# Cutaneous flavobacteriosis — polymorphous skin granulomas from *Flavobacterium capsulatum*

## A case report

G. H. FINDLAY, P. R. HULL, H. E. SMITH, M. M. HENTON


### Summary

A case of multiple eruptive skin granulomas caused by *Flavobacterium capsulatum* is described. The organism was resistant or poorly sensitive to all antibiotics except carbenicillin. Cure was brought about by using maximal doses of this drug. The source of the infection could not be proved, but it dated from an orthopaedic procedure to the elbow which was followed by a chronic cellulitis at the operation site. Since this is an organism known to occur in stored water, it was presumed that the flavobacterium was introduced into the wound from bottles of boiled and cooled water used in the operating theatre.


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This report concerns an unfamiliar clinical condition brought about by an even less familiar organism of the genus *Flavobacterium*.

The flavobacteria live in water. They may multiply in water or watery solutions in many places: natural pool and well waters, plumbing, tap nozzles, shower roses, sink traps, water supplies and purification plants, any reservoirs or stores of water, humidifiers, ice-making machines, disinfectant solutions, multidose vials, etc. They are largely non-pathogenic, and do not survive long on the human skin surface.

*Fl. meningosepticum* is the commonest pathogen. It produces septicaemia with serious lung and brain damage in the newborn, entering the bloodstream through the nasopharynx. Skin rashes do not occur.[1*] In adults it has also caused subacute bacterial endocarditis without skin signs.[2]

*Fl. odoratum* may have been an opportunist pathogen in certain cases of gangrene of the extremities.[3,4] Other flavobacteria have been recovered from clinical specimens and infected material, but they were seldom directly concerned in the clinical condition. They have not been associated with skin eruptions.[5,6] *Fl. capsulatum*, which was recovered repeatedly from embolic skin granulomas in our patient, appears not to have caused disease before.

*Fl. capsulatum* (Leifson, 1962) was first isolated from several sources of laboratory-distilled water in the USA.[7] It has a large capsule, and its general characteristics are summarized by Weeks.[8] Its DNA base composition shows a high guanine-plus-cytosine ratio of 63%,[9] and its ribosomal RNA differs from that of other flavobacteria.[10]

**Department of Dermatology, University of Pretoria**
G. H. FINDLAY, M.D., D.SC., F.R.S. S.AF.
P. R. HULL, M.MED. (DERM.), F.F.DERM.
H. E. SMITH, M.B. CH.B.
**Bacteriology Section, Veterinary Research Institute, Onderstepoort, Tvl**
M. M. HENTON, B.V.SC.

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## Case report

The patient was a 58-year-old housewife who had undergone resection of the head of the right radius after a traumatic fracture. The elbow was otherwise radiologically normal. Thereafter the skin wound had healed but a painful, localized cellulitis had developed at the elbow over the succeeding 3 months, leading to a spotty osteoporosis of the ulna and the humerus in its vicinity, although the remaining radius shaft was unaffected.

We have no proof that flavobacteria were introduced into the elbow during the operation, but several points favour this possibility. Firstly, it was the only discoverable source for the metastatic flavobacterial granulomas which developed subsequently. Before this, she had been healthy, and no infective foci were found after extensive searches elsewhere. Secondly, in the small private nursing home where the operation had been performed, stores of boiled water were used to cool the levers used for elevating the radius and to cool freshly boiled water. The elbow is also a cool site where an organism adapted to room temperature could survive. We therefore suggest that the boiled and cooled water contained the flavobacteria. Thirdly, treatment of the other flavobacterial lesions also cured the elbow lesion, according to clinical and radiological evidence, and remained so for a year afterwards.

Apart from the pain in the elbow after the operation, she suffered over the next 3 months from intermittent fever, headaches, tiredness and lack of appetite, and lost 10 kg in weight. In the same period a series of eruptive spots appeared. These were polymorphic, symptomless, and usually lasted about 10 days each. They occurred mainly on the hands, forearms, feet and legs, with a few over the back. Papules, sheet-like lesions, plaques and invisible deep panniculitic lesions also developed.

