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Case Report

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Acute community-acquired meningoencephalitis with Morganella morganii – a case report

Meningoencefalită acută comunitară cu *Morganella morganii* – prezentare de caz

Brindusa Tilea[1], Edit Szekely[2], Simona Teches[1], Ioan Tilea[3]

1. Infectious Diseases, Department M4, Clinical Sciences, Faculty of Medicine, University of Medicine and Pharmacy Tirgu Mures, Romania, 2. Microbiology, Department M2, Functional and Additional Sciences, Faculty of Medicine, University of Medicine and Pharmacy Tirgu Mures, Romania; 3. Family Medicine, Department M3, Clinical Sciences and Internal Medicine, Faculty of Medicine, University of Medicine and Pharmacy Tirgu Mures, Romania

Abstract

Morganella morganii (M. morganii) is a Gram-negative aerobic and facultative anaerobic rod, belonging to the Enterobacteriaceae family. This pathogen is uncommon in community-acquired infections, most often being found in postoperative nosocomial and urinary tract infections. Infection of the central nervous system with this pathogen is rare. We present the case of a 66-year-old patient who underwent colon cancer surgery, chemotherapy and radiotherapy, had left iliac anus, type 2 diabetes and developed acute meningoencephalitis caused by M. morganii. Cerebrospinal fluid examination revealed increased number of polymorphonuclear neutrophils, modified biochemistry and AmpC beta-lactamase producing M. morganii strain. After initiation of antibiotic treatment, initially with empirical therapy represented by meropenem and vancomycin, afterwards adjusted to meropenem and ciprofloxacin, according to the stain's susceptibility to antimicrobials the patient's evolution was favourable, in spite of the existence of two immune suppressing conditions.

Keywords*: meningoencephalitis, M. morganii, immunosuppression, antibiotic therapy*

Rezumat

Morganella morganii (M. morganii) este un bacil Gram negativ aerob, facultativ anaerob ce aparţine familiei Enterobacteriaceae, prezent atât în mediul ambiant cât şi în flora saprofită intestinală. Este considerat un agent patogen rar întâlnit în infecţiile comunitare, fiind mai frecvent identificat în infecţii nozocomiale postoperatorii şi infecţiile de tract urinar. Afectarea sistemului nervos central este rară. Prezentăm cazul unui pacient în vârstă de 66 ani cu neoplasm de colon operat, chimio şi radio tratat, cu anus iliac stâng, diabet zaharat tip II, care a dezvoltat o meningoencefalită acută cu M. morganii. Examenul lichidului cefalorahidian a relevat o citologie crescută constând din polimorfonucleare neutrofile, biochimie modificată şi cultură bogată de M. morganii, o tulpină

***Corresponding author**: Brindusa Tilea , University of Medicine and Pharmacy Tirgu Mures, Romania, e-mail: brindusa_tilea@yahoo.com

secretoare de AmpC beta- lactamază. După instituirea tratamentului antibiotic, inițial empiric cu meropenem și vancomicină, ulterior conform sensibilității germenului, meropenem și ciprofloxacină, evoluția pacientului a fost favorabilă chiar și în condițiile existenței celor două afecțiuni imunodeprimante.

***Cuvinte cheie**: meningoencefalita, M. morganii, imunosupresie, tratament antibiotic*

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Background

Morganella morganii (*M. morganii*) is a Gram-negative bacteria belonging to the Enterobacteriaceae family. It is a conditional pathogen commonly found in soil, water and normal flora of humans and animals (1). *M. morganii*, initially considered as non-pathogenic, was found to be involved in urinary infections especially in elderly patients with long-term indwelling catheters, as well as in postoperative nosocomial infections and as an opportunistic agent in immunocompromised patients with various diseases (neoplasms, blood disorders, diabetes mellitus, infection with human immunodeficiency virus, etc.) (2, 3).

