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АСПИРАЦИОННЫЙ ПНЕВМОНИТ ПРИ НАЗАЛЬНОЙ ЛИКВОРЕЕ. ОБЗОР ЛИТЕРАТУРЫ

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Aspiration Pneumonitis with Nasal Liquorrhea. Literature Review

Резюме

Повреждение мозговых оболочек в сочетании с наличием дефекта костных структур основания черепа и формированием сообщения с полостью носа или околоносовыми пазухами являются необходимыми условиями назальной ликвореи. Существует целый ряд осложнений назальной ликвореи различного происхождения: инфекционные (менингит, абсцесс мозга), пневмоцефалия, аспирационный пневмонит и гастрит. Проведен обзор литературы, относящейся к аспирационному пневмониту при назальной ликвореи. Было отобрано 4 статьи с описанием 9 случаев. Проведен анализ демографических показателей пациентов, клинических данных, особенностей лечения. Исходя из анализа литературы, аспирационный пневмонит является редким осложнением назальной ликвореи. Для проведения дифференциальной диагностики с другими видами пневмонита необходимо опираться на дополнительные клинические данные, такие как односторонние выделения прозрачной жидкости из носа при наклоне головы, ухудшение состояния и усиление симптомов в горизонтальном положении, отсутствие синдрома системного воспалительного ответ, неэффективность антибактериальной терапии, рецидивирующий характер течения. Антибактериальная терапия не приводит к излечению пациента от пневмонита. Для лечения этой патологии необходимо прежде всего устранить причину аспирации — выполнить пластику дефекта основания черепа при отсутствии противопоказаний со стороны анестезиологического пособия.

Ключевые слова: *аспирационный пневмонит, назальная ликворея, дефект основания черепа, хирургия основания черепа*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

Damage to the meninges in combination with the presence of a defect in the bone structures of the base of the skull and the formation of communication with the nasal cavity or paranasal sinuses are necessary conditions for nasal liquorrhea. There are a number of complications of nasal liquorrhea of various origins: infectious (meningitis, brain abscess), pneumocephalus, aspiration pneumonitis and gastritis. A review of the literature related to aspiration pneumonitis in nasal liquorrhea has been carried out. 4 articles were selected with descriptions of 9 cases. The analysis of demographic indicators of patients, clinical data, treatment characteristics was carried out. Based on the analysis of the literature, aspiration pneumonitis is a rare complication of nasal liquorrhea. For differential diagnosis with other types of pneumonitis, it is necessary to rely on additional clinical data, such as unilateral discharge of clear fluid from the nose when tilting the head, worsening of the condition and intensification of symptoms

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in a horizontal position, absence of systemic inflammatory response syndrome, ineffectiveness of antibiotic therapy, recurrent the nature of the flow. Antibiotic therapy does not cure the patient from pneumonitis. For the treatment of this pathology, it is first of all necessary to eliminate the cause of aspiration — to perform plastic surgery of the skull base defect in the absence of contraindications from the side of anesthetic aid.

Key words: *aspiration pneumonitis, nasal liquorrhea, skull base defect, skull base surgery*

Conflict of interests

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BMI — body mass index, CPAP — constant positive airway pressure, CT — computed tomography

Introduction

CSF rhinorrhea occurs only if damage to the meninges, skull base fracture and a leakage into the nasal cavity or paranasal sinuses are combined [1]. The most common causes of this state include traumatic brain injuries (traumatic CSF leak), as well as endoscopic and neurosurgical interventions (iatrogenic CSF leak). Also, CSF leak can be of idiopathic origin (spontaneous CSF leak); it is often associated with increased intracranial pressure, metabolic and endocrine disorders [2, 3].

Abundant watery nasal discharge may inconvenience the patient with CSF rhinorrhea but poses no direct threat to life and cannot lead to the complete emptying of cisterns and cerebrospinal fluid spaces. Due to compensatory mechanisms, CSF rhinorrhea results in increased production and decreased reabsorption of cerebrospinal fluid [4]. However, CSF rhinorrhea has a number of complications of various origin. These include infectious complications (meningitis, brain abscess), pneumocephalus, aspiration pneumonitis and gastritis [5].