The most obvious lesion was a superficial papule (Fig. 1) about 4 mm in size, with a lichenoid outline, occasional haemorrhage, occasional scaling, and a dark central dot. When fresh, these papules were oedematous, with a surrounding flare and a central punctum. They became red-brown and were sometimes elongated in the tension lines of the skin. Some were grouped, linear or confluent, with vague edges, and showed a slight preference for the extensor surfaces of the joints. Some papules on the fingers were tender and suggested Osler's nodes. There were also vague areas of pink-to-brown sheets of skin, possibly representing subsidence of the papular phases. Plaques in the dermis

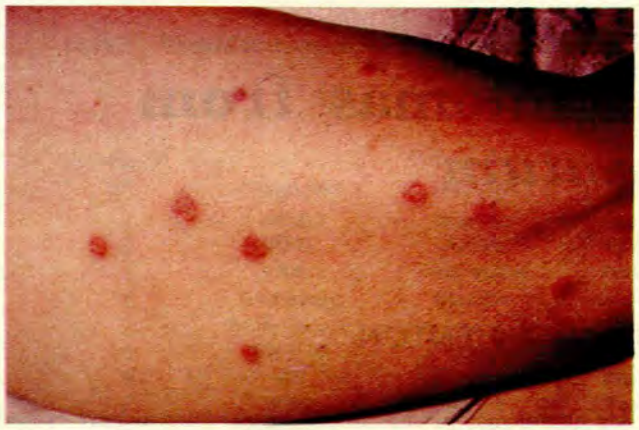

**Fig. 1. Scattered lichenoid papules on the arm.**

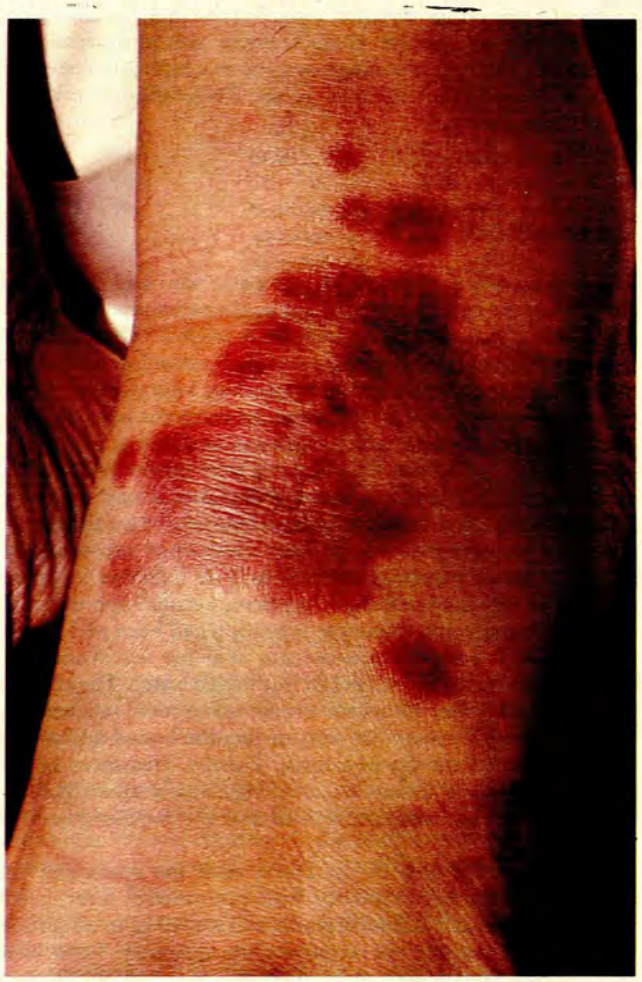

**Fig. 2. Confluent plaques on dorsum of foot.**

attained a size of 10 mm (Fig. 2), with somewhat vague edges. They lay on both surfaces of the hands and fingers, mingled with the papules (Fig. 3). Subcutaneous masses were vague in outline, but also underwent a cycle of eruption and disappearance.

The consistent recovery on culture of material from the lesions of a Gram-negative coccobacillus resistant to almost all antibiotics provided the essential clue to the cause and cure of the condition.

Blood cultures, aerobic and anaerobic, were negative and no organisms were stainable in tissue sections. Fungal and mycobacterial staining and culture of the skin tissues were negative.

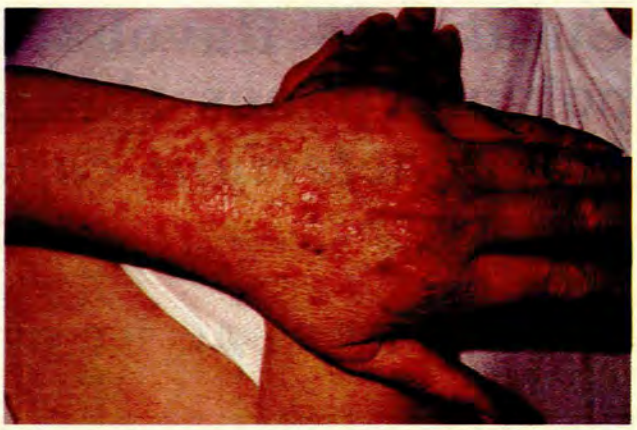

**Fig. 3. Mixture of papules and plaques on dorsum of wrist and hand.**

X-ray and ultrasound examinations of the chest and abdomen were negative; bone scintigraphy showed some isotope concentration in the right carpal and metacarpophalangeal joints, as well as in the ethmoid sinus, which was not thought relevant to the case. Investigation of blood and sputum for various infections was negative. The erythrocyte sedimentation rate was 20 - 30 mm/1st h. Stools, urine, liver function, glucose tolerance curve, muscle enzymes, and serum urea, electrolyte, immunoglobulin, complement and auto-antibody levels and full blood count were normal.

