A Rare Complication of Orbital Cellulitis in a Diabetic Case: Cavernous Sinus Thrombosis

Diyabetik Bir Olguda Orbital Sellülitin Nadir Bir Komplikasyonu: Kavernöz Sinüs Trombozu

Betül EKİZ BİLİR,¹ Bülent BİLİR,² Mücahit DOĞRÜ,³ Evrim POLAT,⁴ Neslihan SOYSAL ATİLE,¹ İbrahim YILMAZ⁵

¹Department of Endocrinology, Republic of Turkey Ministry of Health State Hospital, Tekirdağ, Turkey
²Department of Internal Medicine, Namik Kemal University Faculty of Medicine, Tekirdağ, Turkey
³Department of Radiology, Namik Kemal University Faculty of Medicine, Tekirdağ, Turkey
⁴Department of Ophthalmology, Republic of Turkey Ministry of Health State Hospital, Tekirdağ, Turkey
⁵Department of Pharmacovigilance and Rational Drug Use Team, Republic of Turkey Ministry of Health State Hospital, Tekirdağ, Turkey

Summary

It is that diabetes mellitus increases tendency to develop infections and thrombosis. Impairment of various mechanisms and agents of humoral and cellular immune systems can be expected. Disturbances of platelet function, coagulation factors, and vascular structure predispose diabetics to thrombotic events. The course of both infections and thrombotic events is often worse than in non-diabetic patients. Presently described is 94-year-old male patient with diabetes who had orbital cellulitis that became complicated with cavernous sinus thrombosis (CST). He was admitted to endocrinology clinic with diagnoses of orbital cellulitis, urinary tract infection, hyperosmolar non-ketotic state, acute renal failure, and compensated metabolic acidosis secondary to uremia. Despite immediate antibiotic therapy, hydration, and additional required treatment, patient did not respond and died as a result of CST. There must be awareness, especially for diabetic patients, that orbital infections may spread to nearby cavernous sinuses and cause potentially lethal septic CST. Early diagnosis and immediate treatment are essential.

Keywords: Cavernous sinus thrombosis; diabetes mellitus; orbital cellulitis; rational antibiotic use.

Özet


Anahtar sözcükler: Kavernöz sinüs trombozu; diyabetes mellitus; orbital sellülit; akılcı antibiyotik kullanımı.
Introduction

Diabetes mellitus (DM) has become an epidemic disease and is characterized by increased morbidity, mortality, and healthcare expenses.[1]

DM, classified among chronic diseases, is a global disease threatening almost every age group. In 2010, incidence of adult diabetes was reported at 13.7 percent in this country.[2] In 2013, worldwide total of diabetic patients reported was 362 million, and that year, 5.1 million of those patients lost their lives as result of diabetes and its complications.[3] According to Public Health Institute of Turkey, there were 7 million cases of DM in the country in 2014.[4]

Cavernous sinus thrombosis (CST) is a life-threatening event. Infection is most frequent etiological factor, and in rare instances, probable association with DM has been indicated.[5–7]

Presently described is case of diabetic patient with rarely seen orbital cellulitis and complication of CST.

Case Report

Presently described is report of 94-year-old male patient with history of previous ischemic cerebrovascular disease without sequelae and 20 years of diabetes. He indicated that he did not use antidiabetic drugs. Patient had experienced nausea, vomiting, and inability to eat for 4 days and was diagnosed at another health center with urinary tract infection. Oral ciprofloxacin (1000 mg/d) treatment was initiated; however, due to lack of any improvement after 2 days of antibiotherapy, he was referred to emergency service of our secondary care hospital.

In initial examination, arterial blood pressure (100/60 mm Hg), body temperature (36.6°C), and peak heart rate (90 beats/min) were measured and recorded. Patient was conscious, cooperative, and oriented. Thyroid was nonpalpable, heart rate was rhythmic, and no additional sound or murmur was detected. Respiratory tract examination revealed end-inspiratory crepitant rales over left basal pulmonary segment. Abdominal guarding and tenderness were not seen. Pretibial pitting edema (1+) was noted. Conjunctival edema, hyperemia, and chemosis of right eye were observed; however patient did not report any change in visual acuity.

Patient was hospitalized in endocrinology department with initial diagnoses of hyperosmolar non-ketotic disorder, compensated metabolic acidosis secondary to uremia, urinary tract infection, orbital cellulitis, and acute renal failure. Insulin infusion and hydration were initiated, and intermittent oxygen therapy was provided. Blood and urine samples were obtained for antibiotic susceptibility tests.

