Prolonged fever and involuntary weight loss as manifestations of bacterial endocarditis: A case report

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Abstract. We reported an unusual presentation of prolonged fever and involuntary weight loss in older adult as a manifestation of infective bacterial endocarditis. The patient had pre-existing compensated asymptomatic valvular heart disease without treatment. A positive fecal occult blood test is prompting an investigation of malignancy of gastrointestinal as one of other possible cause of prolonged fever with wasting, evaluation of HIV serostatus shows seronegative. The case fulfilled criteria for definitive infective endocarditis: one major criterion of positive blood culture for Streptococcus mitis, which was one of viridans group streptococci and three minor criteria of fever at least 38°Celsius, immunologic phenomena in the form of glomerulonephritis, and a predisposing heart condition. One course of third-generation cephalosporin successfully cleared the Streptococcus mitis infection proven by culture. Infective endocarditis should be considered as one of the causes of prolonged fever with wasting, especially in cases with the previous history of heart disease.

1. Introduction
The prevalence of prolonged fever among adult hospitalized patient was around 2.9%.¹ The differential diagnosis were more than 200 diseases, although in an adult might be narrowed in several dozen possible causes. The common subgroups of differential diagnosis then finally become the etiology infection (20 – 40%), malignancy (20 – 30%), non-infectious inflammatory response (10 – 30%) and other causes (10 – 20%).²³ Weight loss considered clinically important exceed 5% of body weight over one month or 10% over six months or longer.⁴ Almost any chronic illness with sufficient severity can lead to weight loss ranging from occult infection to malignancy.⁵ Comprehensive evaluation to the otherwise occult cause is mandatory to prevent further morbidity and mortality.

Bacterial or fungal infection of endocardial surface, defined as endocarditis, is associated with significant morbidity and mortality. Identification of risk factor includes prosthetic heart valve, structural or congenital heart anomaly, intravenous drug user, and recent invasive procedure, is one of the keys in diagnosis pathway.⁶ The Duke criteria consist of clinical, laboratory and echocardiographic findings, currently widely used to diagnose infective endocarditis.⁷⁸

2. Case Report
A 60-year-old man was consulted to tropical and infectious disease division of internal medicine with two weeks history of intermittent fever. His body weight decreased involuntarily in the last four month, on admission he weights 14 kilograms less than his previous weight. He suffered from the loss
of appetite and nausea was noted after five months and gradually worsening with stomach pain within the last month.

He had a medical history of heart disease since adolescent, at that time his doctor informed him about his heart murmur. The heart disease was without any prompt cardiac evaluation; he was not attended any regular medical follow up nor taking medication for his heart problem. Medical records for the heart disease diagnosis could not be retrieved. The patient use to smoke more than 20 cigarettes in the past 40 years and currently trying to quit.

On admission, the evaluation revealed conscious and febrile with axillae temperature 38.1°Celsius, blood pressure 130/80 mmHg, pulse rate 92 beats per minute, respiratory rate of 18 times per minute and pain score 2/10 (visual analogue scale) on the epigastrial area. Physical examination revealed normal heart border with diminished cardiac waist on percussion. Heart sound regular with soft second heart sound, distinct grade 3/6 pan-systolic murmur best heard at the apex with radiation to the left axillae with the same intensity. Stigmata of infective endocarditis was not visible and other systems also unremarkable.

Blood test showed elevated white cell count of 12.54 x 10³/μL with neutrophilia (10.45 x 10³/μL; 83.36%). C-reactive protein as inflammatory markers was markedly at the level of 54.68 mg/dL. Urinalysis indicates mild proteinuria (dipstick +1) with microscopic hemoglobinuria of +2 (erythrocyte sediment 8 – 10/pf). The fecal test was positive for a fecal occult blood test (FOBT) with a low level of CEA. HIV antibody test results were non-reactive. Imaging evaluation of cardiovascular status revealed unremarkable chest X-ray, which showed normal heart shape and size with cardio thorax ratio (CTR) of 54% (Figure 1). Echocardiography showed moderate mitral regurgitation due to prolapse of the posterior mitral leaflet (PML) with thickening of cordae tendinea (Figure 2).

Upper endoscopy showed Barrett’s esophagus with superficial gastritis at antrum (Figure 3), and lower endoscopy revealed polyp with a stalk at the colosigmoid junction (Figure 4). Three sets of blood culture collected at 30 minutes intervals grew Streptococcus mitis. The isolates were fully susceptible to penicillin, cephalosporin 3rd generation, azithromycin and clindamycin antibiotics.

