

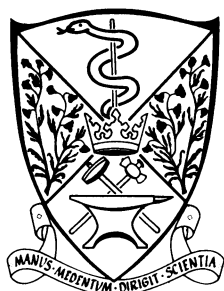
We thank Ms K Soutter and Ms L Poole for their help in organising the meeting.

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2 Pai GR, Haites NE, Rawles JM. One thousand heart attacks in the Grampians:

the place of cardiopulmonary resuscitation in general practice. *Br Med J* 1987;294:352-4.

- 3 ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17 187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet* 1988;ii:349-60.

(Accepted 8 June 1989)



Hammersmith Staff Rounds

Systemic candidiasis: an unusual complication of eating mutton

Commonly affects the skin, eyes, and costochondral joints

The incidence of systemic candidiasis has increased greatly over the past decade.¹ *Candida* is widely known as a pathogen of immunocompromised patients, though evidence now suggests that many candida infections occur in patients without immune deficiencies, possibly owing to prolonged use of broad spectrum antibiotics and more active intensive care practices. We present a patient who developed systemic candidiasis after an abdominal operation and showed two characteristic features that could have led to earlier diagnosis.

History

The patient was a 36 year old farmer who was referred from Greece with a fever of unknown origin. Previously well, he presented in December 1988 with peritonitis. At laparotomy a perforation of the small bowel was found, as was a meat bone—the possible cause. Five days later his condition deteriorated, necessitating a second operation and a temporary ileostomy. Postoperatively he developed the adult respiratory distress syndrome and septicaemic shock. His protracted clinical course included endotracheal intubation and prolonged mechanical ventilation, parenteral nutrition, and treatment with broad spectrum antibiotics. Pus from the wound was reported as growing a pseudomonad and a fungus. The ileostomy was eventually reversed, and he was discharged in February 1989. Shortly afterwards he complained of night sweats, rigors, headaches, bilateral subcostal pain, and visual impairment. He was treated as an outpatient with several short courses of antibiotics. His symptoms did not improve and he was referred to this hospital.

On examination he was unwell and had a temperature, tenderness over the costochondral joints, and evidence of a right sided pleural effusion. His visual acuity was reduced: right eye counting fingers only and left eye 6/18 with glasses. Funduscopy showed many well developed, white fluffy three dimensional lesions



FIG 1—Fundal appearances in candidiasis, showing yellow-white chorioretinal lesions, white vitreoretinal lesions often associated with traction, and fluffy white intravitreal ball-like lesions

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Br Med J 1989;299:557-8

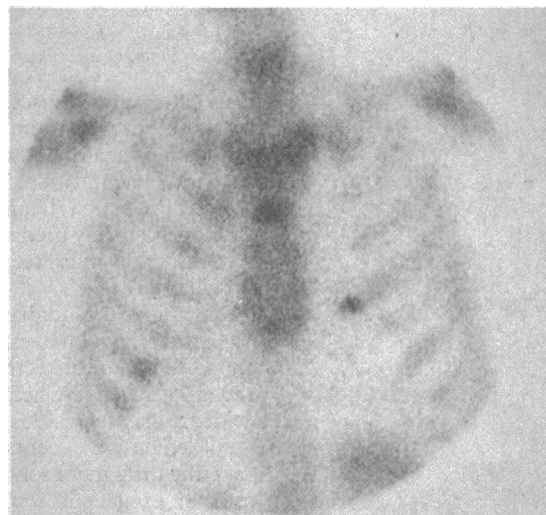


FIG 3—Radioisotope scan of bone showing greatly increased uptake bilaterally in region of costochondral joints of several ribs

extending out from the chorioretina into the vitreous humour, considered characteristic of candidal endophthalmitis (fig 1). The white cell count was $12.2 \times 10^9/l$ (78% neutrophils), erythrocyte sedimentation rate 107 mm in the first hour, and C reactive protein concentration 92 mg/l (normal <10 mg/l). Cultures of blood, urine, and pleural fluid all yielded negative results. Agglutinin and precipitin serological testing for candida yielded positive results. Chest radiography showed right pleural effusion and atelectasis at the base of the right lung. A computed axial tomogram showed multiple soft tissue swellings over the costochondral joints of several ribs (fig 2). A radioisotope scan of the bones showed greatly increased uptake bilaterally over the costochondral joints and in several discrete areas in the maxilla (fig 3). A scan of white cells labelled with indium-111 showed increased uptake in the costochondral joints (fig 4) and was consistent with osteomyelitis.

Disseminated candidiasis was diagnosed, and to prevent further loss of vision treatment was started with amphotericin B and flucytosine. Rib pain and fevers resolved within one week, and his vision improved (right eye 6/18 and left 6/9 with glasses). A vitrectomy was performed and intraocular amphotericin inoculated into the aqueous humour. The patient made a full and uncomplicated recovery and remained well with normal visual acuity.

