ADVANCED ACTINOMYCOSIS OF THE SPINE TREATED WITH PENICILLIN AND STREPTOMYCIN

Report of a Case

M. S. BRETT, LONDON, ENGLAND

From St Mary's Hospital, London

Actinomycosis seldom involves the vertebral column. Only four out of 670 patients with actinomycosis reviewed by Sanford and Voelker (1925) had rib or vertebral involvement. It is clear that in the past the diagnosis has been difficult and that the condition has often been mistaken for Pott's disease. Among the reports of sixty cases of mycosis of the vertebral column Meyer and Gall (1935) found only nine diagnosed correctly before death. The mortality rate was at least 90 per cent.

This case is placed on record because the vertebral column was mainly affected and because of the remarkable response to treatment with penicillin.

CASE REPORT

W. McN., aged forty-two years. Carpenter and part-time fisherman.

History—In 1944 he noticed the gradual onset of a continuous dull aching pain in the right shoulder, which did not prevent him from continuing his work. Six months later a swelling appeared at the back of the right shoulder and increased rapidly in size. He had generalised backache and shortness of breath on exercise. A chronic abscess between the shoulders was treated at the local hospital by drainage and a short course of penicillin (total one and a half million units). Examination of pus on many occasions failed to reveal any specific infection. Radiographs at that time showed evidence of infective changes in the bodies of the third and fourth thoracic vertebrae. There was an opacity in the right upper zone caused by either a paravertebral abscess or a superficial abscess in the soft tissues of the back. During the next two years he attended hospital at intervals and carried on with work whenever possible. Fresh abscesses appeared at the back of the neck and in the lumbar region and required incision and drainage on several occasions. He suffered from as many as eight discharging sinuses at a time. Lassitude, loss of weight, and a slowly developing kyphosis were also noticed, without cough or any other symptoms.

From January to March 1948 he was again in hospital and, although actinomycosis was suspected, no proof was obtained from repeated examinations of the pus. After two short courses of penicillin (total three million and five million units) and a course of 10 per cent iodine solution the sinuses almost healed. A lipiodol sinogram at this time showed an extensive abscess cavity communicating with the sinuses. He was able to return to work but complained of flatulence and increasing shortness of breath on exertion.

In May 1949 he noticed swelling of his ankles and difficulty in walking because of stiffness and pain in the left hip. He also had intermittent diarrhoea and some increased frequency of micturition. He was admitted to St Mary’s Hospital under the care of Mr A. Dickson Wright.

Clinical examination—Extremely ill; very pale, with puffy features. Temperature and pulse normal. Weight 9 st. 2 lb. (128 lb.). There was generalised oedema, particularly in the legs and scrotum. He walked with a limp, and was unable to stand erect because of flexion deformity of the left hip (Fig. 1). On the back, the left side of the neck, and the right side of vol. 33 B, no. 2, May 1951
the chest, there were many sinuses lined by bluish granulations, and many scars at the sites of healed sinuses (Fig. 2). The left hip was held in 80 degrees of fixed flexion. There was marked restriction of hip movements because of pain. The spine showed marked thoracic kyphosis and some lumbar rigidity. The abdomen was distended with ascites. The liver and spleen were not palpable. Radiographs of the spine (Figs. 3 and 4) showed irregular destructive changes in all the vertebral bodies from T.4 to L.1. There was also evidence of new bone formation, most marked on the adjacent surfaces of the vertebral bodies. The intervening disc spaces were slightly narrowed. There was a cavity in the upper posterior part of the body of the first lumbar vertebra. Lipiodol sinograms did not reveal any communication between the sinuses on the back and the spinal column. Intravenous pyelogram showed no abnormality of the kidneys. Bacteriological examination—Culture of the watery exudate from the sinuses was negative.

Pu obtained from a fresh abscess was found to contain “sulphur granules,” and colonies of actinomyces were seen during direct examination with the microscope. The organism was grown from the pus by anaerobic culture. It was extremely sensitive in vitro to penicillin and to streptomycin (Figs. 7 and 8); growth was inhibited in anaerobic culture by 0.06 units per cubic centimetre of penicillin and 10 µg per cubic centimetre of streptomycin.

Treatment and progress—Penicillin was given in doses of half a million units twice daily by intramuscular injection, a total of 140 million units being given in twenty weeks. A low-salt and high-protein diet was given, and two pints of blood were transfused.

