Aberrant form of *Pseudomonas aeruginosa* in sputum and cerebrospinal fluid causing infection in a compromised patient

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**SUMMARY** A patient with non-Hodgkin’s lymphoma developed meningitis due to an aberrant form of *Pseudomonas aeruginosa* observed on Gram stain. The organism was grown on primary isolation media without needing hypertonic media. The significance of aberrant forms in body fluids is discussed.

*In-vitro* changes in the morphology of many organisms by antibiotics is well documented (Lorian and Atkinson, 1975; Klainer and Perkins, 1972; Lorian and Sabath, 1972). Similarly, the identification and significance of organisms grown or isolated only in hypertonic media (bacterial variants known as L-forms or spheroplasts) was recently reviewed by Louria et al. (1976). We describe a patient in whom organisms atypical in appearance and morphology on initial Gram staining were identified subsequently as *Pseudomonas aeruginosa* on routine culture media. The clinical significance of this will be discussed.

**Case report**

The patient, a 60-year-old man, developed painless cervical adenopathy in September 1975. He had had a right orchidectomy for a seminoma in 1963. Postoperatively he received 3000 rads of irradiation to the para-aortic area without evidence of recurrence. Four months before presentation in 1975 he developed a left foot drop, but did not seek medical advice. On admission biopsy of a left supravacular lymph node showed a non-Hodgkin’s lymphoma of follicular type. Treatment consisted of 5000 rads of Cobalt-60 to the cervical, supravacular, and axillary area bilaterally and the upper mediastinal lymph nodes without complications or significant reduction in lymph node size. A second biopsy of an inguinal lymph node was consistent with non-Hodgkin’s lymphoma.

Chemotherapy was begun with cyclophosphamide, vincristine, and prednisone on 11 January 1976. At this time, the patient began to complain of hoarseness of voice and began to have two to three loose bowel movements a day. Throat examination revealed swelling in the arytenoid area. The loose bowel movements continued and a proctosigmoidoscopy on 16 January showed normal mucosa. Stool examination was unremarkable. On 20 January the patient developed dysphagia. A white blood cell count was 300/mm³ (0.3 x 10⁹/l) with a haemoglobin of 8.5 g/dl. Endoscopy on 22 January revealed three to four petechiae in the submucosa of the stomach. One day later his temperature rose to 103°F by mouth. On examination the patient was alert and orientated with a temperature of 103°F, a blood pressure of 110/70 mm Hg, and was in no acute distress. The neck was supple with negative Kernig’s and Brudzinski’s signs. The oropharynx was minimally injected without exudate. The lungs had diffuse bilateral rhonchi with no evidence of consolidation. The remainder of the examination was normal. No new lateralising neurological signs or skin lesions were present. Laboratory examination showed a white blood cell count of 300/mm³, haemoglobin 6.4 g/dl, platelets 27,000/mm³ (27 x 10⁹/l). A lumbar puncture revealed one polymorphonuclear leucocyte but was otherwise unremarkable. Subsequent cerebrospinal fluid blood and urine cultures were negative. Chest
x-ray film showed an interstitial pattern in the right lower lung with calcification of the right pleura which was unchanged from September 1975.

The patient was started on cefazolin 500 mg intravenously every six hours plus gentamicin 60 mg intravenously every six hours. His fever continued, rising to 104°F. Carbenicillin 4.0 g intravenously every four hours was added. Gram stain of the sputum showed a long, filamentous Gram-negative rod (Figure) which on culture grew only *Ps. aeruginosa*. Three to four filamentous Gram-negative rods per high power field were seen. No other organisms were observed. On 27 January an ulcerative lesion developed on the inner aspect of the patient's lower lip. This also subsequently grew *Ps. aeruginosa*. On 29 January the patient became agitated, restless, and incoherent and he had nuchal rigidity with positive Kernig's and Brudzinski's signs. Rales and rhonchi were greatly increased in the right middle lobe area. Chest x-ray film showed a new right middle lobe infiltrate. Repeat lumbar puncture showed a sugar of 78 mg/100 ml, protein 42 mg, polymorphonuclear cells 300/mm³ and red blood cells 40/mm³ (0.04 × 10⁹/l). Gram stain of spinal fluid showed five to six long, filamentous Gram-negative rods per high power field. No other micro-organisms were seen. The stain of the spinal fluid was similar to the Gram stain of the patient's sputum.