Pneumonitis is a disease with pathogenesis based on damage to the walls of alveoli and lung parenchyma, which results in their scarring and fibrotic changes. Pneumonitis can be induced by autoimmune diseases, exposure to chemicals, infectious agents, radiation or aspiration [6]. Aspiration pneumonitis develops when the contents of the oropharynx or stomach enter the lower respiratory tract. Risk factors for aspiration include conditions with impaired consciousness, traumatic brain injuries, and diseases with symptoms of dysphagia [7].

In 2016, Justin Seltzer et al. [8], for the first time, described a case of aspiration pneumonitis in a 44-year-old woman with CSF rhinorrhea. In previous series analyzing skull base defect management, authors focused on the diagnosis and surgical methods for CSF rhinorrhea [9]. Aspiration pneumonitis associated with cerebrospinal fluid leak is underestimated in clinical practice.

Patients with profuse CSF rhinorrhea often complain of coughing at night because, when they are in supine body position, cerebrospinal fluid enters the lower respiratory tract through the nasal cavity and nasopharynx and irritates the mucous membrane of the larynx and pharynx [10].

Objective: review of articles on aspiration pneumonitis with CSF rhinorrhea to identify patterns of development of this complication and develop optimal management for patients.

Materials and Methods

A review of articles from the Pubmed database published between 2000 and 2021 was carried out. Literature was searched using the following keywords: “CSF rhinorrhea”, “skull base damage”, “aspiration pneumonitis”, “complications of CSF rhinorrhea”. Inclusion criteria: articles in English and Russian reporting on aspiration pneumonitis with CSF rhinorrhea and mentioning diagnosis and the approach to the management of this complication. Exclusion criteria: articles with no mention of lung damage associated with CSF rhinorrhea or with insufficient data. We found four articles describing nine cases. Analysis of demographic parameters (gender, age, body mass index (BMI)), clinical data (symptoms, etiology of CSF leak, X-ray data), treatment features (previous conservative therapy, type of approach, plastic surgery materials, use of lumbar drainage) was carried out.

Results

According to the analysis, the average age of patients was 51 years (range 33–76 years). Most of patients were

female — eight (88.9%); male — one (11.1%). Seven (77.8%) patients were overweight, and five (55.6%) had grade 3 obesity. The most frequent complaints included nasal discharge, cough, and shortness of breath. Increased body temperature and typical signs of intoxication were found in two (22.2%) cases. X-ray of the chest in most cases revealed ground-glass opacity pattern. There was no relationship between the damaged side of the skull base and the affected lung; bilateral airiness disorders were often found. According to brain computed tomography (CT), in four (44.4%) cases, the defect was localized in the ethmoid roof, in three (33.3%) cases — in the cribriform plate, in one (11.1) case — in the sphenoid sinus, and in one (11.1) case — in the petrous pyramid of the temporal bone. Demographic and clinical data of patients are shown in Table 1.

The authors used different treatment methods. In their description of the first six cases, Maya Or et al. [11] performed plastic surgery for cerebrospinal fluid fistula without management of pneumonitis during pre- and postoperative periods. Endoscopic endonasal approach was used in five patients, and postaural approach — in one patient (in case of a defect of the petrous pyramid of the temporal bone). Deep fascia of thigh and pedicled nasoseptal flap were used for the correction of defects. Further, patients underwent average follow-up of 20.5 months in the center with the subsequent CT of the chest. The authors report the complete postoperative resolution of pneumonitis after eliminating its causes.

Justin Seltzer et al. [8] report that their patient underwent several courses of antibiotic therapy. However, therapy was ineffective, and she was prescribed symptomatic treatment with glucocorticosteroids, adrenergic agonists and antitussive agents. The patient was referred to a thoracic surgeon who performed a biopsy of the upper lobe of the right lung. However, nothing was revealed apart from signs of acute bronchopneumonitis.