After two weeks’ treatment the pain in the back had completely disappeared—for the first time in four years. There was a full range of painless movement of the left hip without evidence of any spasm of the psoas muscle. The sinuses on the back were either healed or covered by crusts. But there were still ascites and extensive oedema. After nine weeks’ treatment the oedema was confined to the ankles, and the sinuses were soundly healed (Fig. 9). There was no change in the kyphosis, but the lower spine moved almost fully and without pain.

Fig. 1
Condition before intensive penicillin therapy was begun. Note, in Figure 1, the marked flexion deformity of the left hip and widespread oedema; and in Figure 2, the numerous discharging sinuses.
Radiographs of the spine before intensive penicillin therapy was begun. Note, in Figure 4, the small cavity in the body of the first lumbar vertebra, and the destruction of the intervertebral disc between the tenth and eleventh thoracic vertebrae.

Radiographic appearance six months after the completion of intensive treatment by penicillin and streptomycin. There is evidence of reparative change in the bone with increase in bone density.
Blood agar culture plates showing the sensitivity of anaerobic actinomyces to penicillin (Fig. 7) and to streptomycin (Fig. 8). The "ditch" at the bottom of the plate in Figure 7 contains penicillin solution in a concentration of 50 units per millilitre, and in Figure 8, streptomycin solution in a concentration of 500 micrograms per millilitre. In each plate the streak on the left is staphylococcus aureus (Oxford H.). The central streaks are actinomyces. The streak on the right is streptococcus pyogenes (Milne). All four streaks were made right across the plate from top to bottom. The plates were cultured for twenty-four hours aerobically and for seven days anaerobically. Note that growth has been inhibited near the ditch in each plate, indicating sensitivity to the antibiotic. The actinomyces appear to be more sensitive to the antibiotics than the staphylococcus or the streptococcus, but this is explained by the wider diffusion of the antibiotic by the time the colonies of actinomyces appeared (five days).

### TABLE I

**Results of Special Investigations**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>June 1949</th>
<th>August 1949</th>
<th>February 1950</th>
<th>August 1950</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haemoglobin (per cent)</strong></td>
<td>60</td>
<td>80</td>
<td>105</td>
<td>110</td>
</tr>
<tr>
<td><strong>White blood corpuscles (per cu. mm.)</strong></td>
<td>20,000</td>
<td>10,000</td>
<td>16,000</td>
<td>11,000</td>
</tr>
<tr>
<td><strong>Plasma proteins (gm. per cent)</strong></td>
<td>4.1</td>
<td>4.4</td>
<td>5.7</td>
<td>5.1</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.9</td>
<td>1.8</td>
<td>2.7</td>
<td>3.5</td>
</tr>
<tr>
<td>Globulin</td>
<td>3.2</td>
<td>2.6</td>
<td>3.0</td>
<td>1.6</td>
</tr>
<tr>
<td><strong>Blood sedimentation rate (mm. per hour)</strong></td>
<td>64</td>
<td>45</td>
<td>32</td>
<td>30</td>
</tr>
<tr>
<td><strong>Urine:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin Casts</td>
<td>+ (0.9 gm.%)</td>
<td>+ (0.5 gm.%)</td>
<td>+ (0.5 gm.%)</td>
<td>+ (0.5 gm.%)</td>
</tr>
<tr>
<td>Many hyaline and granular</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood urea (mgm. per cent)</td>
<td>26</td>
<td>45</td>
<td>32</td>
<td>50</td>
</tr>
<tr>
<td>Urea concentration test</td>
<td>1.0, 1.2, 1.4%</td>
<td>2.1, 2.0, 2.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congo red test (percentage absorption in one hour)</td>
<td>44</td>
<td>47</td>
<td>29</td>
<td></td>
</tr>
</tbody>
</table>
Since the organism was very sensitive to streptomycin it was decided to give a three weeks' course of this drug (0.5 grammes twice daily) despite the great benefit that had already been gained from penicillin. At the end of the course of streptomycin—that is, twelve weeks after the beginning of penicillin therapy—the patient was discharged, feeling very well. He had slight oedema of the ankles on exercise but returned to work as a carpenter six months after the beginning of intensive treatment. He received penicillin injections as an out-patient for a further period of three months from March to June 1950 (one million units per day; total eighty million units). He is now able to do a full and strenuous day's work without symptoms. Radiographs one year after the beginning of treatment are shown in Figures 5 and 6; the repeated investigations are shown in Table I.

