Disseminated actinomycosis

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Actinomycosis classically involves the cervicofacial, abdominal or thoracic regions.[1] Recent studies indicate that the site most commonly involved is the abdomen (50-63%), next the cervicofacial region (24-30%), and then the thorax (13-20%). A small number of cases are reported in which the primary lesions are in the skin, bones or other sites.[2, 3] Hematogenous dissemination is thought to be uncommon. It was found in only two of 85 cases of pulmonary actinomycosis reviewed by Bates and Cruickshank.[2] However, Graybill and Silverman,[4] in a recent study of seven cases of pulmonary involvement, found evidence of hematogenous dissemination in three cases.

The case reported here is unusual in that the presenting manifestations were those related to the peripheral secondary lesions.

B.P., a 39-year-old white man, presented complaining of painful, swollen areas on some of his fingers and toes. The history of his illness began six weeks earlier when he had a sudden onset of swelling and pain in the fourth and fifth toes of his right foot. The involved toes became bluish, with scaling and desquamation of the skin. Three weeks after the initial symptoms the patient noted swelling and pain in the pulp space of the distal phalanx of the left index finger. Over the next few days several of the distal phalanges of his right hand were similarly affected. During this six-week period he suffered from malaise, anorexia, occasional chills and fever, and a non-productive cough. He also lost 20 lbs. in weight.

On physical examination the patient was in no acute distress. His temperature was 100.3° F. His teeth were in relatively poor condition. He had a non-tender thyroid nodule measuring 1 cm. in diameter. The tip of the spleen was palpable on deep inspiration. All peripheral pulses were palpable and strong. The pulp spaces of the distal phalanges of all the fingers of the right hand (Fig. 1), the left index finger, and the fourth and fifth toes of the right foot (Fig. 2) were warm, swollen, tender and bluish in colour.

Soon after admission several pustules developed in the involved areas of his fingers and toes. Over the course of several days new lesions developed on the lateral aspect of his left foot, over his left sacro-iliac region and on the lateral aspect of his right thigh. The patient ran a constant temperature of around 100° F. The affected areas of his right hand became increasingly painful, so that eventually he was unable to flex his fingers.

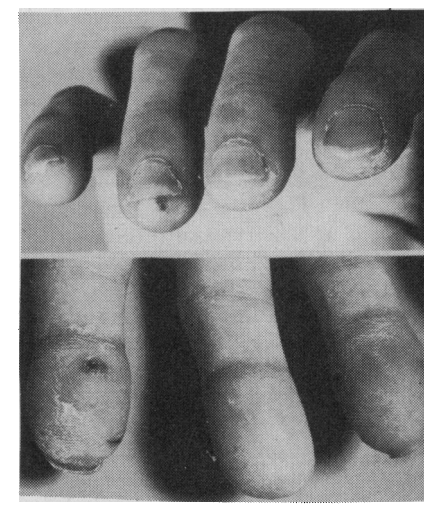

FIG. 1—Photographs showing swelling of the distal phalanges of all the fingers of the right hand. Abscesses can be readily seen on the ring and index fingers.

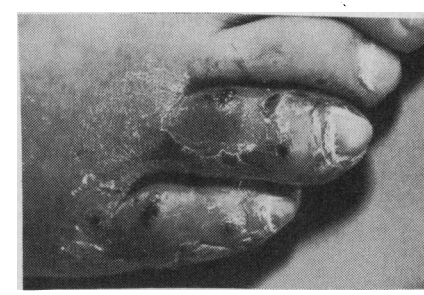

FIG. 2—Lesions on the toes of the right foot showing discolouration and excoriation.

Laboratory tests

On admission the hemoglobin was 11.7 g. per 100 ml., the hematocrit 38% and the leukocyte count 11,600. His corrected erythrocyte sedimentation rate (Westergren) was 30 mm. in the first hour. Blood chemistry estimations were within normal limits. A bone marrow examination was normal. Serum protein electrophoresis was normal. Tests for antinuclear protein and rheumatoid factor were negative, as were fungal and tuberculin skin tests. A chest radiograph revealed several small peripheral lung nodules confirmed by whole lung tomograms. A skeletal survey was normal.

