertebral body is fully developed together with the disk lesions has precluded the recognition of this alternative explanation, the more so because early localization in the bone marrow is characteristic of the Brucella organism. A recently studied case demonstrates the presence of granulomatous destruction limited to the interbody joint. Radiographic and pathologic evidence from other cases also implicates the disk in the pathogenesis of brucellar spondylitis.

BRUCELLA ORGANISMS AND BRUCELLOSIS

Evans,6 recognizing the similarities in the organisms discovered by Bruce (Malta, 1887) and by Bang (Denmark, 1897), suggested the generic name to honor Bruce, who led the investigation that determined the cause of undulant fever in man. Subsequently the organism recovered from aborting sows by Traum (United States, 1914) was added to the genus. Br. melitensis, Br. abortus and Br. suis share serologic and pathogenic properties, but each has distinct cultural characteristics. All are pathogenic for man as well as dogs, horses, wild animals and fowl. Brucellosis is the most common disease transmitted from animal to man.

The disease is widespread in the United States and Canada, but most cases occur in livestock regions. The acute illness, commonly a mild and vague febrile disturbance, usually is neglected. Only 1,300 of an estimated 30,000 to 40,000 cases22 were reported to the U.S. Public Health Service (1956).26 Serologic evidence of infection in animals, the reservoir for human infections, was found in 3 per cent of 5 million cows in 1951.10

The protean manifestations of the acute illness are ill-defined and include fever, malaise, weakness, pain in the joints, headache and loss of weight. Most infections occur in males; children are resistant to the organism. It is an occupational disease of farmers, meat handlers and slaughter-house workers. The diagnosis is confirmed if serum agglutinates Brucella antigen in a dilution of 1:80 or higher.

The most important route of infection is through the skin;15 the respiratory route is involved in certain instances. Regional lymphadenopathy and a transient bacteremia ensue, the organism eventually assuming an intracellular position in the reticuloendothelial system from which an outpouring of bacteria may persist for years.19 The histopathology of the infection has been thoroughly studied by standard infection of the guinea pig7 and confirmed by bone-marrow studies in humans.14 Characteristic granulomatous lesions in liver, spleen, testi-
cle and bone marrow reach full development in 3 to 4 months.

**BRUCELLA SPONDYLITIS**

Involvement in the spine is characterized by a proliferative sclerotic reaction together with a destructive process involving the articulation of the intervertebral body, distinct in its slow progress, and culminating over months and years in ankylosis of the involved region. Lowbeer has made the most extensive review of the subject of brucellar osteomyelitis and spondylitis in his analysis of the pathology in this complication. Mantle found a paucity of reports in the North American literature dealing singly with brucellar spondylitis and implied that bony complications in England and America are rare. Spink has included the problem of spondylitis in his numerous monographs on brucellosis in America and stated that it occurs in more than 10 per cent of cases.

In the cases of brucellosis admitted to the Royal Victoria Hospital in Montreal the incidence of the complication of spondylitis was only slightly higher than in Spink's experience. Four of 26 patients with serologically proven infections were admitted because of spondylitis. Nine of the 26 had pain in the neck and back as a part of the other symptoms, but no special investigations attended these complaints.

Brucellar spondylitis is a well-recognized entity in areas where the more invasive *Brucella melitensis* is endemic. Zammit reviewing cases from Malta, and Granjon and Mouren, reporting on cases from France, have recently emphasized the importance of the radiographic features.

**Clinical Picture.** The constant feature is pain relieved by rest, localized to the affected region of the spine, occurring late in the convalescent period. Commonly occurring before radiographic signs have appeared, this stage is usually unidentified as being brucellosis, the nature of the initial infection having been neglected. Radiating pain of girdle and extremities is present in more than one-half of the cases. Restriction of motion, muscle spasm, tenderness and signs of nerve-root involvement are common. In severe infections paravertebral abscess may also develop, usually in association with the acute disease (Fig. 1). Extradural compression also occurs.

**Radiological Appearance.** The common feature in numerous illustrations from foreign case reports is participation of the articulation of the intervertebral body. The first conspicuous sign is a step-like erosion of the margin of the vertebral body opposing the disk (Fig. 2, middle). Invariably there is already thinning of the disk and faint osteophytic bridging. Abnormality in the disk is emphasized by Zammit in his analysis of cases in which only 3 failed to show a narrow disk space. The areas of rarefaction in the corners of the opposing vertebral bodies mold themselves by a proliferative sclerotic process into characteristic spurs (Figs. 1 and 2). These assume the form of curved beaks bridging the borders of the interspace and are indistinguishable in chronic cases from the ordinary osteophytes of hypertrophic arthritis. Brucellar spondylitis, however, usually is limited to only one level. In the majority of cases the lumbar region is affected, the next most common site being the thoracic region. Frequent involvement occurs in the cervical vertebrae where the changes are of a similar nature.

