Abstract
Leptomeningeal carcinomatosis is an uncommon complication of different types of cancer in which the disease spreads to meninges. It usually presents with clinical features of meningeal irritation, combined with cranial nerve involvement. This report aims to describe vestibular dysfunction as one of the possible and infrequent initial signs of leptomeningeal carcinomatosis. We present a case of a 49-year-old female who has been previously diagnosed breast cancer who developed bilateral vestibular dysfunction due to leptomeningeal carcinomatosis. Leptomeningeal carcinomatosis can be variable in its presentation since any aspect of the nervous system can be affected. Multiple cranial nerve involvement isn’t rare, with most commonly affected third, fifth and seventh cranial nerve (5). In our case, the patient presented with the symptoms of isolated vestibular dysfunction with preserved cochlear part of the nerve. This can be explained by the possible way of propagation of malignant cells via endolymphatic ductus into the inner ear with the obliterated connection between sacculus and cochlea.

Keywords: leptomeningeal carcinomatosis, isolated vestibular dysfunction, breast cancer

Isolated vestibular dysfunction as an initial manifestation of leptomeningeal carcinomatosis due to breast cancer – A case report

Gordana Sičaja1, Marija Ernoić1, Hrvoje Budinčević1,2

1 Department of Neurology, Sveti Duh University Hospital, Zagreb, Croatia
2 Faculty of Medicine, J.J. Strossmayer University, Osijek, Croatia

Sažetak
Izolirana vestibularna disfunkcija kao inicijalna manifestacija leptomeningealne karcinomatoze kod raka dojke – prikaz slučaja

Leptomeningealna karcinomatoza rijetka je komplikacija različitih oblika karcinoma, a podrazumijeva širenje bolesti na moždane ovojnice. Manifestira se kliničkim značajkama irritacije moždanih ovojnica u kombinaciji sa zahvaćenomživca moždanih živaca. Cilj ovog prikaza slučaja je opisati vestibularnu disfunkciju kao jednu od rijetkih inicijalnih manifestacija leptomeningealne karcinomatoze. Predstavljamo slučaj 49-godišnje pacijentice s prethodno dijagnostikiranim rakom dojke koja je razvila izoliranu bilateralnu vestibularnu disfunkciju u sklopu leptomeningealne karcinomatoze. Leptomeningealna karcinomatoza je varijabilna u svojoj prezentaciji jer može utjecati na bilo koji dio živca. Više istražaka zahvaćenja moždanih živaca nije rijetko, s najčešćim tretmanima po općoj smjeti. U našem slučaju pacijentica imala je simptome vestibularne disfunkcije s očuvanim kohlearnim dijelom živca. Isolirano zahvaćanje vestibularnog dijela živca može se objasniti mogućim načinom širenja zloćudnih stanica putem endolimfatičnog duktusa u unutarnje uho uz obliteration sustava.

Ključne riječi: leptomeningealna karcinomatoza, izolirana vestibularna disfunkcija, rak dojke

Copyright (C) 2020 Sičaja G, Ernoić M, Budinčević H. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.
**Introduction**

Leptomeningeal carcinomatosis is a relatively rare complication that occurs in about 5% of patients with cancer. In the last few decades, it has been more frequently recognized due to medical diagnostics and treatment advancements and, therefore, prolonged life expectancy in oncological patients. The most common primary sites to involve the meninges are breast cancer, lung cancer, and melanomas. It usually presents with clinical features of meningeal irritation, combined with cranial nerve involvement.

This report aims to describe vestibular dysfunction as one of the initial signs of leptomeningeal carcinomatosis, which might be of value in a better understanding of this condition's pathogenesis.

**Case report**

**Patient information**

A 49-year old female was admitted to the Department of Neurology due to vertigo accompanied by a headache and loss of balance. The symptoms have begun two months earlier with vertigo and continued to aggravate three weeks before admission with loss of balance, progressive gait unsteadiness, occipital headache and vomiting. Medical history revealed breast cancer metastatic to the lymph nodes, diagnosed nine months before admission, that was surgically removed and subsequently treated with twenty-eight radiotherapies and six chemotherapy cycles (docetaxel, doxorubicin).