## Microbiological investigations

A Gram-negative coccobacillus was isolated from the skin granulomas on three separate occasions. The identification of this organism proved difficult. From the sensitivity tests it was evident that carbenicillin was the antibiotic of choice, the organism being poorly sensitive or insensitive to other antibiotics routinely tested. A special study of the isolate was therefore undertaken at the Microbiology Section of the Veterinary Research Institute at Onderstepoort.

At room temperature fine grey colonies developed in 24 hours; these enlarged markedly after several days, becoming yellow in a week and brown after several weeks, on blood tryptose agar (Difco), using bovine blood. Growth at 37°C was much slower, colonies becoming visible only after 48 hours. At 5°C and 42°C no growth occurred. The isolate was a Gram-negative, encapsulated pleomorphic rod. The culture was non-motile. Biochemical tests were carried out at room temperature according to standard procedures. Positive reactions were found to phosphatase, cytochrome oxidase, hydrogen sulphide production with lead acetate paper and catalase (weakly positive), and negative reactions to indole, nitrate, urease and phenylalanine deaminase. No liquefaction of gelatine or digestion of Loeffler's agar occurred. The organism grew on Simmonds's citrate.

Using Andrade's indicator in peptone water, a heavy growth occurred with the formation of a yellow pellicle, but the carbohydrates tested were not fermented. These were: glucose, lactose, sucrose, maltose, dulcitol, inositol, adenitol, mannitol, raffinose, xylose, salicin, sorbitol, trehalose, rhamnose, starch, glycerol, mannose, galactose, aesculin. Litmus milk became alkaline and peptonized after 1 month.

The isolate was sensitive (*in vitro*) to erythromycin, novobiocin and amikacin, and markedly sensitive to carbenicillin. It was insensitive to penicillin, streptomycin, clindamycin, bacitracin, polymyxin, colistin, co-trimoxazole, gentamicin and kanamycin.

According to the criteria of Weeks,[8] the isolate was identified as *Flavobacterium capsulatum* Leifson (Fig. 4).

**Fig. 4. *Fl. capsulatum* Leifson. Three groups of the organisms, stained with methylene blue, and a stained antigen-antibody precipitate around the capsule from serum raised in rabbits against this strain (procedure as for *Klebsiella* capsule typing) (x 1 000).**

## Histological findings

Six skin biopsy specimens from various types of lesion showed a similar histological pattern throughout, namely a peri-arteriolar and pericapillary histiocytic granuloma with some endothelial swelling and perivascular thickening, without thrombus formation. The placement of this granuloma corresponded to the clinical picture: there were mini-granulomas near the surface around a cluster of capillary tufts corresponding to the smallest visible pink spots. There was also a sharply demarcated band-like upper and mid-dermal infiltrate in the lichenoid spots. These did not abut directly on the epidermis. In the deeper dermis perivascular granuloma occurred around the candelabra-like ascending arterioles. There was a compact conglomerate of small granulomas in the mid-dermis with arterioles interlacing between them, which corresponded with the 'Osler's node' type of clinical lesion (Fig. 5). Granuloma formation at the cutis-subcutis junction with some fat necrosis caused the panniculitis lesions.

