

FEBRILE SYNDROME IN THE DIABETIC ADULT, A DIAGNOSTIC TRAP

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Rezumat

Introducere. Diabetul zaharat este una dintre cele mai frecvente patologii ce afectează populația generală în epoca modernă, infecțiile constituind unul dintre motivele prezentării pacientului diabetic la diverse camere de gardă. Pacientul diabetic poate dezvolta infecții cu germeni și localizări variate, ce au tendință de recurență și de evoluție nefavorabilă, comparativ cu populația generală.

Prezentare de caz. Pacientă, 71 ani, diabetică și cu patologie cardiovasculară importantă, se internează pentru sindrom febril persistent după 7 zile de antibioterapie recomandată pentru intercurență respiratorie. Fusese evaluată recent neurochirurgical pentru durere lombară; radiologic se decelase tasare corpi vertebrali T12-L1, neurochirurgul opinând că intervenția chirurgicală este nerecomandată din cauza patologiei asociate. Clinic se remarcă stare generală gravă, febră, pulmonar: raluri subcrepitante bazal bilateral, TA=100/60 mmHg, AV=100/min neregulat. Biologic s-au decelat leucocitoză cu neutrofilie, sindrom inflamator cu procalcitonină crescută, hiperglicemie, retenție azotată; radiografia toracică arăta stază, iar ecocardiografia FE 25%. Examinarea clinică completă decela abces inghinal drept, care a evoluat lent favorabil după drenaj și antibioterapie conform antibiogramei (hemocultură cu stafilococ, cultură din plagă cu E.Coli). După 2 săptămâni, antibioterapia s-a sistat deoarece evoluția clinică și paraclinică erau net favorabile; după 24 de ore pacienta redevine febrilă, reapar leucocitoza și sindromul inflamator, fără alte modificări clinice. S-a refăcut bilanțul infecțios: culturi din plagă-sterile, urocultură-sterilă, fără vegetații valvulare ecocardiografic, CT toraco-abdomino-pelvin - aspect sugestiv pentru spondilodiscită T12-L1.

Concluzii. Diagnosticul etiologic al sindromului febril la pacientul diabetic poate fi extrem de dificil în practică. În cazul nostru, pacienta nu remarcase prezența abcesului inghinal și, în plus, durerea lombară (care o imobilizase la pat) reprezenta un important semn de alarmă, ușor de ignorat în contextul infecțios evident.

Cuvinte cheie: diabet zaharat, febră, infecție, spondilodiscită.



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Abstract

Introduction. Diabetes mellitus is one of the most frequent pathologies that affect the general population in the modern era, infections being one of the main reasons why the diabetic patient will present to an emergency room. The diabetic patient can develop infections with various germs and locations, that have a tendency to reoccur and have an unfavourable evolution compared to the general population.

Case report. A 71 year old female patient, diabetic and with significant cardiovascular pathology is admitted with a persistent febrile syndrome after 7 days on antibiotic treatment for respiratory infection. She had recently had a neurosurgical evaluation for lumbar pain; radiology had shown a compression of the T12-L1 vertebral bodies, the neurosurgeon stating that surgery was not recommended because of the associated pathologies. Clinical examination reveals a poor general state, fever, pulmonary: bilateral basal subcrepitant rales, BP = 100/60 mmHg, AV = 100 BPM irregular. Blood work showed: leucocytosis with neutrophilia, inflammatory syndrome with high procalcitonin levels, hyperglycaemia, nitrogen retention; chest X-ray shows stasis and the echocardiography EF 25%. The complete clinical examination detected a right inguinal abscess, that had a slow, favourable evolution after drainage and antibiotic therapy according to the antimicrobial susceptibility testing (AST) (blood culture with staph, wound culture with E.Coli). After 2 weeks, the antibiotic therapy was discontinued because of the favourable clinical and lab work evolution; after 24 hours the patient is febrile again, the leucocytosis and inflammatory syndrome reappear without any other clinical changes. The infectious assessment was redone: sterile wound cultures, sterile urine cultures, no valvular vegetation on echocardiography, a CT of the chest, abdomen and pelvic area suggestive for T12-L1 spondylodiscitis.

Conclusions. The etiological diagnosis of the febrile syndrome in a diabetic patient can be extremely difficult in practice. In our case, the patient had not noticed the inguinal abscess and the lumbar pain (that restrained her to bed) represented an important sign, easily ignored in the obvious infectious context.

