CASE REPORT

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Leptomeningeal carcinomatosis can be presenting manifestation of breast carcinoma

Leptomeningealna karcinomatoza kao manifestacija karcinoma dojke

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Abstract

Introduction. Leptomeningeal carcinomatosis (LC) is a serious complication occuring in solid cancer patients with rather poor prognosis. **Case report.** We presented a 47-year-old woman with the 6-month history of diffuse headache, nausea and visual obscuration. Initially, clinical status and brain magnetic resonance imaging (MRI) indicated syndrome of idiopathic intracranial hypertension. Due to clinical progression and high papillary stasis, cerebrospinal fluid (CSF) examination was performed only after ventriculoperitoneal shunt was implanted. This led to a significant although transient clinical improvement. Futher investigations led to the diagnosis of invasive lobular breast carcinoma and repeated CSF analysis revealed malignant breast carcinoma cells. In this case LC was an initial presentation of a malignant disease. **Conclusion.** In the presence of a high clinical suspicion of LC, in spite of initially negative findings, a clinician should persist in repeating relevant tests, such are MRI with larger amounts of gadolinium and high-volume cytological CSF analyses in order to make the diagnosis.

Key words:
breast neoplasms; neoplasm metastasis; meningeal neoplasms; diagnosis, differential.

Apstrakt

Uvod. Leptomeningealna karcinomatoza (LK) je ozbiljna komplikacija koja se javlja kod bolesnika sa karcinomima i ima lošu prognozu. **Prikaz bolesnika.** Prikazali smo 47-godišnju ženu sa 6-mesečnom anamnezom difuzne glavobolje, mučnine i zamagljenja vida. Na početku, klinički status i magnetna rezonanca mozga ukazali su na sindrom idiopatske intrakranijalne hipertenzije. Usled kliničkog pogoršanja i visoke staze papile, pregled cerebrospinalne tečnosti (CST) mogao je biti obavljen tek posle plasiranja ventrikuloperitonealnog šanta. Ovo je dovelo do značajnog, mada prolaznog, kliničkog poboljšanja. Dalje ispitivanje ukazalo je na postojanje invazivnog lobularnog karcinoma dojke, a ponavljanje analize CST otkrile su postojanje malignih ćelija karcinoma dojke. U ovom slučaju LK je bila početna prezentacija maligne bolesti. **Zaključak.** Ukoliko, uprkos početnim negativnim nalazima, postoji visoka klinička sumnja na LK, kliničar bi trebalo da ponavlja relevantne analize, kao što su magnetna rezonanca sa većom količinom gadolinijuma i analize većeg volumena CST, da bi se postavila dijagnoza.

Ključne reči:
dojka, neoplazme; neoplazme, metastaze; meninge, neoplazme; dijagnoza, diferencijalna.

Introduction

Leptomeningeal carcinomatosis (LC) is a serious complication of cancer associated with substantial morbidity and mortality. Leptomeningeal metastases ooccur in 5–15% of patients with cancer but the diagnosis has become increasingly common with the routine use of high-quality magnetic resonance imaging (MRI) and lengthening survival of patients with more effective treatments [1–3]. The most common primary cancers, excluding hematological malignancies, are breast, lung, gastrointestinal tumors and melanoma [1–3]. The disease typically involves multiple levels of the neuraxis, and obstruction of normal cerebrospinal fluid (CSF) flow pathways may result in increased intracranial pressure and hydrocephalus [2]. Identification of malignant cells by CSF cytology had been the diagnostic gold standard, with high specificity but limited sensitivity [1, 2]. In spite of

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advances in diagnosis and treatment, the prognosis in patients with LC remains poor.

Case report

A 47-year-old woman was admitted with a 6-month history of headache, bilateral tinitus, nausea with occasional vomitting and visual obscurations. The patient had been previously in good health with the negative past and family history. In particular, the family history of breast carcinoma was negative.

On admission, her general status was normal. Small painless lump in the upper lateral quadrant of the right breast was noted. No lymphadenopathy was found on clinical examination. On neurological examination the patient was well-oriented, with bilateral papillary edema (4 Dpt), decreased visual acuity bilateraly (20/25) and gait ataxia. Complete blood count and standard biochemistry were normal. A mildly increased D-dimer level (215 μg/L, reference < 125 μg/L) was noted. Brain computed tomography (CT) was normal.

Brain MRI indicated dilatation of both optic nerves with increased perineural CSF, flattening of the posterior sclera, empty sella syndrome, dilatated lateral ventriculs with periventricular edema; conclusion was made that these are typical signs of idiopathic intracranial hypertension (IIH). MR venography (MRV) revealed slower blood flow through sinus rectus without signs of trombosis.

Full coagulation assessment, immunological analyses with antinuclear, antiDNA and anticardiolipin antibodies, ELISA HIV antibodies and serology for syphilis were negative. Repeated D-dimer was normal. Abdominal ultrasound examination was unremarkable. Chest radiography indicated enlarged mediastinal lymph nodes, but thorax CT with contrast showed normal finding in the mediastinum; however, it revealed small lesion in the right breast and enlarged lymph nodes in the right axilla. Mammography confirmed tumorous formation in the upper lateral quadrant of the right breast. The biopsy was performed and histopathological analysis showed invasive lobular breast carcinoma. There was no metastatic lesions on radiography examination of the skull and spinal column.