**Pathology.** The most important contribution to the understanding of the pathogenesis of brucellar spondylitis has been made recently by Villafane Lastra and Griggs. They obtained specimens of spinal columns from fatal cases in Argentina and correlated the gross pathological changes seen in full sagittal sections with the radiographic appearance. Although they concluded that the infection probably starts in the vertebral body, their specimens show distinct participation of the intervertebral disk in initiating osteomyelitis (Fig. 3). Their photomicrograph illustrates the implantation of infected necrotic disk tissue into the cancellous portion of the vertebral body.

To this pathological study can be added the present case, a patient with pain in the
BRUCELLOSIS OF INTERVERTEBRAL DISK

Fig. 1. Brucellar spondylitis complicated by collapse of vertebral body and abscess. A 71-year-old butcher with radiating girdle pain for 6 weeks. Fever was persistent. Brucella agglutination was 1:10,240.

(Left) Changes in thoracolumbar vertebrae interpreted as hypertrophic spurs. Thinning of disk and osteophytes are typical of brucellar spondylitis. (Right) Two and one-half months later, opposing surfaces of T8-T9 were destroyed and there was early paravertebral abscess. Sclerosis of the osteophyte at T10-T11 is more apparent. Process controlled with spinal fusion.

back and sciatica who was operated upon for protruded disk associated with spondylolisthesis. The surgical specimen shows destructive granulomatosis limited to the nucleus pulposus and collagen fibers of the annulus (Fig. 4). There is microscopic invasion of the cartilaginous plate by islands of granulomatous tissue. Elsewhere in the specimen there is an abundance of undisturbed cartilage. The vertebral body was uninvolved radiographically (Fig. 5) and remained so during a 9-month follow-up period. The circumstance was recognized as an opportunity to confirm infection localized in the intervertebral disk. One of Zammit’s cases also showed radiographically the stage of involvement of the disk without subchondral bony erosion, but lacked the histopathological material that can be included in the present study, a rather typical example of brucellar spondylitis.

CASE PRESENTATION

A 36-year-old dairy farmer was admitted Aug. 2, 1958, incapacitated for 3 weeks with low-back pain and right sciatica. Radiating pain in the leg had been sudden and had followed 6 months of low-back discomfort. At the age of 15 he had injured his back in a fall and had limped for 3 months.

In the summer of 1957, abortive disease first appeared in his herd of 50 to 75 cows. He alone handled the heavily contaminated fetal membranes. Government control of brucellosis in his herd had been under way. In the fall of the same year he was in bed for 3 days with a febrile illness and for the subsequent 2 weeks had mild fever and continued to feel weak.

He exhibited restricted movement of the back and a tender prominent L5 spinous process. On the right there was straight-leg-raising pain,
weakness of gluteals and anterior tibial muscles, a hypoactive ankle-jerk reflex, and marked hypesthesia of lateral thigh, leg and foot. Roentgenograms showed a spondylolisthesis of L5-S1 and a myelographic defect on the right at the same level (Fig. 5). The cerebrospinal fluid protein was 150 mg. per cent.

He underwent operation on Aug. 9, 1958. A small, pale, soft mass was found epidurally in the floor of the canal. The disk was friable and necrotic. A bilateral diskoidectomy was done at the single L5-S1 level through a partial laminectomy. The L5 body was stable and the laminal arch was not excessively mobile.

Microscopic study revealed granulomatous tissue (Fig. 4); subsequently serum-agglutination studies for Brucella were strongly positive at a dilution of 1:640.

In the initial postoperative period the patient’s temperature was elevated every afternoon as high as 102°-103°F. He was given a 2-week course of Chloromycetin and streptomycin and was discharged after a month to continue rest in bed at home. Symptomatically he was relieved and radiographically there had been no progression.

Two months later he was allowed limited activity. Serum agglutinins were positive in a dilution of 1:320. By April, 1959 improvement had continued. Serum agglutination was still positive but now at a dilution of 1:80. Roentgenograms of the lumbar spine remained unchanged.