Table 1. *Demographic and clinical indicators of patients*

№, Author	Gender	Age	Etiology	BMI	Complaints	X-ray / CT of the lungs	Defect localization
1 [Maya Or] [11]	F	76	Spontaneous	37	Rhinorrhea on the right, shortness of breath, cough	Central and peribronchial ground-glass opacities in all lobes	Right ethmoid region
2 [Maya Or] [11]	F	51	Spontaneous	36	Rhinorrhea on the right, intermittent cough, meningitis	Bilateral ground-glass opacities with bronchial wall thickening	Right lateral sphenoid
3 [Maya Or] [11]	F	44	Spontaneous	37	Recurrent rhinorrhea on the right, shortness of breath on exertion, cough, hoarseness	Bilateral patchy opacities in lower lobes (left > right)	Right cribriform plate
4 [Maya Or] [11]	F	54	Spontaneous	41	Rhinorrhea on the left, headache	Ground-glass opacities in all right lobes	Left ethmoid region
5 [Maya Or] [11]	F	36	Spontaneous	31	Rhinorrhea on the left, cough, shortness of breath, wheezing	Ground-glass opacities in both upper lobes + left lower lobe	Left ethmoid region
6 [Maya Or] [11]	M	64	Spontaneous	21	Rhinorrhea on the left	Ground glass opacities bilaterally, bronchial wall thickening, borderline bronchiectasis	Left tegmen mastoideum
7 [Justin Seltzer] [8]	F	44	Spontaneous	36,5	Rhinorrhea on the right, cough, shortness of breath on exertion, hoarseness	Bilateral violation of the airiness of the lungs in the lower lobes	Right ethmoid region
8. [Mark G Jones] [12]	F	33	Spontaneous	N/a	Discharge from the nose, cough, heaviness and pain in the chest, fever	Bilateral ground-glass opacities	Cribriform plate
9 [Wasgewatta] [13]	F	53	Spontaneous	35	Discharge from the nose, cough, fever	Bilateral ground-glass opacities in the lower lobes	Right cribriform plate

Note: BMI — Body mass index, X-ray — Roentgen examination, CT — computed tomography

The patient was then referred to an ENT specialist who noticed the constant nasal discharge and prescribed a test to determine β2-transferrin in nasal secretion. The patient was referred to the neurosurgical department, where endoscopic endonasal plastic surgery of the skull base defect was performed. During surgery, lumbar drainage was placed and fluorescein sodium was used. The authors report an uneventful postoperative period. CT of the lungs in 11 months revealed no signs of lung tissue damage. This case demonstrates the late diagnosis of CSF rhinorrhea after unsuccessful management of pneumonitis and confirms the conclusion that the cause of aspiration should be eliminated.

Mark G. Jones et al. [12] reported a similar case. Nasal discharge in this case was described as occasional. The patient repeatedly underwent antibiotic therapy for bilateral pneumonia. However, her clinical picture included signs of intoxication (fever, neutrophilia, swollen lymph nodes). Bronchoscopy revealed *Haemophilus influenzae*. A two-week course of amoxicillin/clavulanate and azithromycin helped improve the patient's condition. However, later on, symptoms of pneumonia recurred since the discontinuation of antibiotics led to worsening. As in the previous case, the patient also underwent a biopsy, but its results revealed nothing but bronchiolitis. Aspiration pneumonitis was suggested, and brain magnetic resonance imaging revealed a defect in the region of the cribriform plate. After the plastic surgical correction of this skull base defect, symptoms of pneumonitis regressed.

Sanjiwika Lalanjani Wasgewatta et al. [13] reported a case of spontaneous CSF rhinorrhea and pneumonia during CPAP-therapy (CPAP — Constant Positive Airway Pressure, mode of mechanical ventilation with constant positive pressure) for obstructive sleep apnea syndrome. After the treatment course, the patient began to complain of coughing, headache, nasal discharge and fever. The patient was prescribed acetozalomide (diacarb), after which the patient noted a decrease in headaches and nasal discharge. Another patient underwent endoscopic endonasal plasty of skull base defect and ventriculoperitoneal shunting. The authors reported that a week after this surgery, a second CT of the chest revealed no signs of lung tissue damage.