Bacteraemia and systemic infections with *M. morganii* were less frequently reported. Most cases of systemic infections occurred in patients suffering from severe immune deficiency (4, 5, 6). The infection of the central nervous system (CNS) often occurs due to secondary hematogenous dissemination having an otogenic focus of infection (purulent otitis media, otomastoiditis). However, meningoencephalitis caused by *M. morganii* is rarely reported. There are few cases reported in literature (1, 7).

Case presentation

We present the case of a 66-year-old male patient, retired, living in a rural area. In 2007 he was diagnosed with colorectal cancer and underwent surgery, when left-sided colostomy was performed, followed by chemo- and radiotherapy. After one year the patient was diagnosed with insulin-dependent diabetes mellitus. In September 2014, 5 days before admission, the patient complained of insidious symptoms such as fever (not measured), low back pain, abdominal pain, headache, nausea, vomiting, loss of appetite. Initially he was examined by a surgeon who invalidated the diagnosis of acute surgical abdomen based on clinical, imaging and laboratory data and was sent home with the prescription of symptomatic treatment. Abdominal pain was improved but the patient became drowsy, disoriented, confused, agitated and aphasic, therefore being referred to Infectious Disease Clinic. Physical examination on admission revealed general malaise, body temperature of 38.6°C, blood pressure: 140/80 mmHg, heart rate: 130 beats/minute, oxygen saturation (SO_2) 95%, respiratory rate: 25 respirations/minute, congested facial expression and periorbital dark circles. Meningeal irritation syndrome was present, with neck stiffness and positive Kerning 1 and 2 signs. The patient presented the clinical signs of CNS impairment: drowsiness, disorientation, confusion, obnubilation, intermittent agitation, unresponsiveness to verbal stimuli, aphasia and a Glasgow coma scale score of (GCS) 6/7. The patient presented symmetrical deep *tendon reflexes* bilaterally diminished, generally low muscle strength without signs of cranial nerve damage, diminished cutaneous reflexes but the pharyngeal reflexes were present. Auscultation of the lungs revealed bilateral tightened vesicular murmur, tachycardia without heart murmurs. Other symptoms and signs were acetone-like halitosis, diffuse abdominal tenderness in the left abdominal cavity on palpation, left iliac anus, normal stools and left parastomal eventration. Complete

blood count showed: leukocytosis (14,680/ml), thrombocytosis (746,000/ml) with a left shift of the leukocyte formula: 88% segmented, moderate anaemia (Hgb): 10.2 g/dl, increased erythrocyte sedimentation rate (ESR): 115/1h, elevated C-reactive protein (CRP): 225.4 mg/l, increased fibrinogen concentration (1048 mg/dl) and hypokalemia: 2.8 mmol/l. Brain computed tomography scan (CT) highlighted diffuse cerebral atrophy whie the fundoscopy was normal. Lumbar puncture was performed and the collected cerebrospinal fluid (CSF) was purulent, Pandy's reaction markedly positive, shwing pleocytosis, 36,000 leukocytes out of which 95% polymorphonuclear neutrophils (PMNs), 5% lymphocytes, low glucose levels 5 mg/dl (the patient being diabetic the blood sugar level was 210 mg/dl when CSF collected), protein level 225.5 mg/dl and chloride 104 mmol/l. Serum immunoglobulins (IgG, IgM, IgA) and complement components (C3, C4) levels were within normal limits. (Table I)

Bacteriological analysis of the cerebrospinal fluid was performed according to routine proto-