We found that the positive blood culture for microorganism consistent with infective bacterial endocarditis (S. mitis as one of viridans streptococci group), the presence of fever and the immunologic phenomenon of glomerulonephritis in a patient with a predisposing heart condition, supporting the diagnosis of infective endocarditis in this case. The clinical sign and symptoms fulfill one major and three minor based on Duke’s criteria for the clinical diagnosis of infectious endocarditis. Predisposing heart condition diagnosed with valvular heart disease, mitral regurgitation moderate due to Rheumatic Heart Disease. The gastrointestinal lesion was Barrett’s esophagus; superficial gastritis pars antrum and polyp pars colo-sigmoid junction.
Figure 1. Chest X-Ray shows normal heart shape and size with cardiothoracic (CTR) ratio of 54 %.

Figure 2. Echocardiography showed moderate mitral regurgitation due to prolapse of the posterior mitral leaflet (PML) with thickening of cordae tendinea.

Figure 3. Upper endoscopy, esophagastroduodenoscopy showed changes in the mucosa of esophagus’ appearance identified as Barrett’s esophagus and erythema with edema at pars antrum.
Figure 4. Lower endoscopy revealed the appearance of colonic polyp (arrow) with a stalk at colo-sigmoid junction pars descendent.

The patient was treated with 2 grams of ceftriaxone antibiotic daily and planned for four weeks of antibiotic regimen, along with valsartan 10 mg once daily and propranolol 10 mg twice daily for underlying valvular heart disease management. Barrett’s esophagus as a common manifestation of gastroesophageal reflux disease (GERD) and superficial gastritis pars antrum were treated with twice daily 20 mg omeprazole with 10 mg domperidone for improving gastric motility and emptying time. The fever subsided within five days of antibiotics therapy, and blood culture has taken on day 7 of ceftriaxone therapy was sterile. Gastric pain improved after the second day of administration domperidone and omeprazole. Appetite improvement was reported after administration of omeprazole and domperidone. The patient was discharged on day 14 of antibiotic therapy and remained afebrile and asymptomatic after discharge. Education about sign and symptoms of infective endocarditis to patient and family has been given for early awareness of recurrence. Awareness on dental health stressing on regular dental evaluation, along with cutaneous hygiene was prompted to encourage infective endocarditis prevention measures.

3. Discussion
Chronic fever with weight loss possesses a challenging task in the diagnosis process. Unintentional weight loss in this case considered as a consequence of advanced chronic disease and related to the prolonged fever.

Despite advances in medical therapy, infective endocarditis remains a high morbidity and occasionally fatal infection if the diagnosis is miss. The inflammation can come from a variety of disease state, but the majority of cases were due to infection. Previously Sir William Osler divided “simple” and “malignant” form of endocarditis. The “simple” endocarditis means more subtle constitutional symptoms and frequently misdiagnosed until has been present for weeks or months, lately the term well known as subacute bacterial endocarditis. The “malignant” forms of endocarditis were acute onset and fulminant clinical findings which were now known as acute endocarditis. The widely accepted criteria used today for clinical diagnosis is the Duke Criteria which use a set of major, minor and pathologic criteria to classify endocarditis as definite, possible or rejected. This case presented a subacute bacterial endocarditis in term of its subtle constitutional syndrome, the loss of body weight first not identified as a result of subacute bacterial infection. The clinical diagnosis of infectious endocarditis was definite and fulfilled one major criterion (positive blood culture for Streptococcus mitis, which was a viridians Streptococcus) and three minor criteria (fever of at least
38°Celsius, immunologic phenomena of glomerulonephritis, and a predisposing heart condition). Viridans streptococcus was the second most common etiology of infective bacterial endocarditis.

Successful treatment for infective endocarditis requires an appropriate antibiotic. Initial antibiotic of choice depends on the severity of symptom which should be adjusted to the culture result. Duration of therapy was measured based on at least two set of sterile blood cultures obtained every 24 to 48 hours, indicate the infection has been cleared from bloodstream and maintained based on culture. The indolent course of subacute endocarditis in this case also manifest in unintentional weight loss. The successful treatment of underlying disease and prevention of recurrence will halt further weight loss. In some study, the risk of gastrointestinal cancers was high soon after diagnosis (after three months) of infective endocarditis and remains high after > 12 months long-term follow-up. The strongest and best-documented relationship between bacterial infection and colonic cancer was Streptococcus bovis infection, specifically the S. gallolyticus subspecies; which has been in some studies were related to the presence of colonic adenoma or carcinoma. The gastrointestinal problem, in this case, was Barrett esophageus due to GERD and colonic polyp. Barrett esophageus as premalignant lesion together with colon polyp, both increase the risk of colorectal cancer. Annual endoscopy is necessary for surveillance in this case.

In summary, prolonged fever and unintentional weight loss should be considered a sign and symptom of subacute infective endocarditis. Since the diagnosis of infective endocarditis carries a high risk for colorectal cancer, the presence of pre-malignant gastrointestinal lesion should be evaluated annually.

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