Keywords: diabetes mellitus, fever, infection, spondylodiscitis.

Introduction

Diabetes mellitus is one of the most frequent pathologies that affect the general population in the modern era, representing one of the main mortality causes, alongside cardiovascular diseases and cancer. Infections are one of the main reasons why the diabetic patient will present himself and be admitted to an emergency room. Alongside rare and extremely severe infections like emphysematous pyelonephritis, malignant otitis externa and rhinocerebral mucormycosis, the diabetic patient can develop infections with various germs and locations, that have a tendency to reoccur and have an unfavourable evolution compared to the general population⁽¹⁾.

Case description

A 71 year old female patient, whose medical history included insulin-dependent type 2 diabetes with nephropathy complications, stage IV peripheral arterial disease (amputated left calf), significant cardiovascular pathology - acute myocardial infarction with multiple stenting, permanent atrial fibrillation and heart failure with oxygen therapy at home, outpatient treatment with digoxin, betablocker, loop diuretic, coumarinic oral anticoagulant and a statin, initially presented to the emergency room of an Emergency Care Hospital because of a general altered state, fever, shortness of breath. Because of the lack of hospital beds she was directed to the Colentina Clinical Hospital.

The time since the onset of her current history was of approximately 10 days and was initially accompanied by cough with mucopurulent expectoration. Her general practitioner had recommended antibiotic therapy, but a week later, the patient presented to the emergency room because of the persisting

symptomatology. The laboratory examinations done in the Emergency Admission Unit showed leucocytosis with neutrophilia and inflammatory syndrome; the EKG revealed atrial fibrillation, the echocardiography detected a left ventricle ejection fraction of 25%, akinetic interventricular septum, hypokinesia, PAPs 60 mmHg, and the chest X-ray revealed an enlarged heart and pulmonary stasis. On admission to our clinic, the patient had an altered general state, was febrile, with dehydrated skin and mucosa, the pulmonary examination revealed bilateral basal subcrepitant rales, SaO₂ with oxygen therapy through the nostrils (3 l/minute) was at 94%, she was tachycardic with an AV 121 BPM, irregular hearts sounds, no detectable murmurs, BP = 100/60 mmHg, without any other significant pathological changes on clinical examination. Blood work confirmed the presence of leucocytosis with neutrophilia and inflammatory syndrome, with high procalcitonin levels, but also hyperglycaemia and nitrogen retention.

After retrieving the patient from the emergency room, the medical history and the clinical examination were reassessed and revealed a right inguinal abscess spontaneously drained; from the patient's reports we learned that she had a secretion that stained her underwear, which she considered to be urinary incontinence. The surgeon incised the abscess, and drained it; macroscopically, the fluid was purulent and fetid, which is why empirical antibiotic therapy was initiated at the recommendation of the infectious disease physician, followed by an adjustment of the antibiotic regimen depending on the bacteriological results of the wound culture. Concurrently, blood cultures were done - one of the identified *Staphylococcus aureus*; in the wound we found the presence of *Escherichia Coli*. In this context, the infectious disease physician



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considered that the sepsis had a cutaneous point of origin and recommended Vancomycin, Imipenem and Metronidazole therapy, adjusting the doses depending on her creatinine clearance rate and monitoring her; concurrently, the balance of electrolyte levels was restored, proper insulin therapy was administered and her background treatment was continued.

After two weeks, the patient's general condition improved significantly, she was afebrile, the inguinal abscess was evolving favourably, laboratory tests showed that the leucocytosis and inflammatory syndrome were subsiding, which is why the infectious disease physician considered it an opportune moment to discontinue the antibiotic therapy, with monitoring of the patient. 24 hours later the fever reappeared, the leucocytosis and inflammatory syndrome were rising, so a more extensive assessment was done to identify an infectious disease - urine culture, wound culture, echocardiography; it was negative.

Reviewing the medical history, we learned that the febrile syndrome initially began 2-3 days after the patient had been evaluated in an outpatient facility by a neurosurgeon for mechanical back pain that was present for at least several weeks; the X-ray taken at the time revealed compression of the T12-L1 vertebrae. Considering the reoccurrence of the fever and the patient's condition, it was considered useful to perform a CT of the chest, abdomen and pelvic regions (without contrast because of the renal involvement) that detected an aspect suggestive for T12-L1

spondylodiscitis. The neurosurgeon recommended continuing the antibiotic treatment for at least 6 more weeks, with reassessment, considering that a possible surgery was extremely risky, because of the severe pre-existing pathologies.