Table I. Evolution of CSF and serum parameters

CSF	**Day – 1**	**Day – 7**	**Day – 14**	**Reference value**
Aspect	Purulent	Slightly opaque	Clear	Clear
Pandy reaction	++++	++	Negative	Negative
Pleocytosis cell/mm^3	36,000 leucocytes	2,400 leucocytes	90 lymphocytes	0-5
Gram stain	95% neutrophils 5% lymphocytes	70% neutrophils 30% lymphocytes	90% lymphocytes 10% neutrophils	
Culture	Positive *Morganella morganii*	Negative	Negative	Negative
Glucose mg/dl	5	10	35	50-55
Proteins mg/dl	270	142	80	15-60
Chloride mmol/l	104	98	100	110-125
SERUM				
White blood cells (10^3/µl)	14.68	12.58	10.03	4-9
Platelets (10^3/µl)	746	610	410	130-360
Neutrophils (%)	88	76	60	54-62
Hemoglobin (g/dl)	10.02	10.0	10.89	12.4-14.9
ESR (mm/1h) Westergren method	115	70	30	<20
C-Reactive protein (mg/l)	225.4	51.3	15	<6
Fibrinogen (mg/dl)	1,048	610	470	200-400
Glucose (mg/dl)	210	100	98	70-100
Urea (mg/dl)	70	50	38.25	7-22
Creatinine (mg/dl)	1.1	0.7	0.76	<1.3
Potassium (mmol/l)	2.8	4	4.3	3.5-5.0
Sodium (mmol/l)	130	134	137	135-145

col. Microscopy of the sediment revealed frequent granulocytes and Gram-negative rods. A *M. morganii* pure culture grew on chocolate and blood agar plates. Identification was carried out on Vitek2 Compact® system (bioMerieux, USA) using GN cards. Antimicrobial susceptibility was tested on AST-N204 cards. EUCAST (European Committee on Antimicrobial Susceptibility Testing) version 4.0 was used for the interpretation of susceptibility results. The strain was resistant to amoxicillin-clavulanic acid, cefotaxime, ceftazidime, and susceptible to cefepime, ertapenem, imipenem, meropenem, amikacin, gentamicin, ciprofloxacin, trimethoprim/ sulfamethoxazol. (Table II)

ESBL (extended spectrum beta-lactamase) production was verified by a double disk method using cefotaxime with and without clavulanic acid and ceftazidime with and without clavulanic acid. The diameter of the inhibition zones around the disks with and without inhibitor was not significantly different, therefore ESBL production was excluded.

AmpC beta-lactamase production was tested by a double disk method using cefotaxime with and without phenylboronic acid and ceftazidime with and without phenylboronic acid. For both 3rd generation cephalosporins the diameters of the inhibition zones have increased with over 5 mm around the disks containing the inhibitor compared to the diameter around the disks without inhibitor, suggesting the presence of an AmpC beta-lactamase.

The presence of family specific plasmid-born *ampC* genes was tested by a multiplex PCR reaction as described by Pérez-Pérez et al (8). A PCR product of 405 bp was detected, corresponding to the DHA type AmpC beta-lactamase encoding gene.

Samples of blood cultures (tested in aerobic and anaerobic environments), urinalysis and stool analysis collected prior to the initiation of antibiotic treatment revealed no bacterial growth. The ENT (ear, nose, throat) specialist found no infectious foci in the patients ears and sinuses. Chest X-ray and electrocardiogram did not show any abnormalities.

Initially, in the first two days the patient was treated with meropenem 5 g/day t.i.d. and vancomycin 2 g/day b.i.d.; on the third day, when the pathogen and its sensitivity were determined, vancomycin was replaced with ciprofloxacin 400 mg/day intravenously b.i.d.. The patient also received immunoglobulins, 5 g/day iv for 3 days, anti-inflammatory steroids (Dexamethasone 16 mg/day iv b.i.d.) for 7 days, Mannitol 20% 125

Table II. Antimicrobial susceptibility tests results of Morganella morganii Vitek2 Compact® method

Sample	***Cerebrospinal fluid***	
Selected organism	***Morganella morganii***	
Phenotype	***AmpC***	
Antibiogram	**Results**	**MIC ug/ml**
Ampicillin	R	>=32
Amoxicillin/ Clavulanic Acid	R	>=32
Piperacillin/ Tazobactam	I	<=4
Cefotaxime	R	16
Ceftazidime	R	32
Cefepime	S	<=1
Ertapenem	S	<=0.5
Imipenem	X	
Meropenem	S	<=0.25
Amikacin	S	<=2
Gentamicin	S	<=1
Ciprofloxacin	S	<=0.25
Norfloxacin	S	<=0.5
Nitrofurantoin	X	
Trimethoprim / sulfamethoxazole	S	<=20
Tigecycline	X	

S – sensitive, I – intermediate sensitive, R – resistant, X – untested
MIC- Minimum Inhibitory Concentration

ml iv b.i.d. for 5 days, Lantus (Insulin glargine) - 24 IU/day, antipyretics as well as iv group B vitamins.

