A magician's tale

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CASE PRESENTATION

A 19-year-old male university student and part-time magician presented with a two-week history of fever with rigors, nausea, vomiting, headaches and migrating polyarthralgia. The patient's medical history was significant for a childhood murmur that was presumed benign. The patient denied use of illicit drugs and was not on any medication at the time of presentation. The patient owned several pets, including a dog, a monitor lizard and rabbits used for his magic tricks.

On initial assessment, the patient did not appear to be in distress, was afebrile and hemodynamically stable. The physical examination was remarkable for two murmurs: a grade 2 of 6 apical systolic murmur and a grade 2 of 6 short early diastolic murmur at the left upper sternal border, without any peripheral signs of chronic aortic insufficiency or subacute infective endocarditis. Laboratory data were significant for an elevated leukocyte count of $24.5 \times 10^9/L$ (93% neutrophils). Chest radiography was unremarkable. An electrocardiogram showed sinus tachycardia at a rate of 100 beats/min and a mildly prolonged PR interval of 0.22 s.

Three sets of blood cultures were immediately drawn. A transthoracic echocardiogram performed on the same day confirmed severe aortic insufficiency and demonstrated numerous abnormalities, including vegetations on the aortic valve, a perforated aortic cusp and a large aortic root abscess. Moderate mitral insufficiency was also present. The patient was started on an empirical regimen of vancomycin and gentamycin, and was transferred to the coronary care unit for monitoring.

Within 3 h of admission, the patient developed complete heart block with acute pulmonary edema requiring emergency cardiac surgery. At the time of surgery, the heart was massively dilated. The right coronary cusp of the aortic valve was completely destroyed and replaced by vegetations. The aortic abscess that extended into the interventricular septum was drained, the septum was reconstructed and the aortic valve was replaced with a homograft.

Direct examination of intraoperative swabs revealed fine Gram-negative rods, and ceftriaxone was added to the regimen. On postoperative day 2, blood cultures became positive, and filamentous Gram-variable rods were detected by microscopy. After 48 h, both blood and intraoperative specimens grew pinpoint colonies on blood agar incubated under 5% carbon dioxide. Direct examination of the bacteria revealed thin, nonbranching, Gram-variable rods. The organism could not be identified using either the VITEK 2 automated system (bioMérieux, USA) or the API-20E test kit (bioMérieux, USA); it did not ferment any carbohydrates, was negative for catalase, oxidase and indole, and appeared susceptible to vancomycin by disc diffusion, leading the treating team to suspect a Gram-positive bacterium. Pending identification of the isolate by the reference provincial public health laboratory, susceptibility testing was performed by Etest (AB Biodisk, Sweden) and revealed a minimum inhibitory concentration for penicillin of 0.094 (interpreted as probably sensitive) and for vancomycin of 0.38 mg/L (probably sensitive). Ampicillin was added, and ceftriaxone discontinued.

On postoperative day 9, persistent fevers with leukocytosis prompted a repeat echocardiography, which showed new vegetations on the interventricular septum and the aortic homograft, as well as more severe mitral insufficiency. On postoperative day 10, the provincial public health laboratory reported that the results of fatty acid analysis were consistent with an *Actinomyces* species, but that the isolate would be sent to the federal public health laboratory for definitive identification. Ampicillin and gentamycin were discontinued, and penicillin G (18 million units intravenously/day) was added to the vancomycin. Because fevers persisted, the diagnosis of an *Actinomyces* species as the etiological agent was questioned. The isolate was sent to a research laboratory for amplification and sequencing of the 16S rRNA gene. What was the etiological agent of this fulminant endocarditis?

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DIAGNOSIS

By means of amplification and sequencing of the 16S *rRNA* gene, the isolate was rapidly identified as *Streptobacillus moniliformis*, a Gram-negative organism that normally resides in the oropharynx of rodents (1-3). Upon repeated questioning, the patient admitted to breeding rats to feed his 0.93 m long lizard, and that he often sustained bites while handling the rats.

The antibiotic regimen was changed to high-dose penicillin G (24 million units intravenously/day) with gentamycin. The patient remained febrile, and eventually required repeat surgery to evacuate blood clots and drain mediastinal abscesses eroding the ascending aortic root. This procedure was complicated by rupture of the aortic root, leading to cardiac arrest and emergency cardiectomy. The septal leaflet of the tricuspid valve was found to be embedded in a large vegetation and sealing off a ventricular septal defect. The tricuspid valve was replaced with a bioprosthesis, the ventricular septal defect was closed and the aortic root was reconstructed. The patient recovered from surgery and completed an eight-week course of antibiotics. The patient was still well three years after his illness, and has returned to his studies and his magician tricks (although without the lizard).

DISCUSSION

The present case illustrates two points. First, that a detailed social history is instrumental not only in making clinical diagnoses but also in making microbiological ones. With prior knowledge of the patient's exposure to rats, rat-bite fever, a rare but well-described zoonosis (4-7), would have been suspected and the microbiology laboratory could have been directed to take the necessary steps involved in identifying the culprit organism. Second, the importance of molecular diagnostics for rapid identification of unusual and fastidious organisms is highlighted.

S moniliformis is a fastidious organism that grows preferentially in an atmosphere of low oxygen tension in a medium supplemented with serum. Its isolation from blood can be inhibited by the anticoagulant used in most commercial blood culture bottles, and characteristic 'fluff balls' have been

described in liquid culture media (8). In the present case, the organism was isolated from commercial blood culture bottles and grew on solid media without serum supplementation, but could not be identified using automated systems. In fact, although the Gram stain appearance of the organism was initially that of a Gram-negative bacterium, identification was confounded by its subsequent Gram-variable appearance, its susceptibility to vancomycin and its biochemical inertness, misleading the treating physicians toward a Gram-positive organism. Other traditional phenotypic methods, including fatty acid profiling performed in a reference laboratory, failed to provide an accurate identification and, hence, adequate therapy for this organism.

The DNA amplified from this isolate showed 99% similarity with the GenBank sequence Z35305 corresponding to the 16S *rRNA* of the type strain of *S moniliformis* (American Type Culture Collection strain 14647). In theory, any sequence variability could suggest a different species; however, in practice, a sequence difference of 1% or less is generally considered acceptable for an isolate to be designated as belonging to the same species as the type strain (9). The isolate was eventually confirmed by the federal public health laboratory as being *S moniliformis*.

CONCLUSION

We describe a nearly fatal case of rat-bite fever caused by *S moniliformis* in a young adult, where accurate microbiological diagnosis depended on the use of molecular diagnostic methods. The disease required both medical and aggressive surgical management for cure.

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