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Pickwickian syndrome – the tip of the iceberg in extremely obese patients

Пиквик синдром – врх леденог брега код екстремно гојазних пацијената

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SUMMARY

Introduction Pickwickian syndrome, also known as hypoventilation syndrome in adults, consists of three factors: obesity (Body Mass Index – BMI >30 kg/m²), daytime hypercapnia and sleep disordered breathing, after ruling out other disorders that may cause alveolar hypoventilation. Timely recognition of PS is of utmost importance because such patients have significant morbidity and mortality. However, recent data indicate that PS is under-recognized and under-treated. We report a case of early-identified PS at pre-hospital level with a favorable outcome after hospital treatment.

Case report A 67-year-old female patient was diagnosed prehospitally, and the diagnosis was later confirmed in hospital. Diagnostic criteria were as follows: BMI > 45,7 kg/m² (height 170 cm, weight 132 kg), hypercapnia, hypoxemia and respiratory acidosis (pCO₂ – 41 mmHg, pO₂ – 56 mmHg, ph 7.45) in the absence of other causes of hypoventilation. During hospitalization, the following diagnostic procedures were performed: standard laboratory analyses, chest radiography, electrocardiography, abdomen, and heart echocardiography. An attempted sleep study (polysomnography) was interrupted due to a drop in oxygen saturation levels. Non-invasive mechanical ventilation and diet were used as the first line of therapy. However, due to the development of a global respiratory insufficiency, the patient was intubated and placed on a mechanical ventilator. After 30 days of hospital treatment, the patient was released in a satisfactory general condition with recommendations for weight reduction and symptomatic therapy.

Conclusion As obesity is becoming an epidemic of modern society, early recognition and treatment of PS is of crucial importance.

Keywords: obesity, Pickwick, syndrome, early, recognition, treatment

САЖЕТАК

Увод Пиквик синдром (ПС) познат и као хиповентилациони синдром одраслих чини тријада: гојазност (Body Mass Index-БМИ >30 kg/m²), целодневна хиповентилација, и поремећај дисања током спавања у одсуству алтернативних узрока алвеоларне хиповентилације. Благовремено препознавање ПС је од изузетног значаја јер овакви пацијенти имају сигнификантни морбидитет и морталитет. Међутим, новији подаци указују да је ПС недовољно препознат и недовољно лечен. Приказујемо случај рано препознатог ПС на прехоспиталном нивоу са повољним исходом након болничког лечења.

Приказ случаја: 67.-годишњој пацијенткињи постављена је прехоспитална дијагноза ПС која је потврђена и у болници. Дијагностички критеријуми били су: БМИ > 45,7 kg/m² (висина 170 cm, маса 132 kg), хиперкапнија, хипоксемија и респираторна ацидоза (pCO₂- 41mmHg, pO₂- 56mmHg, ph 7,45) у одсуству других узрока хиповентилације. Током хоспитализације урађене су следеће дијагностичке процедуре: стандардне лабораторијске анализе, радиографија грудног коша, електрокардиограм, ултразвук срца и абдомена. Покушана студија спавања (полисомнографија) је прекинута због пада SaO₂ (сатурације крви кисеоником). Као прва линија терапије примењени су неинвазивна механичка вентилација и дијета. Међутим, због развоја глобалне респирацијске инсуфицијенције пацијенткиња је интубирана и стављена на механички вентилатор. Након 30 дана болничког лечења отпуштена је кући у задовољавајућем општем стању са препоруком за редукцију телесне тежине и применом симптоматске терапије.

Закључак: Гојазност постаје епидемија савременог друштва, те је од круцијалног значаја рано препознавање и лечење ПС.

Кључне речи: гојазност, Пиквик, синдром, рано, препознавање, лечење

INTRODUCTION

The increase in the prevalence of extreme obesity in the last decade is a health, economic and demographic problem of global proportions. Overweight and obesity cause 3.4 million deaths a year [1]. Classification of obese adults based on body mass index – BMI (obese class I - BMI 30.0-34.9; obese class II - BMI 35.0-39.9; obese class III - BMI ≥40.00)

and relative risk assessment of morbidity (elevated, moderately elevated and highly elevated) was made by WHO in 1997. [2]. According to the results of the 2013 Health Survey in the Republic of Serbia, based on the measured BMI, more than half (56.3%) of the population was overweight (35.1% pre-obese and 21.2% obese) [1]. The average BMI value in the adult population of Serbia is 26 ± 4.74 kg/m².