**DISCUSSION**

**Mode of infection**—It is generally accepted that the organism may enter the body by way of the digestive tract, often through the mucous membrane of the mouth, oesophagus or ileocaecal region (Cope 1938). This case is of particular interest because of the extensive lesion in the spine without neighbouring gross lesions in the thorax or abdomen. There was radiological evidence of a soft-tissue abscess, possibly mediastinal, at the clinical onset of the disease, and a study of the serial radiographs showed regression of this shadow with spread of the disease down the spine. It is probable that the organism entered the mediastinum by penetrating the oesophageal wall and later invaded the spine by direct extension.

**Clinical picture**—The symptoms presented no unusual features. They corresponded closely with those described by Meyer and Gall (1935), namely: persistent pain, recurrent abscess formation and mild deformity, followed later by psoas irritation, shortness of breath and oedema. The patient's condition had deteriorated steadily for four and a half years before the diagnosis was established.

Amyloid disease was suspected because of the presence of anasarca and heavy albuminuria, despite the fact that there was no palpable enlargement of the liver or spleen; it was confirmed by the congo red test (Table I). It is interesting that there has been marked regression of the amyloid condition with great improvement in renal function and restoration of the albumin/globulin ratio to normal coincidentally with the disappearance of the oedema. There was no evidence of spinal cord involvement, described by Dixon (1939).

**Radiographic appearances**—The radiographic appearances in actinomycosis of the spine have been well described by Lubert (1944). In this case the affected vertebrae showed a characteristic mottled appearance from sclerosis around the many small abscess cavities in the bone. The intervertebral discs between the seventh and eighth, and between the tenth and eleventh thoracic vertebrae appeared to have been partly destroyed. This is an unusual happening in actinomycosis, whereas it is frequent in tuberculosis of the spine. It has been recorded by Dixon (1939) and by Lubert (1944). The compact margins of the vertebrae, the pedicles, the laminae and the spinous processes may all be affected by direct spread of the disease and in this case there was radiological evidence of involvement of the ribs and transverse processes. Meyer and Gall (1935) stated that when infection of a vertebra takes place by vascular metastasis the margin of the vertebra is unaffected and cavities are formed in the cancellous bone of the vertebral body. It is tempting to regard the single abscess
cavity in the body of the first lumbar vertebra as a metastasis carried by a spinal vein rather than a lesion produced by direct spread of the disease from the adjacent tissues. Since the beginning of intensive treatment, radiographs at six-monthly intervals have provided striking evidence of reparative new bone formation with return towards a normal trabecular structure of the bone (Figs. 5 and 6).

**Treatment**—There are numerous reports of the success of large doses of penicillin in the treatment of actinomycosis, and it is now of proved clinical value. The importance of continuing treatment until long after the symptoms have subsided has been stressed by Cope (1949). No similar case of extensive actinomycosis of bone treated with penicillin or streptomycin has been found on record in the literature. The sensitivity of actinomyces to penicillin appears to vary considerably (Sanford and Barnes 1949). It is of interest that in this case the organism was very sensitive *in vitro* both to penicillin and to streptomycin. It is also remarkable that the patient did not develop allergic phenomena after such large and prolonged doses of penicillin (220 million units in all).

**Streptomycin**—There have been recent reports of the value of streptomycin in the treatment of actinomycosis but only two have concerned bony lesions—in the jaw and in a cervical vertebra (Costigan 1947, Torrens and Wood 1949). In this case the clinical response to treatment by penicillin was remarkable, but the sensitivity of the organism to streptomycin *in vitro* suggests that streptomycin alone would also have brought about a very great improvement.

**Prognosis**—It is not possible to regard this patient as cured, but it is certain that a very advanced actinomycotic disease process has been, at least temporarily, arrested, and the patient has been changed from a chronic invalid to a normal individual who is able to do a strenuous day's work without symptoms. Watch must be kept for signs of reactivity so that immediate treatment may be given if the need should arise.*

**SUMMARY**

A case of extensive spinal actinomycosis, undiagnosed for nearly five years, responded dramatically to large doses of penicillin, which was later supplemented by streptomycin.

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* Since this report was sent to press this patient has been readmitted (April 6, 1951) with a fresh abscess on his back, slight generalised oedema and early renal failure, for which he is receiving energetic treatment.

I am grateful to Mr A. Dickson Wright for his help and criticism, and for permission to publish this case. I am also indebted to Mr V. Zachary Cope for his interest, to Dr E. Rohan Williams for his help with the radiographs, to Dr G. W. S. Andrews for carrying out the sensitivity tests, and to Dr P. N. Cardew for the clinical photographs. This patient was shown at a meeting of the Clinical Section of the Royal Society of Medicine in February 1950.

**REFERENCES**