Table 1. Primary analysis of the patient

<table>
<thead>
<tr>
<th>Biochemical, hormonal parameters, and hemogram</th>
<th>Arterial blood gas</th>
<th>Complete urinalysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-reactive protein 55 mg/L</td>
<td>pH 7.36</td>
<td>Ketone: negative</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate 20 mm/hr</td>
<td>pCO2 25.6 mmHg</td>
<td>Glucose 2 (+)</td>
</tr>
<tr>
<td>Erythrocyte 6100/mcl</td>
<td>pO2 47.6 mmHg</td>
<td>Protein (+)</td>
</tr>
<tr>
<td>Hemoglobin 15.43 gr/dL</td>
<td>sO2 90.3%</td>
<td>12-13 WBC</td>
</tr>
<tr>
<td>Hematocrit 48.1%</td>
<td>HCO3 16.7 mmol/L</td>
<td>Nitrite (–)</td>
</tr>
<tr>
<td>Plt 136000/mcl</td>
<td></td>
<td>Leukocyte esterase 2 (+)</td>
</tr>
<tr>
<td>Glucose 568 mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urea 120 mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine 1.77 mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted sodium 135 mEq/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma osmolarity 312 mosm/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total bilirubin 0.9 mg/dl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase 23 U/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alkaline phosphatase 475 U/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gamma-glutamyl transferase 147 U/L</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results of biochemical analysis included total protein 4.42 gr/dL, albumin 2.78 gr/dL, erythrocyte sedimentation rate: 20 mm/hr, glycated hemoglobin 12.3%, and levels of serum sodium, potassium, and chlorine were within normal limits. Creatinine level increased while in care to 2.96 mg/dL and fluid therapy was pursued. Urine culture was positive for Escherichia coli (100,000 CFU/mL) resistant to ciprofloxacin; no bacterial growth was detected in blood culture. Biochemical analysis results are summarized in Table 1.

Abdominal ultrasound revealed presence of stage 2 hepatic steatosis, increase in thickness of gallbladder wall, hyperechogenicities consistent with renal parenchymal disease in right (stage 2) and in left (stage 1-2) kidney, a few simple cysts in left (max. 63 mm) and right (max. 56 mm) kidney, microcalculi in right kidney, and cystaloid echogenicities in renal collecting system. Acute renal failure developing from chronic renal failure was determined.

Patient complained of decrease in visual acuity of the right eye on second day of follow-up, and eye pain, redness, and swollen eyelids were observed. Patient could see to count fingers at a distance of 1 m with right eye and 0.5 m with left eye in ophthalmological examination. Right eyelid and periorbital soft tissue were edematous and hyperemic. Movement of right eye was restricted in all directions. Movement of left eye was unrestricted. Right eye was negative for reaction to direct light and left eye was positive. Relative afferent pupillary defect was detected on right side. On biomicroscopic examination, right conjunctiva was intensely and completely chemotic and hyperemic, cornea was lucid, and bilateral nuclear cataract (based on Lens Opacities Classification System III) was detected. Intraocular pressure was normotonic. Examination of fundus revealed vascular tortuosity on right side. Optic disc on right side showed bulging with indistinct contours. Fundus signs of left eye were within physiological limits.

Based on evaluations of ophthalmologist and specialist in infectious diseases, initial diagnosis of orbital cellulitis was made and intravenous (IV) treatment of metronidazole (2000 mg/d) plus ceftriaxone (2000 mg/d), and topical ofloxacin (5x1 drop/d) was initiated. Orbital magnetic resonance imaging (MRI) was also requested.

On the second day of treatment, metabolic acidosis was relieved; insulin infusion was discontinued and replaced with basal+bolus insulin regimen administered 4 times a day. IV antibiotherapy was changed to imipenem plus cilastin. Upon further restriction of eye movement, ophthalmologist was requested to evaluate results of imaging. MRI revealed changes in signal intensities, increased thickness with edema, and inflammation of right retro-orbital conal and extraconal fat planes, periorbital cutaneous, and subcutaneous layers consistent with orbital cellulitis. In addition, mild increase in thickness of retro-orbital ocular muscles, and edematous appearance compared with contralateral counterpart, and some loss of signal intensity in superolateral part of right cavernous sinus (suspect thrombus) were detected. Increased mucosal thickness
in right half of right ethmoidal air cells, sphenoid sinus, and in right maxillary sinus suggested sinusitis, which restricted aeration, and patchy areas of mucus retention cysts were interpreted as complications that developed secondary to neighboring sinusitis (Figure 1).

