Short report

Trichosporon capitatum causing recurrent fungal endocarditis

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Fungal endocarditis is usually seen in patients with prosthetic heart valves or in drug addicts. Diagnosis may prove difficult because blood cultures may be negative and serological tests misleading. Medical treatment alone is rarely successful in eradicating infection, and even when combined with surgery the prognosis remains poor.

We report a case of Candida endocarditis presenting as a mycotic aneurysm of the right pulmonary artery. At operation the patient was found to have complete destruction of a homograft valve which had been inserted, together with a Dacron conduit, at an earlier operation to correct pulmonary atresia.

Despite gross fungal infection a combination of medical and surgical treatment led to recovery. The patient died of pneumonia two years later, with evidence of fungal endocarditis caused by a different organism, Trichosporon capitatum. We can find no previous report of Trichosporon endocarditis.

Case report

The patient presented at the age of 18 months with a systolic murmur. He had been a full-term infant. During infancy he had frequent chest infections. Cardiac catheterisation, performed at one year, showed a single arterial trunk and a VSD.

At annual review he complained of tiredness and effort dyspnoea, and remained below the third centile for height and weight. Reassessment at 14 years of age revealed no cyanosis or clubbing, but there was a systolic thrill accompanied by an ejection systolic murmur in the pulmonary area, and a single second heart sound. A chest radiograph revealed reduced pulmonary blood flow and a prominent left-sided aortic arch. The ECG showed right atrial and biventricular hypertrophy. Cardiac catheterisation demonstrated pulmonary atresia and a VSD, the pulmonary artery being supplied by a collateral vessel from the descending aorta. Other collateral vessels supplied the upper and lower lobes of the right lung.

In September 1976, the collateral vessels were ligated and the VSD was closed with a Dacron patch. Pulmonary atresia was found at valvar level and bypassed by an extracardiac composite conduit made of Dacron and an antibiotic-preserved fresh homograft valve. The antibiotic preservative contained neomycin, carbenicillin, cephaloridine, polymixin B, and nystatin. Gentamicin and cloxacillin were given for one week after operation. Recovery was excellent apart from a transient pyrexia four days after stopping antibiotics, which resolved spontaneously.

The patient remained well for nine months. He then developed a sore throat followed by anorexia, weight loss, and intermittent fever. On examination there was a harsh ejection systolic and an early diastolic murmur in the pulmonary area. A blood count showed a normochromic, normocytic anaemia (haemoglobin 9g/dl), a total white cell count of 10 × 10^9/l (80% neutrophils), and an ESR of 60 mm/hr.

A yeast (Candida sp) was isolated from one of three broth of a single set of blood cultures. There were 20 negative blood cultures. Tests for Aspergillus and Candida precipitins and Candida agglutinins were all negative. There was no microscopic haematuria. Because the pyrexia continued it was decided to treat the patient with penicillin and gentamicin. Despite adequate blood levels of gentamicin there was no improvement. The patient then had haemoptyses, the diastolic murmur became more prominent, and a right-sided rhonchus was noted. A chest radiograph (figure) showed a mass at the right hilum which proved to be pulsatile on screening and the diagnosis of aneurysm of the right pulmonary artery was confirmed angiographically. At operation the homograft valve was found to be totally destroyed and inflammatory tissue formed a false aneurysm in the anterior aspect of the right ventricle. There was also an aneurysm of the right pulmonary artery with surrounding necrosis. After removal of remnants of the first homograft, a new aortic homograft was inserted, and a right pneumonectomy had to be performed.

Candida guillermondii was isolated from portions of the homograft and from a blood culture taken at operation. Analysis of sera showed a rise in titre of Candida guillermondii agglutinins from 1/8 to 1/16 over a period of four months. Since this only represents one dilution it was not completely diagnostic. Histological examination of the resected lung revealed a mycotic aneurysm of the right pulmonary artery.

After operation the patient was treated with intravenous 5-fluorocytosine 100 mg/kg/day (5 FC) for three months. The organism was sensitive to 5 FC and the mean inhibitory concentration (MIC) was 5 mg/l. Serum levels were satisfactory (trough level 22 mg/l). However, he developed
Trichosporon capitatum causing recurrent fungal endocarditis

Figure  Chest radiograph showing mass at right hilum.

a bronchopleural fistula and empyema which yielded a profuse growth of Klebsiella aerogenes, Escherichia coli, and Staphylococcus aureus. He was treated with gentamicin and cotrimoxazole and eventually the fistulae were resected, the pleural cavity was decorticated, and thoracoplasty of the upper seven ribs performed (Mr AJ Gunning).

He made a good recovery and was well and working for two years. He then developed a chest infection and deteriorated rapidly despite a course of cotrimoxazole at home. On arrival in hospital he suffered a respiratory arrest. Despite attempts at resuscitation he died later that day. Blood cultures were negative.

At necropsy there was evidence of pneumonia, which was considered to be the cause of death. Soft necrotic vegetations were found at the base of the conduit and on the cusps of the graft valve. Histological examination of the valve revealed fungal hyphae, with arthrospore formation. There were scattered areas of fungal infiltration around blood vessels in the lung. Trichosporon capitatum was isolated from the vegetations, in which the fungal hyphae could be demonstrated by indirect immunofluorescence. Candida albicans was also isolated from the lung and vegetations, but could not be demonstrated in these tissues by immunofluorescence and so may have been a contaminant. Candida guillermondii was not isolated, and its serum antibody level had fallen to 1/4. This fall in titre of two dilutions strengthened the diagnosis of a previous C guillermondii endocarditis. There were no detectable antibodies to C albicans at any stage of his illness. The Trichosporon capitatum was resistant to 5-fluorocytosine with an MIC of 8 mg/l.