Clinical evolution gradually improved, on the fifth day of treatment the patient regained consciousness and was cooperative. CSF and acute phase reactants (CRP, ESR) changed favourably. On the seventh day of hospitalization CSF pleocytosis was 2,400 leucocytes/mm^3 with 70% PMN's, 30% lymphocytes, increased glucose level 10 mg/dl and negative CSF culture. On the 14th day of hospitalization and treatment the CSF's aspect was clear, 90 lymphocytes/mm^3, negative cultures, biochemistry much improved, acute phase reactants normal but close to the upper limits of the reference range. Antibiotic treatment was stopped after 16 days (Table 1).

Informed consent was obtained from the patient involved in the study.

Discussions

M. morganii is a Gram-negative rod belonging to the Enterobacteriaceae family, being a ubiquitous bacterium of the environment and human intestinal normal flora. *M. morganii* is an opportunistic microbial agent involved in both community-acquired and nosocomial infections. The involvement of this etiologic agent in CNS infections is rare with only few cases being reported in literature (1, 9). The patient whose case we presented developed acute meningoencephalitis with *M. morganii* confirmed by cultivation from the CSF, but not from blood samples collected prior to initiation of antibiotic treatment. The patient was immunosuppressed due to the two underlying conditions: terminal colorectal cancer and type 2 insulin-dependent diabetes. We assume that the meningeal infection appeared due to secondary hematogenous dissemination as the patient was not identified with an otogenic focus of infection, adjacent or remotely located, facts proven by the cranial CT scan and ENT examination. Presumably, the starting point of the initial bacteremia was the digestive tract. Our patient complained of recurrent bowel disorders, normal consistency stools alternating with diarrhoea. Literature specifies that *M. morganii* was more frequently isolated in patients with gastrointestinal problems compared to healthy individuals (10, 11).

In our patient's case, bacteremia was probably transitory and was not identified in blood cultures. In a study involving 2084 cases of bacteremia in the UK, *M. morganii* accounted for only 1% of cases, meaning that it represents a rare cause of bloodstream infections (12).

M. morganii species were more frequently isolated in urinary tract infections in elderly patients with long-term indwelling catheters, the wounds of diabetic patients with necrotizing fasciitis, patients with purulent peritonitis, chorioamniotitis, neonatal sepsis, pneumonia, otitis media, meningitis, brain abscess and in immunocompromised patients (2, 13, 14, 15, 16). We assume that in case of our patient, with terminal colorectal cancer and diabetes mellitus, an imbalance occurred in the saprophytic microflora which led to the dislocation of the bacteria, transient bacteremia and penetration into the CSF. Lee and Liu reported 74 positive blood cultures from 10,639 (0.69%) cases of infections with *M. morganii* over a period of two years in a medical centre in Taiwan (17). In our hospital, during a 5-year period, 7 strains of *M. morganii* were identified (2 from blood cultures, 3 from urine samples and 2 from peritoneal secretions), no isolates being recovered from CSF (unpublished data). This was the first case of acute meningoencephalitis with *M. morganii* isolated from CSF hospitalized and treated in our clinic in the last 20 years (18).

Most of the patients described by Lee and Liu who developed bacteremia with *M. morganii* also presented concomitant diseases, such as neoplastic tumours, diabetes and chronic kid-

ney disease (17). Like other etiological agents of the Enterobacteriaceae family, *M. morganii* has natural resistance to many beta-lactam antibiotics, aminopenicillins, cephalosporins and macrolides from the first and second generations, but it is usually sensitive to aminoglycosides, carbapenems, extended spectrum cephalosporins and fourth generation fluoroquinolones and trimethoprim-sulfamethoxazole (2, 3).

