LETTER TO THE EDITOR

RARE COMBINATION OF INFECTIVE ENDOCARDITIS IN A DRUG ABUSER WITH HENOCH-SCHOENLEIN PURPURA

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To the Editor,

The course of infective endocarditis (IE) is frequently complicated by heart failure (HF), uncontrolled infection, embolic events, infectious aneurysms, acute renal failure, rheumatic complications, splenic abscess, myocarditis, pericarditis, etc (1). Henoch-Schonlein purpura (HSP) is very rare in IE. The aim of the paper is to present a case with such a combination and to suggest possible practical implications.

Case report

A twenty-nine-year-old female with a history of drug abuse (heroine, methadone) was admitted because of dyspnea, fever, cough and arthralgia, to the Department of Pulmonology. Her prior medical history includes Hepatitis C. The chest X-ray showed diminished transparency in medium and lower lung fields, abscess apically and shadows in costophrenic sinuses, as well as very enlarged cardiac silhouette. A multi-slice computer tomography revealed pneumonia with multiple abscesses as well as both pleural and pericardial effusions, without signs of pulmonary embolism. Her laboratory values were as follows: WBC 9.6 $x10^9$/L (normal range, NR 4.0-9.0); RBC 2.5$x10^{12}$/L (NR 3.80-5.30); Hgb 99g/L(NR 110-170); Hct 31% (NR 36-56); Plt 274$x10^9$/L (NR 120-380); Creatinine 103.2µmol/L (NR 53.0-115.0); BUN 12mmol/L (NR 2.5-7.5); Glycemia 7.9mmol/L (NR 3.9-6.1); AST 51U/L (NR 10-31); ALT 32.8U/L (NR 10-32); LDH 589.4U/L (NR 220-450); CRP 108mg/L (NR 0.0-5.0); Proteins 56.4g/L (NR 62.0-81.0) Albumins 23.5g/L (NR 35-52); Procalcitonine (PCT) 118ng/mL (NR 0.0-0.05); D-dimer 1761µg/L (NR <550); Brain natriuretic peptide (BNP) 4432pg/mL (NR 0.0-100.0).

Klebsiella was identified in sputum, Acinetobacter and Klebsiella in repeated blood cultures and Enterobacter in urine cultures. Blood gases showed: pH 7.18; $PaCO_2$ 18mmHg; HCO_3 6.7mmol/L; BE -19.8mmol/L; PaO_2 100mmHg; SpO_2 96%. She was treated with antibiotics according to antibiogram (including: meropenem, vancomycine, levofloxacin, metronidazole).

Her clinical course was complicated by an acute kidney injury (BUN concentration up to 24.3mmol/L, Creatinine up to 504.4µmol/L, acidosis). Meanwhile, the echocardiogram showed verrucae on the tricuspid

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valve (dimension 14.9mm x 5.3mm) accompanied by severe tricuspid regurgitations (right ventricular systolic pressure 46 mmHg). The left ventricle (LV) was slightly enlarged with preserved ejection fraction (58%); moderate to severe aortic and mitral regurgitation were also present. Pericarditis was confirmed (maximum 13 mm in diastole).

IE was diagnosed according to Duke`s criteria: two major (verrucae confirmed with the echocardiography and positive blood cultures) and two minor criteria (intravenous drug abuse, fever). The patient was transferred to the Cardiology Department and continued to receive antibiotics as suggested by antibiogram (including: meropenem, vancomycin, levofloxacin, metronidazole, doxicyclin and cilastatin) together with fluconazole, eubiotic and corticosteroids.

Solid LV contractility allowed an intensive volume load and the renal function improved (BUN 10.0mmol/L; Creatinine decreased from 504.4μmol/L to 93.7μmol/L at discharge). During the further clinical course, the size of verrucae on the tricuspid valve had diminished (dimension 11mm x 7mm) (Fig. 1).

On the 13th day purpuric lesions became obvious on her hands, trunk and legs (Fig. 2). The clinical picture, confirmed by histopathology, and presence of symptoms of arthritis and kidney disease, confirmed the diagnosis of HSP.

The patient was discharged without visible verrucae both by echocardiography and MRI, with mild tricuspid and mitral regurgitation, without aortic insufficiency, and with discrete pericardial effusion. Blood cultures were negative. Laboratory values at discharge were: Troponin 13ng/L (NR 0.0-40ng/L), BNP 82.2pg/mL (reduced from 4432pg/mL), CRP 0.9mg/L, PCT 0.19ng/mL (diminished from 118ng/mL).