Discussion

Fungal endocarditis is rare and is most often seen in drug addicts or after open-heart surgery, where the causative organism is usually C albicans. Endocarditis caused by C guillermondii has been found in drug addicts and after cardiac surgery. The diagnosis of Candida endocarditis can be difficult and repeated negative blood cultures are not uncommon. In this case a Candida sp was isolated from one of many blood cultures; his subsequent course emphasises that Candidaemia should never be disregarded in any patient at risk. Serological tests are often employed, but false-negative results may occur in the presence of invasive disease, and the tests may not include unusual species such as Candida guillermondii. Furthermore a high agglutinin titre to Candida may be misleading. The precipitin test, which employs somatic antigen, is more specific but such antibodies can develop in patients undergoing open-heart surgery in the absence of systemic infection, possibly because of postoperative superficial colonisation of the gut by yeasts. Despite these anomalies serological tests remain a valuable aid, but they should be made before operation in order to assess the relevance of subsequent changes.

Eradication of Candida infection of a valve is seldom achieved by medical means alone. Excision of the infected valve still results in a poor prognosis, which might be improved by four to six weeks' postoperative therapy with either amphotericin B, 5 FC, or both. Despite gross infection in our patient the fungal endocarditis with C guillermondii seemed to have been cured. There was a recurrence of fungal endocarditis with a different organism, Trichosporon capitatum. This is normally found in superficial lesions, is generally regarded as non-pathogenic, and is rarely invasive. If one assumes that this organism was introduced into our patient at operation, then it seems to have flourished in the presence of 5-fluorocytosine, to which it was resistant.

We wish to emphasise that major fungal endocarditis can be present despite negative serological tests, especially if the organism is an unusual one. Even with gross disease a combination of excision of the infected valve and chemotherapy may lead to recovery. We would recommend close observation of any such patient for possible recurrence of endocarditis, and also consideration of the possibility of a reinfection.

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References

Plasma catecholamines in exercise-induced asthma

Sir,—The results of Zielinski et al (Thorax 1980; 35: 823) on plasma catecholamines in exercise-induced asthma must be interpreted with extreme caution. Plasma catecholamines were determined by a fluorimetric assay which lacks both specificity and sensitivity and is inadequate for the measurement of plasma catecholamines. The basal values reported for adrenaline are five to ten times higher, and for noradrenaline three to five times higher than those measured by radioenzymatic assay (Barnes et al, Clin Sci 1981; 60:18P), or by high pressure liquid chromatography with electrochemical detection or by gas chromatography-mass spectrometry. The pre-exercise values reported by Zielinski et al correspond to those attained during infusions of 0.075 \( \mu \)g/kg/min noradrenaline and 0.05 \( \mu \)g/kg/min adrenaline (FitzGerald et al, Eur J Clin Invest 1980; 10:401) which cause marked cardiovascular and metabolic effects and produce significant bronchodilatation in asthmatic subjects (Barnes et al, N Engl J Med 1980; 302:263).

Using a fluorimetric assay any changes in catecholamines during exercise are very difficult to evaluate. Their demonstration that adrenaline does not rise and that noradrenaline only rises by 50% during submaximal exercise in normal subjects is in conflict with previous studies where a three to fivefold rise in adrenaline and five to tenfold in noradrenaline have been reported (Galbo et al, J Appl Physiol 1975; 38:70), and are almost certainly the result of the insensitivity of the fluorimetric assay used. Comparisons between normal and asthmatic subjects are therefore invalid. We have recently measured the catecholamine response to exercise in asthmatic and non-atopic normal subjects using a sensitive radioenzymatic assay. The normal subjects showed a threefold rise in adrenaline and a fivefold rise in noradrenaline whereas the asthmatic subjects showed no rise in adrenaline and only a twofold rise in noradrenaline, suggesting an impaired sympathoadrenal response to exercise in asthmatic subjects (Barnes et al, Clin Sci 1980; 58:4P). The results are discussed in more detail elsewhere in this issue of Thorax.

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Sir,—I fully agree that radioenzymatic assay is more sensitive and specific in measuring plasma catecholamines than the fluorimetric method. Moreover, much less blood is needed. We would have used it if it had been available. Nevertheless I would not agree that the method in question is inadequate for such measurements. Sensitivity of the fluorimetric method is sufficient for plasma measurements if a large sample of plasma is used and measurement procedures are meticulously performed (Jiang et al, Mayo Clin Proc 1976; 51:112). Some authors have reported comparable values of plasma catecholamines using both fluorimetric and radioenzymatic methods (Miura et al, J Lab Clin Med 1977; 89:421, Campese et al, J Lab Clin Med 1980; 95:927). In the papers to which we referred to in our paper, plasma catecholamines were determined using the fluorimetric method. We were not especially interested in basal values which vary depending on the time of the day and can increase in anticipation of muscular exercise (Mason et al, Psych Med 1973; 35:406). We were interested in changes of adrenaline and noradrenaline levels in plasma brought about by physical exercise in three different groups of subjects. For that specific purpose I would find our methods satisfactory.

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