Signs of clinical progression, comprising increased headache and vomiting, generalized tonic-clonic seizures and papillary stasis progressing to 6 Dpt, precluded CSF examination. An intense antiedematous therapy was administered (dexamethasone, mannitol). A repeat MRI showed the same finding. The ventriculoperitoneal (VP) shunt was implanted, leading to significant clinical improvement, decrease in papillary stasis (2.5 Dpt) and enabled CSF sampling. First CSF analyses showed normal biochemistry with one lymphocyte and polymorphonuclear each. CSF cytology indicated rare mononuclears with signs of atypia in some, but the finding was inconclusive. Oligoclonal bands were absent. CSF bacterial and fungal cultures were negative. A week later CSF analysis was repeated, showing mildly increased proteins (0.6 g/L), hypoglicorachia 2.3 mmol/L (glyceamia 6.8 mmol/L), 3 polymorphonuclears and 3 lymphocytes *per* 1 mL. Larger amount of CSF was sent to second cytological analysis, which revealed a large number of malignant cells corresponding to breast carcinoma (Figure 1). The patient was referred to the Oncology Unit for further treatment. Standard symptomatic and palliative care was applied and the patient died 4 months later.

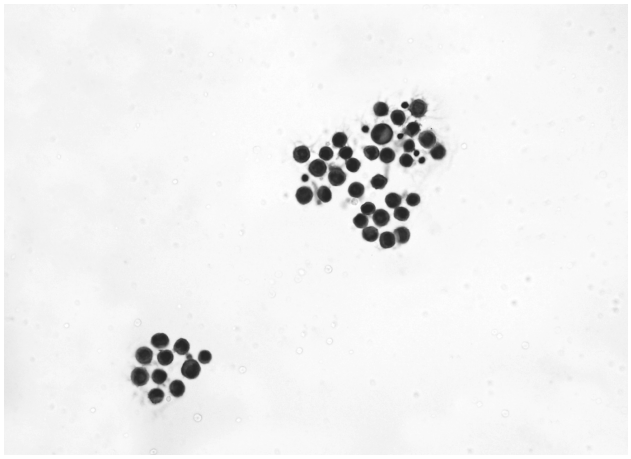

Fig. 1 – Clusters of breast lobular carcinoma cells in cytospin preparation of cerebrospinal fluid sample (haematoxylin and eosin, × 400).

Discussion

Breast cancer is the leading nonhematologic cause of LC [3]. We reported an illustrative case of a patient presenting with LC as initial manifestation of breast malignant disease. Initially, possible dural sinus thrombosis were suspected. However, no direct signs of sinus thrombosis were visualised, D-dimer normalized and no prothrombotic condition was identified. Only VP shunting led to a significant clinical improvement and enabled the diagnosis of metastasing breast neoplasma.

Althought CSF cytology, the gold standard of LC diagnosis, was immediately required, examination could not be performed untill VP shunt was placed. VP shunt is shown to significantly improve symptoms in patient with LC, which was the case in our patient as well [1, 3]. Only the second high-volume CSF analysis confirmed the diagnosis of LC. Positive CSF cytology is found on the initial examination in only 50% of LC patients, and in about 85% of those undergoing three high-volume (> 10 mL) lumbar punctures [1, 2]. The specificity of the test is excellent but there is a substantial frequency of false-negative results [2, 4].

There were no clear signs of meningeal pathology on MRI scan in this case. MRI of the brain and spine with a T1-weighted gadolinium-enhanced sequence, combined with fat-suppression T2-weighted scans, is recommended examination in LC, with the sensitivity reported to be up to 71% [2, 5]. However, sensitivity can depend on the quantity of gadolinium used [1, 5].

Our patient presented with several features atypical for LC. LC is the presenting symptom of malignant disease, seen in only 5–10% of the cases [5]. LC from solid tumors is usually detected in an advanced stage of systemic disease, in the setting of widespread metastases, which were absent in the presented patient [1, 2, 5]. Also, there was long symptoms duration of 6 months before the diagnosis and only 4 months after, while

median survival of treated patients with LC is known to be overall only 2–6 months [2, 5]. Nevertheless, 1-year survival rate can be as high as 25% [3]. MRI indicated IIH but not meningeal pathology, which is seen in at least 30% of cases [5].

Conclusion

Leptomeningeal carcinomatosis is one of the most serious complications occurring in solid cancer patients with rather poor prognosis. It can occasionally be the first manifestation of malignant disease. VP shunting can result in considerable clinical stabilization of the patient and can be vital in the diagnostic process. Lower sensitivity of conventional MRI and CSF examination can be diagnostic pitfalls, but in the setting of a strong clinical suspicion of LC, the clinicians should persist in repeating MRI with larger quantity of gadolinium and high-volume cytological CSF analyses.

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R E F E R E N C E S

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