**Clinical findings**

Neurological examination revealed slight bilateral dysmetria in the finger-nose test, atactic gait without any side preference and a positive Romberg sign. There was no primary position, nor gaze-evoked nystagmus. The rest of the examination was unremarkable.

**Diagnostic assessment**

Blood and urine tests, X-ray of the cervical spine, duplex ultrasound of carotid and vertebral arteries, transcranial Doppler sonography, electromyoneurography (EMNG) of upper and lower extremities was performed and revealed normal results. Neuroradiological imaging using computed tomography and magnetic resonance of the brain did not show any significant intracranial pathology, while the fundoscopy revealed initial bilateral papilledema. Pure tone audiometry produced a slight hearing loss that was age-appropriate, but the caloric test detected bilateral unresponsiveness of the vestibular nerves (Figures 1 and 2).

![Figure 1. Audiometry findings](image1)

![Figure 2. Caloric test](image2)
Cytological examination of the cerebrospinal fluid (CSF) showed an abundance of atypical cells with the morphological characteristics of the adenocarcinoma (Figure 3). Biochemical analysis of the CSF showed elevated protein level (637 mg/L) and decreased glucose level (1.4 mmol/L).

Therapeutic intervention, Follow-up and Outcomes
The patient was initially admitted to the Department of Neurology of our hospital where the diagnostic evaluation was made and the patient was treated with antiemetics, benzodiazepines, infusion solutions and other symptomatic therapy. After the final diagnosis was made, the patient was transferred to the Department of Oncology at University Hospital for Tumors to continue specific, oncological treatment. In total, two cycles of intrathecal chemotherapy (carmustine, cisplatin) were administered, shortly after which the patient died.

Discussion
Leptomeningeal carcinomatosis is one of the most challenging complications of systemic tumors. In most cases, symptoms of leptomeningeal carcinomatosis arise in patients with a known malignancy, although the symptoms sometimes may precede the diagnosis of the primary tumor. In our case, the patient presented with the symptoms of isolated vestibular dysfunction with preserved cochlear part of the nerve. In the recent literature, a bilateral hearing loss is described as a rare and unusual presentation of leptomeningeal carcinomatosis, while an isolated lesion of the vestibular nerves has not yet been described.

There are several possible routes of spreading of malignant cells to meninges, as they may occur either directly from an adjacent tumor or the distal tumor by hematogenous spread or perivascular of perivascular lymphatics. From subarachnoid space, the cells can extend into the temporal bone to the point of the geniculate ganglion where the subarachnoid space terminates, but can penetrate the cribriform area of the labyrinth. Our patient was diagnosed with cancer of the breast nine months before the symptoms of carcinomatosis arose. The CSF analysis confirmed the infiltration of the nervous system, revealing an abundance of metastatic adenocarcinoma cells (Figure 3) with an increased CSF protein and decreased glucose levels. The cerebrospinal fluid examination is usually the most valuable aid for the diagnosis of leptomeningeal carcinomatosis. Although, in our case the first test revealed positive cytology, sometimes several lumbar punctures are required to avoid false-negative results.

Conclusion
Leptomeningeal carcinomatosis can start with a wide variety of symptoms and often represent a challenge for clinicians since it can affect any aspect of the neuroaxis and therefore mimic various conditions. Although extremely rare, and to our knowledge not yet published, an isolated bilateral vestibular dysfunction can be a manifestation of leptomeningeal carcinomatosis, as a consequence of the propagation of malignant cells from leptomeningeal space via endolymphatic ductus into the inner ear. This can be explained by the possible way of propagation of malignant cells via endolymphatic ductus into the inner ear, which can lead to consecutive vestibular dysfunction. Since ductus reuniens, connecting sacculus with the membranous cochlea, is usually obliterated in adults, the cochlear part of the labyrinth is not necessarily affected, and vice versa.
Literature:

Conflict of interest
All authors listed declare that they have no conflict of interest.