DISCUSSION

We have presented a patient with severe dominantly right-sided IE, typical for intravenous drug abusers, complicated by heart and renal failure. Underlying causative agents Klebsiella and Acinetobacter belong to the Gramm-negative group of non-HACEK (Haemophilus species, Actinobacillus, Cardiobacterium, Eikenella and Kingella species) microorganisms that are less common causes of IE,

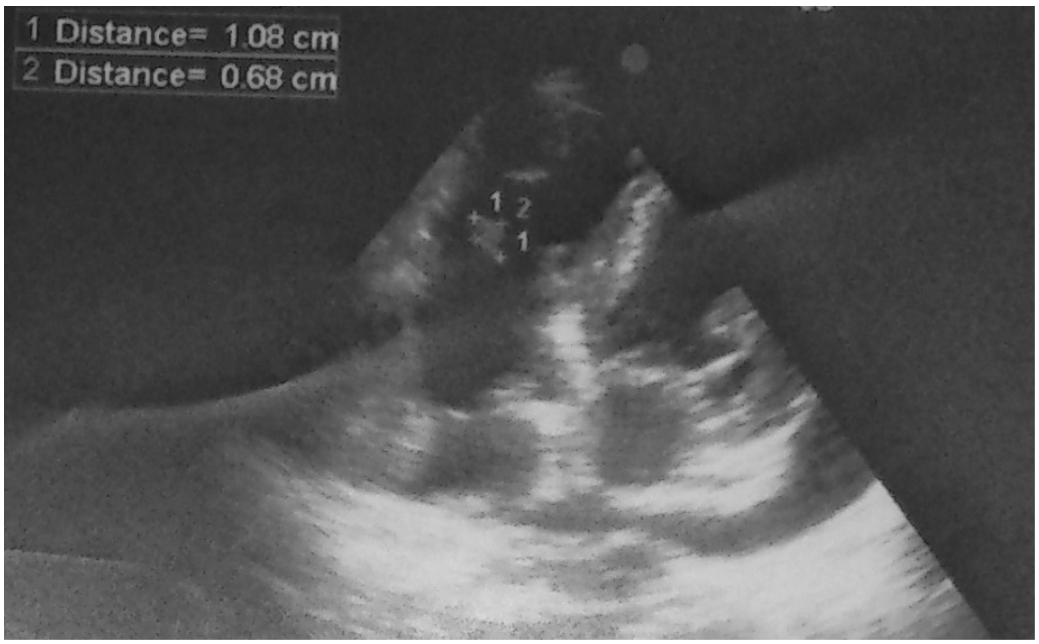

Fig. 1. *Verrucae on the tricuspid valve (dimension 11mm x 7mm), accompanied by severe tricuspid regurgitation.*

even in drug abusers (2). An uncommon feature in IE in our patient was the clinical finding of vasculitis. The distribution of the rash with typical palpabile purpura in this case, was similar to that seen in classic HSP. It is primarily a childhood disease that is typically self-limited, but 10% of the cases occur in adults, when features and outcomes may vary. HSP is usually a hypersensitive reaction to bacteria (streptococcae or mycoplasma pneumoniae) or viruses, but some drugs may also act as antigens. HSP is usually associated with arthritis, nephritis, gastrointestinal disorders, and sometimes with lung hemorrhage, and respiratory tract infection may precede its onset. Purpuric lesions usually appear on the legs and buttocks, but may also be seen on the arms, face and trunk, as in the case of our patient.

The association of IE and HSP has been reported only in a few patients in the medical literature (3-6). None of them was an intravenous drug abuser, nor had other relevant microbiological features and comorbidities, which makes our case unique. The literature search revealed only one case report of cutaneous rash due to leukocytoclastic vasculitis associated with pneumonia caused by Klebsiella pneumoniae (7) and no similar cases of vasculitis associated with Acinetobacter or Enterobacter infection.