Comment

Candida albicans is part of the normal gut flora, and microbial interference is an important factor in preventing colonisation. Alterations in host resistance and the presence of portals of entry primarily allow colonisation and subsequent haematogenous spread.²

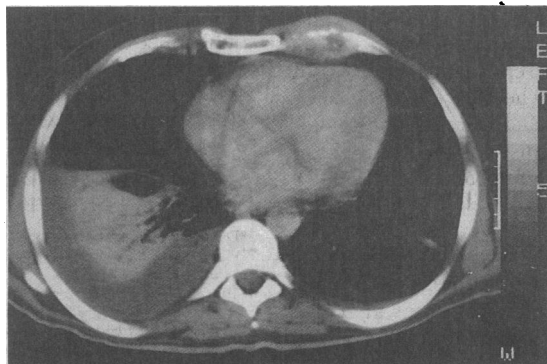


FIG 2—Computed tomogram of thorax showing right sided pleural effusion and left costochondral lesions with soft tissue swelling and bony destruction

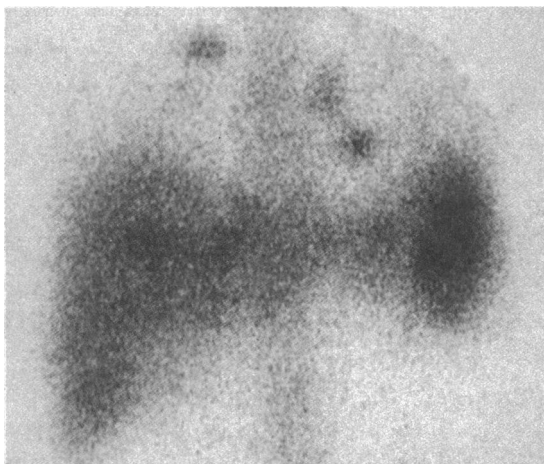


FIG 4—Scan of white cells labelled with ^{111}In showing increased activity in costochondral joints

Thus patients most susceptible to systemic candidiasis are those with gastrointestinal disease, complicated postoperative states, indwelling intravenous catheters, and parenteral nutrition. This patient had all these risk factors. Prolonged treatment with broad spectrum antibiotics not only predisposes to colonisation but also complicates the interpretation of cultures taken during surveillance.

Disseminated candidiasis affects the skin, eyes, and osteoarticular joints especially the costochondral joints. The clinical picture has been well described among intravenous heroin abusers, in whom the incidence has increased greatly, coinciding with the use of lemon juice (contaminated with *C albicans*) to make the drug more soluble. Although the candida is from an exogenous source, this group of patients illustrates the pattern and time course of the clinical features of systemic candidiasis,^{3,4} which may be obscured in the context of complex medical or surgical illness.

Typically, the initial symptom is of a transient episode of fever lasting up to 10 days, which is followed by haematogenous spread to various sites. The first features are often painful nodules or folliculitis, or both. After the initial effect on the skin there is usually a further delay of up to 20 days before the characteristic ocular lesions and candidal endophthalmitis develop. Patients may complain of painful red eyes, photophobia, and impaired vision. In about half of cases the bones and joints are affected some 10 weeks after the first symptom. Interestingly, in most patients, as in our patient, the costochondral joints are affected.

It is worth noting that candida can be readily isolated from cutaneous and bony aspirates even though blood cultures may repeatedly yield negative results. A surprisingly high incidence has been reported in patients receiving parenteral nutrition after operation.^{5,6} In one study 10% of patients who had a protracted postoperative course and were receiving parenteral nutrition showed signs of candidal endophthalmitis.

In clinical practice fungal septicaemia needs to be considered in any patient who has the above risk factors. Evaluation should include careful fundoscopic examination as treatment of disseminated candidiasis is associated with an excellent outcome.

Discussion

JCa: The case shows some features of systemic candidiasis that may be unfamiliar. In this patient it was recognition of the fundal abnormalities that helped in making the correct diagnosis. The effects on the ribs and cartilage are interesting and should have also alerted us to the possibility of *C albicans*.

CTD: Are the fundoscopic appearances characteristic? What features should we be looking for?

ES: The clinical picture is rather characteristic. The features that I look for on examination are threefold: yellow-white chorioretinal lesions, white vitreoretinal lesions often associated with traction, and fluffy intravitreal ball-like lesions.

CTD: Do those fluffy white lesions associated with the vitreous humour grow candida?

ES: One would expect so but in fact that is usually not the case. The vitreous humour was not cultured here as we wanted to measure the concentration of amphotericin B.

JCo: Disseminated candidiasis is increasingly common, and fungal infections generally have been identified as an important missed treatable cause of death. Most infections are due to *C albicans*, though in immunocompromised patients *C tropicalis* is also important. The diagnosis is difficult as blood cultures will generally give positive results in fewer than half of cases, and serological tests are of limited use in clinical management. We should therefore maintain vigilance in susceptible patients. The rapid improvement in the patient's eyesight after treatment was begun was striking. Interestingly, the effectiveness of amphotericin B is not related directly to its tissue concentrations—for example, in fungal meningitis the drug is effective despite cerebrospinal fluid concentrations being low because the drug does not cross the blood-brain barrier.

CTD: Flucytosine will cross the blood-brain barrier.

JCo: That is correct. Resistance to flucytosine, however, is common in candida, and I would not use this as a single agent treatment. When it is given with amphotericin there is often synergism, hence their combined use in this patient.

CTD: This patient must still have a substantial fungal load. I would be concerned about the long term prognosis here. Can you truly eradicate the pathogen from, for example, the costochondral lesions?

JCo: The fundal lesions have regressed rapidly with treatment, and if these are representative of the lesions elsewhere then it would seem that they can be sterilised in the short term. Whether the lesions will reactivate when treatment is stopped is certainly an important question, but generally the prognosis is excellent. The main exception is when candida affects a foreign body, as in prosthetic valve endocarditis; in these cases relapse is almost inevitable unless the prosthesis is removed.

CTD: Was the case as straightforward as your presentation indicates? What were your differential diagnoses initially?

JB: The persistent fever in association with a right sided pleural effusion and the history of recent complicated abdominal surgery all pointed towards a subphrenic abscess. Infection with *Actinomyces israelii* was also considered as multiple bony lesions can be found with this and there may be a history of abdominal surgery. The fundal lesions, however, could not be explained on this basis and led us to search for another infective cause.

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