*Clinical Infectious Diseases*

IN THE LITERATURE

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## CASE VIGNETTE: INFLAMMATORY PSEUDOTUMOR OF LIVER MISTAKEN FOR A LIVER ABSCESS

Vaquer-Grimalt P, García IM, Antón E, et al. IgG4-related disease mimicking a liver abscess [published online ahead of print 2 February 2024]. Rev Esp Enferm Dig doi: 10.17235/reed.2024.10265/2024. PMID: 38305673.

A 37-year-old man with a history of chronic pancreatitis was admitted to hospital with a history of fever for 4 weeks, together with anorexia and right upper quadrant abdominal pain. The patient's physical examination findings were unremarkable. His white blood cell count was normal but his C-reactive protein level was 23 mg/dL (normal <0.5 mg/dL). Results of hepatic tests were mildly abnormal, with total bilirubin of 1.9 mg/dL (normal, <1.2 mg/dL), alkaline phosphatase of 174 U/L (40–150 U/L), and gamma-glutamyl transferase of 127 U/L (12–64 U/L); transaminase levels were normal. Computed tomographic scanning revealed a 10-cm heterogeneous mass in the liver, along with several smaller lesions. Biliary tract abnormalities were not observed.

Empiric treatment for a possible liver abscess was initiated with piperacillin-tazobactam and metronidazole, but fever persisted. Blood and urine cultures were negative, as were results of serological tests for infection with *Echinococcus* and *Entamoeba histolytica*. Liver biopsy was performed, and, rather than pus, histological examination of the specimen revealed fibroinflammatory proliferation with abundant plasma cells. Immunohistochemical staining of the specimen demonstrated increased immunoglobulin (Ig) G4–positive cells. The serum IgG4 concentration was 236 mg/dL (normal, 8–140 mg/dL). These findings led to a diagnosis of inflammatory pseudotumor of the liver and treatment with prednisone with eventual complete resolution of the lesion.

Inflammatory pseudotumor (IPT) is commonly believed to often result from an unusually exuberant response to a pathogen, although an organism is infrequently detected [1]. Of note is that among the reported associated infections, is syphilis, which does not appear to have been excluded in this case and which could have responded to the piperacillin-tazobactam that was given for treatment of a possible liver abscess.

Wang and colleagues state that the "diagnosis of IgG4-RD hepatic IPT should be made after considering infections such as syphilis and excluding IPT mimics, and in conjunction with clinical data such as IgG4 serum level, extrahepatic organ involvement (particularly pancreatic involvement), and, if steroids have been initiated, confirmation of steroid responsiveness."

### Reference

1. Wang D, Misdraji J. Inflammatory pseudotumor of the liver. Surg Pathol Clin **2023**; 16:565–80.

## CHAGAS DISEASE—COMMUNITY- AND HOSPITAL-BASED SCREENING, EVALUATION AND MANAGEMENT

Reifler KA, Wheelock A, Hall SM, et al. Chagas cardiomyopathy in Boston, Massachusetts: identifying disease and improving management after community and hospital-based screening. PLoS Negl Trop Dis 2024; 18(1):e0011913. doi: 10.1371/journal.pntd.0011913. PMID: 38241361; PMCID: PMC10830043.

In 2017, the Strong Hearts project, a Chagas disease screening and treatment initiative based at the East Boston Neighborhood Health Center, recommended screening of all adults <50 years of age who had resided in Mexico, Central America or South America for ≥6 months. This group has previously reported that screening had identified a 0.97% prevalence of Chagas in the selected population.

A positive enzyme-linked immunosorbent-linked assay test led to confirmatory testing at the Centers for Disease Control and Prevention with an alternative method, and those with both antibody tests proving positive were referred to the East Boston Neighborhood Health Center. There, the routine investigations include electrocardiography (ECG), blood chemistry, complete blood cell count, troponin, B-type natriuretic peptide (BNP), and, in most patients, transthoracic echocardiography (TTE), with further testing as indicated.

In a retrospective examination of recorded cases, Reifler and colleagues identified 109 patients with Chagas disease, with 86 (79%) having been identified by screening, in the remaining 23 (21%), testing had been performed because of clinical suspicion. Sixty-seven patients (61%) were female, with one-fifth being of childbearing age; 15% of the 67 were pregnant. Overall, the mean age of the total cohort was 43 years; 27% were >50 years of age, and 95% had migrated from Central America, primarily (85%) from El Salvador

One-fourth of the entire cohort complained of palpitations, 17% had chest pain, and 14% reported exertional dyspnea, but 52% were asymptomatic. The serum troponin level was elevated in 5 of 54 (9%), and the BNP level was >100 pg/mL in 10 of 43 (23%); all 5 with elevated troponin and 9 of 10 with elevated BNP has signs or symptoms of cardiac disease.

The ECG was normal in 51%, but signs or symptoms of cardiac disease were present in one-third. The most common abnormalities detected were right bundle branch block (partial or complete), left anterior fascicular block, and T-wave changes. Low voltage was present in 12%.

Abnormalities were detected at TTE in 46 of the 94 patients (49%) in whom it was performed. These included 23 of the 44 asymptomatic patients (52%), 13 of 42 (31%) who had a normal ECG, and 25 of 64 (39%) who were <50 years of age. The most frequently identified

abnormalities were dilatation of the left atrium (21%), diastolic dysfunction (17%), and apical hypokinesis (11%). In 10 patients (11%), the left ventricular ejection fraction was <50% and all 10 had left ventricle apical abnormalities.