Discussion

Aspiration is defined as the accidental transfer of oropharyngeal or gastric contents (endogenous factors) or fluid and particulate matter (exogenous factors) into the lower respiratory tract. Clinical response to aspiration depends on the nature of the aspirated material, airway microbiocenosis, and colonization by pathogenic organisms [14].

With profuse CSF rhinorrhea, CSF can enter bronchi and alveoli, which may lead to irritation in the respiratory tract. Although patients with skull base defects often complain of coughing in supine body position, cases of pneumonitis as a complication of CSF rhinorrhea have not been adequately described in the literature.

All patients in this study had spontaneous CSF rhinorrhea, which is more common in menopausal women with obesity. There are studies that prove the relationship between obstructive sleep apnea syndrome and spontaneous CSF rhinorrhea [15, 16]. According to a meta-analysis conducted by Bakhsheshian J. et al. (2015), the risk of CSF rhinorrhea is 4.73 times higher in patients with obstructive sleep apnea syndrome than in the control group [17]. However, we found in the literature only a handful of reports of cases of spontaneous CSF rhinorrhea after the start of CPAP therapy [18, 19]. The mechanism of this complication is believed to be associated with changes in intracranial pressure and venous pressure of cerebrospinal fluid [20].

X-ray is used for the diagnosis of pneumonitis (radiography, chest CT). The most common symptom in patients was ground-glass opacity, which is an indicator of lung tissue density and a sign of interstitial infiltration. Ground-glass opacity is represented by a certain area with moderately reduced lung tissue airiness.

This phenomenon is caused by the thickening of interalveolar septa and their partial filling [21]. Differential diagnosis with other types of pneumonitis should be based on additional clinical data, such as unilateral discharge of clear liquid from the nose when the head is tilted, state worsening and intensification of symptoms in a lying position, the frequent absence of systemic inflammatory signs (according to SIRS: fever >38.0 °C or hypothermia <36.0 °C, tachycardia >90 beats per minute, tachypnea >20 breaths per minute, leukocytosis $>12\times10^9$/l or leukopenia $<4\times10^9$/l), absence of a response to antibiotic therapy, and a recurrent disease course. In our country, CSF rhinorrhea is diagnosed based on a laboratory test to determine glucose in nasal secretions, endoscopic examination, CT cisternography, and high-resolution CT [22].

All authors reported that antibiotic therapy was ineffective since lung damage was caused not by infectious agents but by aspiration. Symptoms quickly regressed after successful reconstruction of cerebrospinal fluid fistula. These data suggest that the resolution of pneumonitis depends primarily on the management of the underlying cause (chronic aspiration); antibiotic therapy has no effect on the outcome. Therefore, at the stage of differential diagnosis of lung damage associated with CSF rhinorrhea, it is very important to pay attention to additional clinical signs, such as unilateral nasal discharge of

clear liquid, increased coughing in lying position, and no signs of intoxication.

This analysis is limited by the small number of publications, cases, and retrospective study design. To obtain reliable results, a large-scale prospective study is required.

Conclusion

Aspiration pneumonitis is a rare complication of CSF rhinorrhea that is associated with chronic nasal cerebrospinal fluid leakage via CSF pathways due to skull base defects. This type of aspiration pneumonitis is resolved only after eliminating the cause of CSF rhinorrhea.

Differential diagnosis with other types of pneumonitis should be based on additional clinical data, such as unilateral discharge of clear liquid from the nose when the head is tilted, state worsening and intensification of symptoms in a lying position, no systemic inflammatory signs, no response to antibacterial therapy, and recurrent course of disease. This disorder should be managed, first of all, by eliminating the cause of aspiration, i.e., performing plastic surgery of skull base defect if there are no contraindications for anesthesia.

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