Discussions

Literature data show that diabetes mellitus is associated with a high risk of infections; among these stand out urinary tract infections and sepsis, skin infections and pneumoniae⁽¹⁾. It seems that the presence of comorbidities and complications, especially ones such as sensory neuropathy and constant hyperglycaemia are risk factors for infection in diabetic patients⁽²⁻⁴⁾. The pathogenic mechanism is complex, and the decrease in the innate immune response plays a part - the alteration of the neutrophils' function due to hyperglycaemia⁽⁵⁾. Furthermore, it's been proven that a colonisation of the skin and mucosa with *Staphylococcus aureus*, often methicillin-resistant, exists in diabetic patients; small injuries and insulin administration are favourable conditions for developing infections, locally and at a distance - through transitional bacteria⁽⁶⁾. Our patient had *Staphylococcus aureus* present in her blood work, probably secondary to a skin colonization, and also an inguinal abscess with *E.Coli*, from a probable digestive source, an infection that appeared secondarily from a minor injury (from her underwear) in a bedridden patient with diabetes and multiple

complications and comorbidities. One of the most common infections in diabetic patients compared with the general population is osteomyelitis⁽⁷⁾. For that matter, diabetes mellitus, along with other immunosuppressive illnesses, corticosteroid therapy, administering IV medication and spinal surgery are risk factors for spondylodiscitis. The disease affects mostly people over the age on 50, diagnosed predominantly in males (M/F sex ratio=2/1)⁽⁸⁾. 50% of the cases diagnosed with spondylodiscitis in the general population are caused by the infection with *Staphylococcus aureus* by way of blood-borne infections mostly⁽⁹⁻¹¹⁾. Diagnosing spondylodiscitis is a real challenge in practice, because the initial symptomatology can be represented by pain that subsides with rest - pain that is almost typical with the most common rheumatologic disorder in the elderly - arthrosis.

The pain gradually increases within weeks, even months up to the moment of diagnosis⁽¹²⁾. Furthermore, less than half of the patients with spondylodiscitis are feverish, especially during the onset of the disease⁽¹³⁾. In a spondylodiscitis suspected patient, a very careful clinical examination has to be performed, to evaluate the existence of any risk factors, suggestive lab work (leucocytosis, inflammatory syndrome), afterwards performing imaging scans - X-rays, MRIs, CT scans, concurrently with extensive bacteriological tests to identify the responsible germ⁽¹⁴⁻¹⁶⁾. If the blood cultures reveal a germ that is often involved in spondylodiscitis, such as *Staphylococcus aureus*, it is not necessary to perform a CT guided biopsy at the vertebral lesion for a certain diagnosis (according to *UpToDate 2018*)⁽¹⁷⁾. The antibiotic treatment must be immediately initiated, first empirically, afterwards depending on the result of the bacteriological examination and antimicrobial susceptibility testing; the recommended duration of the treatment is at least 6 weeks, depending on the evolution, existing comorbidities, associated neurological complications^(18,19). The current prognosis for

spondylodiscitis is marked by the reoccurrence of the symptomatology in up to a third of cases, with a mortality rate of approximately 10% according to literature⁽²⁰⁾. The risk factors for an unfavourable outcome and death are: delayed diagnosis, neurological complications, infections with *Staphylococcus aureus*, but also existing comorbidities - diabetes mellitus, liver cirrhosis, cancer, advanced chronic kidney disease^(20,21). In our case, the diagnosis was delayed - technically, the onset of the back pain was at least 2 weeks prior to admission to the clinic, she had blood cultures positive for *Staphylococcus aureus* and presented multiple comorbidities, among which diabetes mellitus with nephropathy.

Conclusions

The etiological diagnosis of the febrile syndrome in a diabetic patient can be extremely difficult in practice, often requiring a multidisciplinary evaluation. Once again, we notice the importance of an extremely thorough and targeted medical history and especially of a complete clinical examination, difficult to conduct in a patient that has multiple comorbidities. Even though the diagnosis seems obvious in the ER, our case illustrated the extent of the bacterial spectrum that can occur in a diabetic patient, that needed extensive lab work. Fever associated with lumbar pain is a red flag, especially in a patient with a immunosuppressive disease.

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