Ambulatory monitoring was performed in 24 patients with various ventricular events detected, including nonsustained ventricular tachycardia in 5. Seven patients (6%) required placement of a cardiac pacemaker or an internal cardioverter defibrillator. Exercise tolerance testing revealed chronotropic incompetence in 6 of 27 (22%). Twelve patients underwent cardiac magnetic resonance (MR) imaging, and 2 of these had significant apical abnormalities not detected with TTE.

Patients were classified according to the American Heart Association system, in which class A is indeterminate (positive serology without evidence of disease) and class B is asymptomatic but with structural heart disease. The most severe class, class D, indicates the presence of dilated cardiomyopathy with refractory heart failure. Half of the patients were classified in category A, and one-third in B.

Current recommendation state that all patients with serological evidence of *Trypanosoma cruzii* infection undergo a resting 12-lead ECG with a 30-second rhythm strip. The experience reported by Reifler and colleagues is indicative that further routine testing is warranted, particularly TEE, findings of which proved to be abnormal in half of asymptomatic patients and in one-third of those with a normal ECG. The investigators suggest the wider use of ambulatory cardiac monitoring and, in selected cases, cardiac MR imaging.

Early identification of infection and of complications is critical to management. Treatment of Chagas disease is strongly recommended for adults up to 50 years of age with chronic infection who do not already have advanced cardiomyopathy. This justifies early identification of infection, while additional studies may provide evidence indicating the need for other interventions, even if treatment of the infection may not be warranted based on current data. The results summarized here confirm the authors' approach to screening and evaluation starting with performance of an ECG and, with recognition that a normal ECG does not rule out cardiac disease, a TTE. Ambulatory cardiac monitoring may be warranted, and in some instances cardiac MR imaging may provide clinically actionable information.

Generalization of the results may be limited by their retrospective nature, the relatively small sample size, and the fact that 85% of case patients were migrants from El Salvador, where one of the 6 *T. cruzi* "discrete type units" is dominant, thus possibly affecting the manifestations and course of clinical illness.

## WHOLE-GENOME SEQUENCING PROVIDES INSIGHTS INTO ANTIBIOTIC RESISTANCE IN *ENTEROCOCCUS FAECIUM*

Coll F, Gouliouris T, Blane B, et al. Antibiotic resistance determination using *Enterococcus faecium* whole-genome sequences: a diagnostic accuracy study using genotypic and phenotypic data. Lancet Microbe 2024; 5(2):e151-e163. doi: 10.1016/S2666-5247(23)00297-5 PMID: 38219758.

Coll and colleagues evaluated the accuracy of antibiotic resistance (AMR) determination using whole-genome sequencing (WGS) compared with phenotypic testing of *Enterococcus faecium*. They studied 4382 isolates for which publicly available WGS and AMR phenotypes were available. The isolates were recovered from 2000 to 2018 in 11 countries.

The authors curated a total of 316 AMR-associated genetic determinants, including 103 single mutations, 100 combinations of mutations, 82 single horizontally acquired genes, and 27 multiple acquired genes (operons) that affected 17 antibiotics. These results were compared with reported phenotypic susceptibility results using European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints, and some of the results follow.

The sensitivity of WGS identification of ampicillin resistance (minimum inhibitory concentration [MIC], >8 μg/mL) was 99.7%, and the specificity was 97.9%, with almost identical results in detection of nonsusceptibility (MIC, >4 μg/mL). In each case the lack of full susceptibility was due only to mutated *pbp5*. Similar sensitivity (98.0%) and specificity (98.8%) of WGS prediction of resistance to ciprofloxacin (MIC, >4 μg/mL) were also observed with resistance due to combinations of *gyrA* and *parC* mutations.

The sensitivity and specificity for prediction of vancomycin resistance (MIC, >4 μg/mL) by WGS were each 98.8%, with the *vanA* operon detected in 94.3% of 2309 vancomycin-resistant isolates, *vanB* in 3.2%, and both in 0.3%. Of note, this result was based not just on the presence or absence of the operons but also on the integrity of all genes in the operons. This approach was dictated by knowledge of the existence of vancomycin-susceptible isolates carrying *vanA* operons that had lost critical genes and proved essential. Thus, simple detection of the presence of each operon without this step would have reduced the specificity to 93.3% without affecting sensitivity.

Resistance to doxycycline was due to *tet*, singly or in combination with other factors. The sensitivities of WGS prediction of resistance to doxycycline and tetracycline were 97.0% and 99.5%, respectively, but the respective specificities were only 81.0% and 71.0. Two reasons for discrepancies were identified: errors in phenotypic susceptibility testing (resistant by Vitek but susceptible by E-test) and silencing of *tet* genes which were nonetheless detected by WGS.

The sensitivity of WGS for detection of high-level resistance to gentamicin (MIC, >512 μg/mL) was 96.8%, while the specificity was only 82.2%. The latter was the result of MICs below the breakpoint threshold despite the presence of aminoglycoside resistance genes. Focusing on isolates with MICs ≥32 μg/mL the identification of silenced aminoglycoside resistance genes.

The specificities of WGS for daptomycin (93.9%), tigecycline (99.7%), and linezolid (98.3%) were high, but sensitivities were

remarkably low at 73.6%, 38.3%, and 58.5%, respectively. The latter largely resulted from a relatively inadequate knowledge of the genetic causes of resistance to these antibiotics.

Among the significant findings in this extensive study that affected the results were the detection of inactive *van* operon variants, truncated gene variants (eg, frame shift mutations in *tet*), and other factors. Simple detection of AMR genes may be inadequate—attention must extend to their functionality. A very important observation is that use of genetic methods to predict resistance is obviously dependent on accurate and complete knowledge of AMR mechanisms. Finally, susceptibility/resistance is often nonbinary and often exists along a continuum around critical antibiotic concentrations.

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