**DISCUSSION**

Infection in the intervertebral disk may be dependent upon organisms in the reticuloendothelial cells in the marrow of the adjacent vertebral body, invading by way of the perforated bony end-plate, for the adult disk has no blood or lymph vessels. This implies exception to the time-honored concept that the disk, because of accessibility only by osmosis and intercellular lymph spaces, is rarely affected primarily by infection. Perhaps one may assume that in the disk tissue, a metabolic requirement is fulfilled for the
organism to exhibit destructive multiplication. The absence of invasiveness in the marrow reservoir itself where the organism resides intracellularly for years is well recognized in brucellosis. The logic in Schmorl's idea that abnormality in the intervertebral disk is a prerequisite for development of osteophytes in hypertrophic osteoarthritis\textsuperscript{21} lends support to the theory of primary involvement of the disk in brucellar spondylitis in view of the remarkable marginal spur formation which also occurs in this disease (Fig. 1 and Fig. 2). Isolated rarefaction of a vertebral body, as in one of Zammit's cases,\textsuperscript{28} is an exception to the usual pattern of destructive and proliferative arthropathy of the interbody.

If the disk tissue is thought of as being embryonic in its derivation from the notochord, one might reconcile the particular localization in the intervertebral disk with the infectious agent since the \textit{Brucella} organism seems to have a predilection for embryonic tissue. Bacteriologists are aware of the fastidious requirements of growth of the \textit{Brucella} organisms and the suitability of the chick embryo as a culture medium. Other examples of localization in special tissue inherent to the organism are localization in the udder, invasion of the fetal membranes resulting in placentitis in the female bovine, and the orchitis that occurs commonly in the male animal.

\textbf{Fig. 3.} Brucellar spondylitis. Photograph of autopsy specimen showing multiple areas of degeneration and herniation of disks caused by brucellosis. "B" is a Schmorl node resulting from implantation of infected tissue from disk in the marrow of the vertebral body. (Courtesy Villafane Lastra and Griggs and Industrial Medicine and Surgery\textsuperscript{27})

\textbf{Fig. 4.} Present Case. Brucellar spondylitis. (Left) Granulomatous destruction of the disk bordering on the uninvolved cartilaginous plate of the vertebral body. (Center) Early inflammatory involvement of collagen fibers of annulus fibrosus. (Right) Microscopic invasion of cartilaginous plate by islands of granulation tissue. The ragged upper aspect bordered on the destroyed substance of the disk.
It is not known what role hypersensitivity plays in the mechanism of pains in the joints in acute brucellosis. Congestion and swelling in peripheral joints is common in brucellosis, and such a process in the disk might compress nerve roots and explain the radicular pain which is so common during the systemic complaints. Goldfain's cases of a distinct monoarticular arthritis associated with brucellosis and the demonstration of a high percentage of positive Brucella agglutinin reactors among a series of patients with arthritis are of interest in this respect.

Brucellar involvement of the spine is also common in swine. The specimens that Feldman and Olson obtained from slaughter houses show that the involvement, as in man, is in the lumbar vertebrae and centers about the interbody space. Pressure of the spinal cord by the necrotic tissue causes "hind-quarter paralysis."

The present case may also be cited as an instance of infection in a "locus minoris resistentiae," a characteristic of brucellosis. The spondylolisthesis was undoubtedly a pre-existent deformity. This unique property is best exemplified in the case of an abscess which occurred around an old plated femur in a patient who had consumed unpasteurized milk for years. Infections are known to have occurred years after the acute illness in a site of current injury. The dissemination probably stems from the bone marrow where intracellular organisms exist chronically. It is also recognized that brucellar spondylitis is most frequent in the lumbar region, and it is here that degenerative disease of the disk predominates.

Early identification of the infection in brucellar spondylitis and immobilization by rest in bed prevent the complication of a protracted infection. The therapeutic impli-
Pott's disease," simulates. In tuberculosis, on the contrary, the resistance to destruction of the disk and cartilage has been recognized.4,20

SUMMARY

The radiologic and pathologic appearance of advanced brucellar spondylitis suggests that destructive invasiveness begins in the intervertebral disk rather than as an extension from the bony matrix. A case is included in the present report which demonstrates histopathological evidence of destruction of the intervertebral disk, a notochordal derivative, may be explained by the predilection of the Brucella organism for embryonic tissues. Brucellosis may be added to the few entities that cause particular involvement of the intervertebral disk.

REFERENCES

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