Microbiology

Several specimens of blood, bone marrow, sputum, urine and stool were sent to the laboratory for in-

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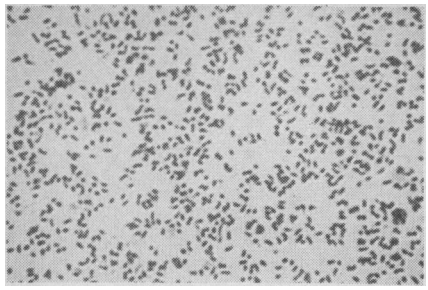

FIG. 3—*A. actinomycetemcomitans* showing the coccobacillary shape. These stain gram-negative (× 1000).

TABLE II
Identification of *A. israeli*

	A. israeli	*A. bovis*	*A. naeslundii*	*Anaerobic diphtheroids*	*Papaleo strain*
Catalase	—	—	—	+	—
Starch hydrolysis	+ or —	+	—	—	±
Glucose	A	A	A	A	A
Xylose	A (20%)	A	A (20%)	—	A
Starch	A (20%)	A	A (20%)	—	A
Glycerol	—	—	—	A	±
Nitrate	+	—	+	+	++

vestigation. Cultures of all of these were negative for bacteria and fungi. All bacterial agglutinations, including those for Pasteurella and Brucella, were also negative. Material was aspirated from the pustules on the fingers; a gram-stained smear revealed no organisms. The fluid was cultured aerobically, anaerobically and in a 10% CO_2 atmosphere. After three days of incubation at 37° C. the aerobic and anaerobic cultures showed no growth. The CO_2-incubated chocolate agar plates showed a light growth of small, smooth, greyish colonies about 1 mm. in diameter. There were fine granules floating in the tryptose broth and the Brewer's meat broth. Gram stains from both the agar colonies and the broths showed gram-negative coccobacilli (Fig. 3). The bacteriological differential diagnosis included Brucella, Pasteurella, Hemophilus and Actinobacillus. The organisms were not agglutinated by Brucella or Pasteurella antisera. Using special strips with X and V factors (Case Laboratories) it was shown that these substances were not required for growth. Two organisms, *A. actinomycetemcomitans* and *H. aphrophilus*, although presently classified in two different genera, are very similar. Their differentiation and hence the final identification of *A. actinomycetemcomitans* in this case was according to the specific cultural reactions seen in Table I.[5, 6] A serum inhibition test was performed with the patient's serum. The growth of the patient's strain of Actinobacillus was inhibited by his own serum in a dilution of 1:16.

On the seventh day another growth appeared in the anaerobic broth (Brewer's meat) in the form of white fluffy balls. Gram-stained smears showed the presence of gram-positive branching rods in addition to the previously identified actinobacilli (Figs. 4 and 5). Cultural characteristics and sugar fermentations identified this organism as *Actinomyces israeli* (Table II).[7, 8]

Sensitivity tests for both organisms were performed. The *Actinobacillus actinomycetemcomitans* was sensitive to tetracycline, streptomycin and chloramphenicol and resistant to penicillin, ampicillin and neomycin. The *Actinomyces israeli* was sensitive to penicillin, tetracycline and chloramphenicol and resistant to streptomycin.

Treatment and course

Streptomycin, 500 mg., was given intramuscularly twice daily, and tetracycline, 500 mg., orally every six hours. The patient became afebrile after four days on this regimen and has remained afebrile since then. The fingers gradually became less tender and the pustules resolved. After three weeks of therapy the pulmonary nodules had decreased in size. He was discharged to his home while receiving 2 million units of penicillin daily, to be continued for a period of three months.

Six weeks after discharge the patient was readmitted for biopsy of the thyroid nodule. At that time there was complete healing of the lesions on his fingers and toes. A radiograph of his chest showed that the pulmonary lesions had also cleared. At operation the nodule was found in the left lobe of the thyroid gland and was attached to the sternothyroid muscle. Microscopic examination revealed a healing granulomatous lesion; no bacteria were evident at this stage.

Discussion

Despite negative sputum cultures, radiological studies suggest that the patient reported here had actinomycotic infection of his lungs. This suggests that the primary site of disease was the lung, and the occurrence of mul-

TABLE I
Differentiation of *H. aphrophilus* and *A. actinomycetemcomitans*

	H. aphrophilus	*A. actinomycetemcomitans*	*Papaleo strain*
SS or citrate	—	—	—
Urea	—	—	—
Gelatin	—	—	—
Indole	—	—	—
H_2S	+	+	(+)*
Lactose	A	—	—
Raffinose	A	—	—
Trehalose	A	—	—
Sucrose	A	—	—
Mannitol	—	A or —	—
Xylose	—	A or —	A
Catalase	—	+	+

*Weakly positive.