Among the many complications of obesity, respiratory tract disorders are in the shadow of metabolic and cardiovascular complications in the first place, so they have been extremely rarely mentioned in our surroundings [3]. Types of respiratory disorders in obese people may be different:

1. respiratory function disorders without alveolar hypoventilation,
2. obesity hypoventilation syndrome – OHS,
3. obstructive Sleep Apnea Syndrome – OSAS,
4. risk during and after surgical interventions [3].

OHS, also historically described as the Pickwickian syndrome (PS), is defined as daytime hypercapnia and hypoxemia ($\text{PaCO}_2 > 45$ mm Hg and $\text{PaO}_2 < 70$ mm Hg at sea level) in an obese patient ($\text{BMI} > 30$ kg/m²) with sleep-disordered breathing in the absence of any other cause of hypoventilation [4]. OHS is a diagnosis of exclusion. Other causes of hypoventilation, such as COPD; severe interstitial lung disease; mechanical respiratory limitation (for example, chest wall disorders such as kyphoscoliosis); myopathies (such as myasthenia gravis); neurological diseases; central causes (such as cerebrovascular disease and untreated hypothyroidism); and congenital causes (such as Ondine's syndrome), should be ruled out. OHS often remains undiagnosed until late in the course of the disease. Its exact prevalence is unknown, but it has been estimated that 10% to 20% of obese patients with obstructive sleep apnea have hypercapnia [5]. Early recognition is important because these patients have significant morbidity and mortality. Effective treatment can lead to significant

improvement in patient outcomes, underscoring the importance of early diagnosis and early treatment [6].

We report a case of early-identified PS at pre-hospital level with a favorable outcome after hospital treatment.

CASE REPORT

An emergency medical service (EMS) team intervenes due to the severe choking of a 67-year-old female patient. She lives alone. The EMS doctor finds that the patient is extremely obese in central (android) type, BMI 45.7 kg/cm² (height 170 cm, weight 132 kg), moving with difficulty. In medical history, the patient states difficulties breathing, worsening in the lying position, fatigue even during minor activities, as well as all-day drowsiness. The problems have been more pronounced over the last seven days. Furthermore, she has urinary incontinence and "swollen stomach". The patient treats hypertension with fosinopril, which she takes irregularly. She has been smoking for the last 40 years (3 packs a day). The patient denies any loss of consciousness, allergies, previous pulmonary, otorhinolaryngological, neurological, cardiological, metabolic (diabetes mellitus) and endocrinological diseases, as well as chronic use of sedatives. On examination, the patient is mildly somnolent (Glasgow Coma Score 13), oriented, afebrile, dyspnoic (respiratory rate 20 / min), facial plethora, cyanotic (central cyanosis), anicteric. Severe patient aspect. Above the lungs weakened respiratory noise, crackles basal left, oxygen saturation (SaO₂) 44%. Heart action is rhythmic, tones somewhat quieter. Blood pressure is 160/90 mmHg. The palpation of internal abdominal organs is difficult due to pronounced obesity. No peripheral edema. Electrocardiography (ECG): sinus rhythm, heart rate (HR) 110 / min, S wave in D1 and from V1 to V6, without acute changes in the ST segment. 100% O₂ is applied through an oxygen

mask at a dose of 6 l / min. The patient was transported to hospital under the diagnosis of suspected PS.

On admission to hospital, the patient's status remains unchanged, with slightly corrected SaO₂ (58%). Gas analyses with no oxygen therapy when awake are: pO₂ 56mmHg, pCO₂ 41mmHg, ph 7.45. Due to the development of a global respiratory insufficiency (pO₂ 34mmHg, pCO₂ 67mmHg, ph 7.24) and the need for ventilatory support, the patient is moved to the Respiratory Unit. She is initially connected to non-invasive mechanical ventilation (NIV). Because of an inefficient gas exchange, the patient is intubated and placed on a mechanical ventilator. After being stabilized, the patient is extubated, connected to NIV and then on oxygen therapy.

Table 1 shows diagnostic procedures performed during hospitalization.

Laboratory test results are shown in Table 2.