Fundus examination performed on fifth day, when visual acuity of the patient had decreased such that he could only count fingers at a distance of <50 cm, revealed papilledema and increased vascular tortuosity. Contrast-enhanced cerebral MR venography was requested with thought that thrombosis might develop secondary to cavernous sinus infection with orbital cellulitis. A prominent filling defect consistent with thrombus in right cavernous sinus was detected (Figure 2).

Consultation with department of neurology was requested. Since heparin with proteoglycan structure (C12H19NO20S3) could not be administered to treat thrombosis because of advanced age of the patient, subcutaneous injection of low-molecular weight heparin, enoxaparin sodium (12,000 IU/d), was recommended as thrombolytic agent. No bacterial growth was detected in blood culture, and after consultation with rational antibiotic use team, combination of carbapenem group of beta-lactam antibiotic imipenem (1000 mg/d), an inhibitor of cell wall synthesis, and cilastatin sodium, a renal dipeptidase dehydropeptidase inhibitor, was replaced with glycopeptide antibiotic vancomycin (1000 mg/72 hr), another inhibitor of cell wall synthesis.

On sixth day of hospitalization, when he received first dose of this treatment regimen, patient developed nosebleed, cloudy consciousness, and hypoglycemia, followed by fatal cardiac arrest.

Written, informed consent was obtained from the sons of the patient when preparing this case report.

**Discussion**

CST, which can appear at any age, is the most critical intracranial septic thrombosis because of complex nervous, vascular, and anatomical relationships. It can be a long-term complication of midfacial or paranasal sinus infections and has high mortality and morbidity rates. *Staphylococcus aureus* is the responsible pathogen in 70% of cases, while *Streptococcus pneumoniae*, gram-negative bacilli, anaerobes, and fungi such as *Aspergillus* sp. or *Rhizopus* sp. may also be etiological agents. Until effective antimicrobial agents were more widely available, mortality rate for CST was 100%; however, now mortality rate has dropped to 30% with early diagnosis and accurate treatment. Mortality generally occurs as an outcome of sepsis or nervous system infection.

Symptoms may have acute, subacute, or chronic onset. Morbidity rate remains high, and complete cure is not generally observed. One-sixth of cases face visual impairment, and half of patients suffer from disorders of cranial nerves. Although CST can develop in a completely healthy individual secondary to infection, patients with diabetes, chronic sinusitis, or depressed immune system are particularly at risk.

Contrast-enhanced cranial tomography or MRI is used for diagnosis. Lack of venous blood (void signal) flow is also very helpful in making diagnosis. Despite name of cavernous sinus thrombosis, first treatment procedure should be institution of appropriate antimicrobial therapy at early stage, rather than thrombolytic agent.
Broad-spectrum antibiotic effective on gram-negative and gram-positive aerobics and anaerobics should be preferred course while waiting for results of antibiotics. Based on results, proper IV antimicrobial drugs effective on bacteria grown in the culture should be selected and treatment should last for 3 to 4 weeks.

Various mechanisms have been proposed to explain increased tendency for infection in diabetic patients. Some infections are seen more frequently in diabetic cases, while some others are seen only in diabetics. Some infections lead a more serious course in diabetic cases and become complicated at a higher rate.

Preseptal (peri-orbital) cellulitis and orbital (post-septal) cellulitis are the 2 main orbital infections. Preseptal cellulitis is more frequent, but orbital cellulitis is more dangerous. Orbital cellulitis may stem from external infection focus, such as skin wound, extension from nasal sinuses, or dental infections, or may be endogenous spread of infection originating in any region of the body. They are seen more often in pediatric age group than adults.

Diagnosis of orbital cellulitis is based on anamnesis, physical examination, and imaging methods (CT, MRI). It can manifest with presentation of eye pain, discoloration, swelling, fever, limitation of eye movement, proptosis, or decrease in visual acuity; however, primary symptoms are proptosis and ophthalmoplegia. It may cause intracranial complications as meningitis, CST, or development of abscesses.

In conclusion, CST is an intracranial complication of orbital cellulitis, and high rate of mortality can be reduced with proper, early treatment. Diabetic tendency to activation, aggregation, and coagulation of platelets, as well as to CST, should be remembered. Especially when clinical manifestations progress rapidly (e.g., increase in proptosis, development of mydriasis and pupillary dilatation, dilatation of retinal veins, decrease in visual acuity, presence of CST), orbital cellulitis should be suspected.

Conflict of interest
None declared.

References