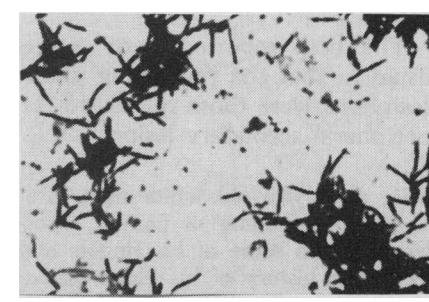

FIG. 4—Mixed culture of *A. israeli* and *A. actinomycetemcomitans* (× 1000).

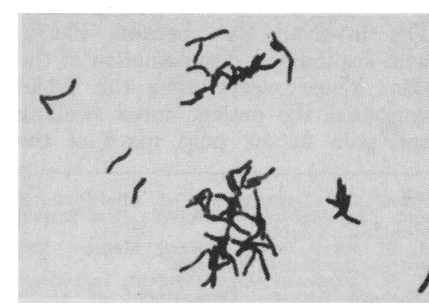

FIG. 5—*A. israeli* in pure culture illustrating the typical branching rods. These are gram-positive (× 1000).

tiple peripheral lesions in the fingers, toes and other sites was a result of hematogenous dissemination from this focus. The granuloma in the thyroid gland was undoubtedly another actinomycotic lesion; the absence of demonstrable organisms was attributable to the antibiotic therapy.

Holm,[9] in a study of material from 650 patients with actinomycosis, concluded that actinomycotic disease was due to a multiple or combined infection with Actinomyces and another aerobic or anaerobic organism. Most human cases are due to *A. israeli*, a normal constituent of the oral flora. Rarely the causative organism is the variety found in cattle, *A. bovis*.[7] Recently a case of thyroiditis due to *A. naeslundii* was reported.[10] Although the accompanying organisms were not all identified in Holm's series,[9] he stated that the second most common organism was *A. actinomycetemcomitans*. The exact role of the Actinobacillus in actinomycosis is speculative. Some believe that it may play some role in the initiation of the infection by making the environment more favourable for the Actinomyces or that it is in part responsible for the dissemination of the disease.[9, 11] In the tissue the role of these organisms would possibly be to reduce the oxygen tension, thus making conditions more suitable for the growth of the Actinomyces.

A. actinomycetemcomitans was, until recently, believed to be only of pathogenic importance in its association with actinomyces. In 1962, King and Tatum[5] reported a study of 32 cases of human infection with *A. actinomycetemcomitans* unaccompanied by Actinomyces. Positive blood cultures were obtained from 25 of these patients.[12] Bacterial endocarditis was diagnosed in 23 of these cases; the other seven cases were of soft tissue lesions.

A. israeli is sensitive to penicillin, and this remains the drug of choice for lesions caused by this organism.[13] Actinomycosis is a chronic disease and is more difficult to treat since it produces a fibrotic tissue reaction. Therefore it is often necessary to use high doses of antibiotics over a prolonged period of time. Treating thoracic cases, Bates and Cruickshank[2] report the use of 10 to 20 million units of penicillin per day for approximately one month, followed by surgical excision of the lesions. Postoperatively the patients are continued on 2 to 5 million units of penicillin daily for one year. For actinomycosis in other sites, 1 to 6 million units of penicillin daily for six to eight weeks appears to be adequate.[7]

Of 37 strains of *A. actinomycetemcomitans* checked for sensitivities by Page and King,[12] all were susceptible to streptomycin, tetracycline and chloramphenicol. However, most strains were moderately resistant to penicillin and ampicillin and quite resistant to methicillin. The studies of Sutter and Finegold[6] revealed similar findings.

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Do biomedical engineering and medical assistants, separately or together, provide the patient the security he may need regarding his state of health, the explanation he seeks for his symptoms, and the basis he requires for rational acceptance of his disease? For all that biomedical engineering may provide, it does not, at present at least, deal empathetically and effectively with personality factors of human beings. Our assistants in medicine do, however. Who are our best assistants? In my life they are my secretary and my wife. An experienced secretary uncannily knows how to schedule patients according to their needs. A good wife may say to her tired husband as he comes home in the evening, "Mrs. Jones called." Her husband asks, "Is she sick?" The wife replies, "Yes, but you can eat your dinner first." He is assured that his wife, who shares his concerns for his patients, has made accurate clinical assessment. He knows also that she would send him promptly on, famished and fatigued, if necessary.—S. P. Asper: *Ann. Intern. Med.*, 73: 325, 1970 (August).