The treatment included: therapeutic diet (VLCD - very-low-calorie diet), crystalloid infusions, electrolytes, antibiotics (ceftazidime, moxifloxacin, vancomycin), anticoagulants (LMWH, then oral), ACE inhibitors, Ca antagonists, gastrointestinal agents and other symptomatic and supportive therapies.

Due to paroxysms of atrial fibrillation (**Figure 1**), amiodarone was included. The patient was converted to sinus rhythm with occasional AF paroxysms.

After 30 days of hospital treatment, the patient was released in a satisfactory general condition with recommendation of the following therapy: lifestyle interventions (dietary changes and physical exercise), amiodarone tbl. 200 mg 1x1 (five days), enalapril tbl. 10 mg 2x1, amlodipine tbl. 5 mg 1xa, furosemide tbl. 40 mg 1x1 with 1gr KCl, acenocoumarol tbl. 1x1 / 2 until INR medical check-up (goal INR between 2 and 3), pantoprazole tbl. 20 mg 1x1. Scheduled appointments with pulmonologist and cardiologist in 15 days, and glycemia and HbA1c tests in a month.

DISCUSSION

A high suspicion of PS is critical for setting the PS diagnosis [7]. Our patient fulfilled the clinical criteria (SpO₂ 44%, dyspnoea on exertion, but also at rest, in unbecoming and uncomfortable positions of the body, facial plethora, elevated level of bicarbonates in blood). According to some data, targeted anamnesis and/or heteroanamnesis have a high sensitivity of 90% to 100%, but significantly lower specificity: 50% to 70% [8]. Obesity per se leads to a greater likelihood of diseases such as systemic arterial hypertension, diabetes, dyslipidemia, and hypothyroidism [4]. Additional questions are directed towards sleep, snoring, daily somnolence, possible cyanosis, and pulmonary and cardiovascular symptoms. In physical examination, respiratory noises are mostly reduced due to a thick layer of subcutaneous tissue on the thorax. In uncomplicated cases, early inspiratory basal crackles can be detected (in our patient on the left side). Heart tones are usually quiet, but during the aggravation of the illness, there may be arrhythmia. The ECG finding in our patient indicates an atrial fibrillation that has been arrested with amiodarone. Frequent finding is arterial hypertension due to obesity, smoking, hypoxemia (in our case SaO₂ was 44%), and other factors. Evidence of right ventricle enlargement from pulmonary hypertension that complicates advanced OHS may be seen on ECG and echo [9].

Obesity hypoventilation syndrome (OHS) cannot be diagnosed on history and examination alone but requires the demonstration of daytime hypercapnia [5]. Certain laboratory results complete the anamnesis and physical examination (elevated serum bicarbonate (> 27 mEq/L), hypercapnia (arterial pressure of carbon dioxide [PaCO₂] > 45 mmHg), hypoxemia (PaO₂ < 70 mmHg), polycythemia). Patients suspected of having OHS can initially be screened by pulse oximetry and by determination of serum levels of venous bicarbonate. SpO₂ values < 93% on pulse oximetry would be suggestive of hypoventilation. A serum bicarbonate level \geq 27 mEq/L had a sensitivity of 92% and a specificity of 50%,

justifying its use in screening [10]. A raised bicarbonate (> 27 mmol/L) or base excess (> 3 mmol/L) in the absence of another cause for a metabolic alkalosis in an obese individual with a $\text{PaCO}_2 < 45$ mmHg may be an early indicator of OHS, warranting closer investigation [11]. We noted similarly. Blood tests are also recommended for the identification of hypothyroidism and polycythemia. A chest radiograph should be performed to exclude parenchymal lung disease, chest wall disease, asymmetrical elevation of a hemidiaphragm (ie, diaphragm paralysis), and cardiomegaly.

The "gold standard" for diagnosing OSAS is polysomnography (PSG), which involves non-invasive measurement of vital parameters during sleep. According to published allegations [9] 90% of PS patients have coexisting OSAS, however due to unsuccessful polysomnography and missing heteroanamnesis (the patient lived alone) we were unable to confirm this theory. Because symptoms are nonspecific, the diagnosis of PS is frequently delayed. It is commonly misdiagnosed as asthma or chronic obstructive pulmonary disease [12] and some patients are not diagnosed until hospitalization for acute-on-chronic respiratory failure occurs. However, recent data indicate the obesity hypoventilation syndrome is under-recognized and under-treated [13].