The patient died within six hours. Permission for necropsy was not obtained. The cultures of spinal fluid, blood, and sputum were all positive for *Ps. aeruginosa* in 24 hours. Interestingly, the *Ps. aeruginosa* isolated from the cerebrospinal fluid was resistant by Kirby-Bauer disc diffusion to carbenicillin unlike all other *Ps. aeruginosa* isolated from the patient, which were sensitive to carbenicillin. The organism grew on primary isolation media without the need for hypertonic media. Both the biochemical activities and colonial morphology in primary culture were not unusual and on primary isolation media it had lost its aberrant morphology. The *Ps. aeruginosa* was not tested for haemolysin production or serologically tested.

**Discussion**

Infections in patients with underlying disease and altered host defences are difficult to treat. Bacteraemias due to Gram-negative organisms, especially *Ps. aeruginosa*, seem to have an affinity for the compromised host (Freid and Vosti, 1968; Young and Armstrong, 1972). McBride et al. (1976) showed that compromised patients are colonised with Gram-negative bacilli, including *Ps. aeruginosa*. However, not all colonised patients become infected with these organisms even when they are present in the patient's immediate environment.

Al-Dujaili and Harris (1975) have looked at the colony morphology, pyocine typing, and haemolysin production of *Ps. aeruginosa* in the sputum from hospitalised patients and from their environment to try to discover when *Ps. aeruginosa* becomes
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The only factor that was closely associated with the ability to produce infection was the in-vitro production of haemolysin. This was not tested in our isolate of Ps. aeruginosa. Other predisposing factors such as abnormal immunoglobulins and neutropenia that may allow the colonising Gram-negative organism to become infectious are operative in the compromised patient (Tapper and Armstrong, 1974).

The terminology of organisms that are atypical in morphology or which require specialised media for growth is confused. Multiple terms, including 'abnormal form', 'aberrant form', 'L-form', and 'spheroplast' are used interchangeably but have specific clinical or microbiological significance for a particular investigator (Lorian and Atkinson, 1975; Louria et al., 1976; Lorian and Waluschka, 1972). The phrase 'aberrant forms' is the most general term and signifies only bacteria that are atypical in appearance but which will grow on routine culture media. Lorian and Atkinson (1975), Lorian and Sabath (1972), and Klainer and Perkins (1971, 1972) have excellent illustrations of the in-vitro effects of antibiotics on staphylococcus and Gram-negative organisms, primarily the Enterobacteriaceae.

The morphology of bacteria can be altered by a variety of factors, including the culture media used, but the most common cause is the presence of antibiotics. Bacterial appearance can be altered not only by the cell wall-acting antibiotics—for example, penicillins or cephalosporins—but also by agents such as chloramphenicol or nitrofurantoin (Lorian and Atkinson, 1975; Lorian and Sabath, 1972; Klainer and Perkins, 1971, 1972) The mechanism for the production of the abnormal or aberrant forms, which are characteristically elongated, is thought to result from the inhibition of autolytic enzymes that initiate seption (Lorian and Atkinson, 1975). Aberrant forms have been isolated from the urine, cerebrospinal fluid, and in blood cultures (Lorian and Sabath, 1972; Louria et al., 1976; Lorian and Waluschka, 1972; Louria et al., 1969). Our case shows the in-vivo morphological effect of antibiotics on a direct smear from the cerebrospinal fluid and sputum. The appearance was so atypical that the possibility of an anaerobe such as Fusobacterium spp. or Bacteroides spp. was considered.

The aberrant or abnormal forms observed in vivo are in contradistinction to other organisms which require specialised media for growth in the following ways: L-forms are cell-wall deficient and propagate on osmotically stabilising media; protoplasts are usually derived from Gram-positive organisms, lack cell walls, and require appropriate media to grow; spheroplasts are derived from Gram-negative bacteria and usually retain some cell wall but require hypertonic media. Our patient's organism was isolated within 24 hours on routine culture media and did not show the abnormal form on Gram stain in vitro.

In summary, we feel the term 'aberrant' or 'abnormal' forms refer to those organisms that are atypical in morphology on Gram stain; which will grow on routine media; and, as demonstrated by this case, can be clinically significant and initially confusing. 'L-form', 'protoplasts', and 'spheroplasts' should be terms reserved for organisms that require specialised media for growth and identification.

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