IE patients frequently exhibit positive ANCA tests (Antineutrophil cytoplasmic antibodies directed against proteinase-3 ANCA-PR3 or myeloperoxidase–ANCA-MPO) and mimic ANCA-associated vasculitis (8). In a recent study, 18% of patients with IE had cytoplasmic ANCAs and/or perinuclear ANCAs and 8% had PR3-ANCAs or MPO-ANCAs, some with very high titers (8). There is evidence of their association with prolonged bacterial or Hepatitis C virus (HCV) infection and heroin addiction in patients with IE. Cutaneous and renal blood vessel vasculitis in ANCA-positive patients with IE is frequent but not consistent. In patients with persistently normal levels of alanil transferase and serological evidence of HCV infection, both polyclonal IgG and either polyclonal or monoclonal IgM rheumatoid factor (RF) (mixed cryoglobulinemia), could be found. HCV exerts a chronic stimulus on the immune system, which may lead to the proliferation of B cell clones producing IgM with RF activity. In 10-42% of the patients, cryoglobulins were associated with a systemic vasculitic disorder of the small and, less frequently, medium-sized arteries and veins. It is

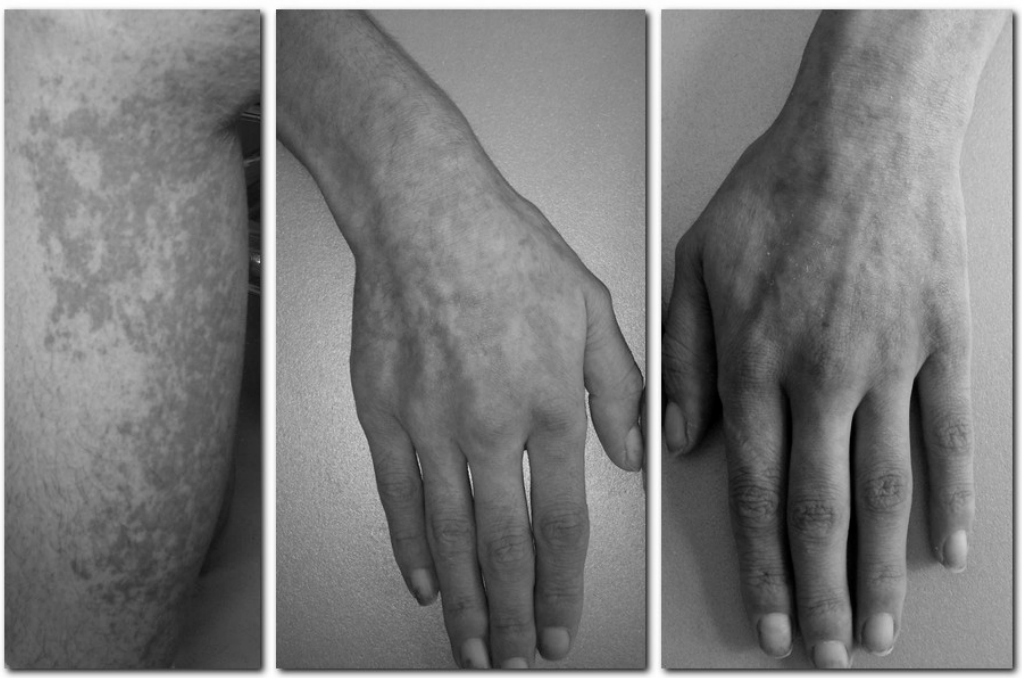

Fig. 2. *Typical palpable purpuric lesions on buttocks and dorsal side of hands.*

characterized by the deposition of immune complexes containing the RF, IgG, HCV RNA, and complement on endothelial surfaces, eliciting vascular inflammation with clinical signs as palpable purpura similar to HSP, renal involvement, arthropathy, peripheral neuropathy or Raynaud phenomenon.

Renal lesions in IE can range from microscopic hematuria to glomerulonephritis and acute kidney injury. Acute renal failure occurs in approximately one-third of IE patients and predicts a poor outcome. Causes are numerous: immune complex and vasculitic glomerulonephritis, renal infarction, hemodynamic impairment due to HF, severe sepsis, or after cardiac surgery, antibiotic toxicity (acute interstitial nephritis), notably related to aminoglycosides, vancomycin and even high dosage of penicillin, nephrotoxicity of contrast agents used for imaging (1).

In the presented case, renal insufficiency was probably the result of a complex interplay of infection, IE itself, hemodynamic compromise in HF, toxicity of antibiotics and immunologic changes in kidney vessel walls induced by immune dysregulation due to HCV-induced crioglobulinemia, ANCA vasculitis, and heroin addiction (9). In our case, the aggressive steroid therapy led to complete renal recovery and disappearance of cutaneous purpuric lesions, which is a regular treatment of purpura.

We report an exceptionally rare case of IE with HSP. This association represents an additional threat to the renal function and warrants its close follow-up, together with the minimization of drugs that are potentially nephrotoxic. Likewise, the onset of HSP may be an alarming sign for searching for possible causes and comorbidities other than those usually expected.

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