M. morganii can develop resistance to beta-lactam antibiotics through the production of various beta-lactamases, such as ESBL, AmpC beta-lactamases or carbapenemases (19, 20). The *M. morganii* strain isolated from our patient's CSF produced a DHA type plasmid-borne AmpC beta-lactamase.

AmpC beta-lactamases lead to resistance to penicillins, oxymino-cephalosporins, cephamycins and monobactams. AmpC genes are present on the chromosomes of several species belonging to the Enterobacteriaceae family and induce high-level resistance in case of hyperproduction of the enzyme. When associated with porin deficiency, AmpC beta-lactamases may cause decreased susceptibility to carbapenems. The emergence of plasmidic AmpC genes represents a new threat due to the possibility of horizontal gene transfer (21).

Although plasmids carrying AmpC encoding genes often harbour additional resistance genes, our isolate was susceptible to non-β-lactam antibiotics.

To our knowledge, there are no case reports about the involvement of AmpC producing *M. morganii* strains in meningitis. Patil AB et al. presented a case of cerebral abscess caused by a biogroup A strain of *M. morganii* resistant to ampicillin and ofloxacin, which did not produce ESBL or AmpC beta-lactamase (3). Nakazawa T et al. described a case of *M. morganii* meningitis, caused by a bacterial strain resistant only to ampicillin and first generation cephalosporins (1).

The *M. morganii* strain described in this case report presented a susceptibility pattern similar to other strains isolated earlier in our hospital, from different samples.

As molecular analysis was not performed for the previously isolated strains, AmpC production can only be assumed.

Our patient was initially treated empirically with meropenem + vancomycin started on admission (due to immunosuppression and the two underlying conditions we considered a possible Gram-negative bacilli and Gram-positive cocci etiology at the beginning of the treatment) and from the third day with a combination of meropenem and ciprofloxacin. The patient was treated for 16 days, taking into account the dynamic changes of the monitored CSF parameters. On the fifth day of treatment the patient regained consciousness and his appetite improved. On the seventh day of hospitalization CSF showed a markedly favourable development compared to results obtained on admission.

Mortality in case of CNS infections with *M. morganii* is 38%, comorbidities (diabetes, neoplasms, etc.) and inadequate therapy or late established therapy being significant factors contributing to the death of patients (17, 22, 23). Although the immunological status of the presented patient was precarious because of the existing comorbidities, colorectal cancer and insulin-dependent type 2 diabetes, his clinical evolution was spectacular without the development of any neurological complications (brain abscess, subdural empyema, intracranial septic thrombophlebitis etc.), more likely due to the early initiation of antibiotic and immunoglobulin therapy.

Conclusion

This case of acute bacterial meningoencephalitis with an opportunistic infectious agent demonstrates the pathogenic potential of *M. morganii* in immunocompromised patients. Ear-

ly initiation of antimicrobial therapy resulted in a favourable evolution of the patient.

Conflict of interest

The authors have nothing to disclose. No competing financial interests exist.

Abbreviations

B.I.D. – Twice a day (from Latin *bis in die*, on medical prescription)
CNS – Central Nervous System
CRP – C- Reactive Protein
CSF – Cerebrospinal Fluid
CT – Computed tomography
ENT – Ear, Nose, Throat (otolaryngology)
ESBL – Extended spectrum beta-lactamase
ESR – Erytrocyte Sedimentation Rate
EUCAST – European Committee on Antimicrobial Susceptibility Testing
GCS – Glasgow Coma Scale
HgB – Hemoglobin
IV – Intravenously
MIC – Minimum inhibitory concentration
PCR – Polymerase chain reaction
PMN – Polymorphonuclear neutrophils
T.I.D. – Three times a day (on medical prescription)

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