In our case, the diagnosis of PS was based on: $\text{BMI} > 45.7$ kg / m², hypercapnia, hypoxemia and respiratory acidosis (pCO_2 - 41mmHg, pO_2 -56mmHg, pH 7.45) in the absence of other causes of hypoventilation. Comorbidities such as heart failure, coronary artery disease, and *cor pulmonale* are more common in patients with OHS, and the likelihood that such patients will require invasive mechanical ventilation or ICU admission is also increased. Noninvasive positive airway pressure together with weight loss are the initial first line therapies for patients with OHS [14, 15]. After a global respiratory failure had developed, our patient was intubated and placed on a mechanical ventilator. Mortality rate in PS is increased due to the respiratory and cardiac consequences of obesity as such.

Because obesity has become a national epidemic, it is critical that physicians are able to recognize and treat obesity-associated diseases. OHS is still a poorly recognized entity in Serbia. Delayed diagnosis of OHS is associated with an increase in morbidity, mortality, and costs of care of patients who are more severely ill.

Informed consent

Written informed consent in Serbian for the case to be published (incl. images, case history and data) was obtained from the patient for publication of this case report, including accompanying images.

Conflict of interest: None declared.

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Table 1. Diagnostic test and results

Diagnostic test	Results
Chest x-ray	Left basal accentuated vascular markings with suspected initial signs of consolidation. Slightly voluminous chylous. No signs of pleural effusion.
Echocardiographic (Echo) examination of the heart complicated by the constitution.	LP dilated 46 cm seems free. MV degenerately altered velum, mild MR and transmitral flow in the type of pseudonormalisation are recorded. LV of normal dimensions, hypertrophic walls 14/12mm, preserved global systolic functions EF 45-50%. The assessment of regional kinetics is difficult but there seems to be no regional asynergy E/e` 13.6. Ao of normal diameter at the root and the ascendent part with atherosclerotically altered walls. AoV of degenerately altered velum, partly sclerotic, preserved coaptation and disturbed separataion. Increased flow rates over AOV Vmax 2.26 m / sec, mild SOAS. Dilated right cavities, limit functions RV TAPSE 22mm, mild TR and SPRV of about 35mmHg registered. Pericardium is not split. Fat pad in front of the RV.
Abdominal echo	In the accessible part the liver is homogenous, steatosis, without focal lesions. The gallbladder, bile ducts, pancreas, aorta, and retroperitoneal space (not fully visualized) without visible changes. Spleen and both kidneys N.A.D. Bladder almost empty, a catheter placed. No free fluid in the abdomen.
Polysomnography	As there was suspicion of sleep apnea syndrome, a sleep study (polysomnography) was attempted, which was interrupted due to a drop in SaO2 levels and the necessity to resume oxygen therapy.

Table 2. Laboratory test details

Laboratory test	Result		Laboratory test	Result	
	max	min		max	min
Reference ranges	max	min	Reference ranges	max	min
WBC 3.9-10x10 ⁹ /l	10.8	6.1	Urea 2.8-7.2 mmol/l	10.1	3.7
Neu 40-70%	84.7	70	Cre 53-124 µmol/l	158	86
Eo 0-6%	10		CK 26-192 U/L	2511	33
RBC 3.86-5.08 x 10 ⁹ /l (women)	4,51		CKMB 24 U/L	66	44
Hgb 110-180 g/l	154		ALT 8-41 U/L	63	57
PLT 140-450 x 10 ⁹ /l	189		AST 7-36 U/L	86	33
CRP <5 mg/l	57.9	10.9	LDH <241 U/L	353	188
TPI <0.75 mmol/l	<0.20		gGT 5-35 U/L (women)	122	51
Na 136 – 145 mmol/l	140		TP 66 – 81 g/L	1.36	
Ca 2.25 – 2.75 mmol/l	1,9		Fe 8.9-30 µmol/l	7	
K 3.5 – 5.0 mmol/l	5.2	3.7	UIBC 2 5 - 59 µmol/l (women)	56	
HCO ₃ 24-29 mmol/l	32		TIBC 49 – 75 µmol/l (women)	62	
Glu 3.5-6.1 mmol/l	10.1	5.0	Pro BNP < 125 pg/ml	2800	243
Oncomarkers and thyroid gland hormones are in the reference range.					
Microbiological analysis			Corynebacterium spp.- diptheroids in the smear in the tip of the tubus		
Urine culture sterile.					