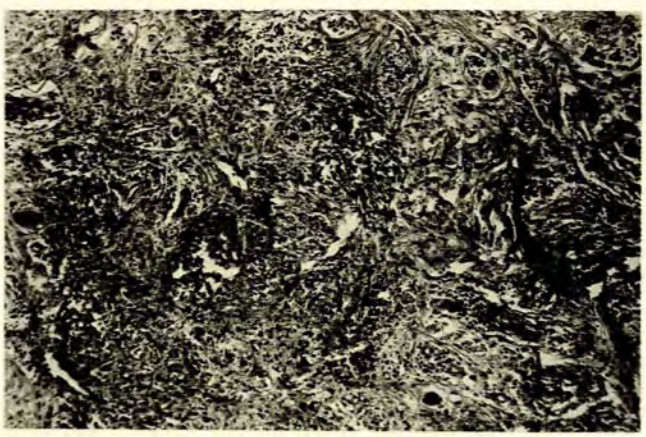

**Fig. 5. Inflammatory reaction in flavobacteriosis. Perivascular histiocytic granuloma in the mid-dermis (x 100).**

The perivascular granulomas contained a loosely packed collection of histiocytes arranged in ascending or horizontal bands and in rounded masses. The cytoplasm was eosinophilic. In the centres of a few granulomas there was a little crumbly disintegration of the cells. There was no caseation, little oedema, few polymorphs and no karyorrhexis. There were signs of mild breaking up and shrinkage of the collagen and haemorrhage in varying amounts. The blood vessels showed endothelial swelling with narrowing of the lumen. No distinct thrombi were seen. Around the granulomas, dilated thin-walled venous and lymphatic spaces were prominent, while in their remote vicinity there were small dense clusters of pericapillary lymphocytes and a few polymorphs.

In areas where scaly lichenoid lesions with upper-dermal band-like granulomas were seen, the overlying epidermis showed necrobiosis of its outer half, with underlying basal layer regeneration and oedema of the papillary layer. The epidermal change comprised karyolysis, a collapse of the cell cytoplasm and at times a shaggy necrosis and disappearance of cells in the outer malpighian and granular layers. There was no spongiosis or production of eczema vesicles. These epidermal changes corresponded exactly to the extent of the underlying granuloma. In the underlying fat there was some foam cell and giant cell production around the granulomas and the associated areas of fat cell necrosis.

## Treatment

Of the antibiotics tested on the cultures, only carbenicillin showed a wide zone of inhibition. Carbenicillin was therefore given for 2 weeks at the dosage advised for adults with normal renal function for severe systemic infections with sensitive organisms. Thus, for the first week, 5 g in 150 ml 5% dextrose-water was given 6-hourly as a side-drip over 30 minutes in an intravenous infusion. Daily serum urea, electrolyte and creatinine clearance determinations and the full blood count showed no abnormality during treatment. Then a thrombophlebitis at the drip site and an extensive purpura developed. For another week carbenicillin was given intramuscularly at a dose of 3 g 6-hourly. The drug-induced purpura then subsided.

On this regimen alone all the skin lesions and the elbow swelling disappeared completely, and remained healed during a follow-up period of 1 year.

## Taxonomy of the pathogen

Reporting our findings on the causative organism to the National Collection of Type Cultures, Colindale, UK, the curator Dr L. R. Hill replied: '. . . we would probably identify this organism as *Pseudomonas paucimobilis*. We have a paper in preparation in which *Flavobacterium capsulatum* results as a synonym of *Pseudomonas paucimobilis*.' If these two names are to be placed in synonymy, we feel justified in adhering to the established name, since their *Pseudomonas* is flagellate and non-encapsulated. First described as a new species of *Pseudomonas* in 1977,[11] its known pathogenicity is at present restricted to a leg ulcer[12] and meningitis.[13] Nothing resembling our case appears to have been seen before.

Because of the remaining uncertainty, Dr Hill kindly examined our cultures. Computer taxonomy in his laboratory based on 68 tests yielded yet another answer: a *Ps. diminuta* (Ref. NCTC 5.5.82; 143/82 Run T1, M624 Lab 5) was diagnosed, but with unusual features. It scored a low value with an organism we had not considered — *Flavobacterium* group II F.

We are reluctant to alter our identification of the isolate, for several reasons: (*i*) its growth under anaerobic conditions (*Pseudomonas* is an obligate aerobe); (*ii*) its non-motility (this difference is acknowledged in the computer study); (*iii*) its capsule (capsulation is not part of *Pseudomonas* identification); (*iv*) its differing reaction to aesculin and McConkey agar (as against *Ps. paucimobilis*); (*v*) its differences on gelatine, in pigment production and motility (as against *Ps. diminuta*).

Further comment appears to be unprofitable at this stage. It is not yet possible to assign a classificatory significance to any given finding. Neither Dr Hill, to whom we are deeply obliged, nor we ourselves wish to regard the identification as altogether final.

## Comment

The clinical picture seen in our patient was that of a bacterial embolism to various depths in the skin, occurring mainly in the

distal parts of the extremities. The lesions produced were short-lived but recurrent. One presumes that the organisms were rapidly altered after arrival in the skin, since none were stainable in the sections, despite yielding positive results on culture. No heart lesions, clubbing or splenomegaly were detected to support the idea of an infective endocarditis, nor were visceral lesions found to account for the patient's deterioration. Having cultured a water-borne organism from the lesions and cured the condition by eliminating it with the correct antibiotic, we assumed that the focus for an intermittent bacteraemia was the infection of a superficial operation wound acquired in the operating theatre from stored water. Because the organism grows poorly at 37°C, the development of granulomas at the lower temperature of the skin may account for the absence of ascertainable lesions elsewhere.

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