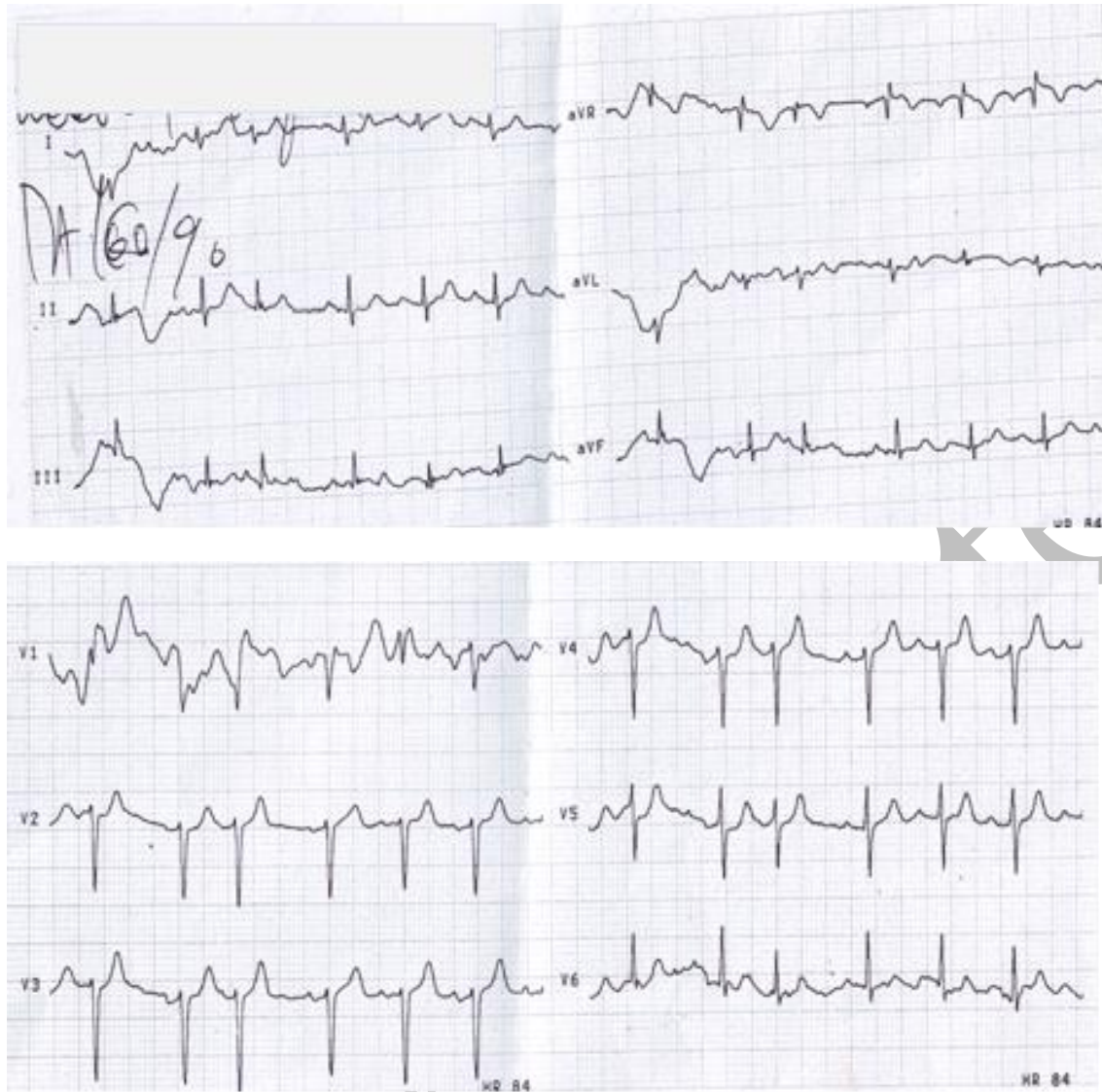


Figure 1. Paroxysmal atrial fibrillation ECG