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Case Report

RARE CASE OF LEPTOMENINGEAL METASTASES FROM POORLY DIFFERENTIATED PAROTID CARCINOMA

Tiara Aninditha[1,2], Dyah Ayu Puspita Anggarsari[1,2], Eka Susanto[1,5], Radius Kusuma[1,4], Erwin Danil Yulian[1,3], Irma Savitri[1,2], Henry Riyanto Sofyan[1,2]

[1]Faculty of Medicine, Universitas Indonesia; dyah.ayu13@alumni.ui.ac.id
[2]Departement of Neurology, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia
[3]Departement of Surgical, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia
[4]Departemen of Radiologi, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia
[5]Departemen of Pathological Anatomy, Dr. Cipto Mangunkusuma Hospital, Jakarta, Indonesia

ABSTRACT

Introduction: Leptomeningeal metastasis (LM) from poorly differentiated parotid carcinoma is a rare and difficult-to-diagnose condition, requiring radiologic imaging and cerebrospinal fluid (CSF) cytology for confirmation. Secondary headache, often a critical "alarm" sign, may indicate intracranial involvement.
Case Report: A 27-year-old woman with a history of poorly differentiated parotid carcinoma and liver metastases presented with severe secondary headache, dizziness, and vomiting. She had undergone chemotherapy (CAF regimen) and was free from cancer pain after initial treatment. Physical examination revealed facial nerve palsy, ataxic gait, dysmetria, and postural tremor. The patient's headache was relieved with high doses of dexamethasone and acetaminophen. Imaging studies, including CT and MRI, revealed vasogenic edema and leptomeningeal enhancement in the right cerebellar hemisphere and a solid lesion in the left parotid gland. CSF cytology showed malignant cells with features consistent with poorly differentiated carcinoma. The patient was diagnosed with leptomeningeal metastasis and will undergo craniospinal irradiation.
Discussion: Leptomeningeal metastasis from parotid carcinoma is an uncommon complication, with secondary headache often presenting in the posterior fossa. Diagnosis requires a combination of CSF cytology showing malignant carcinoma cells and MRI findings of leptomeningeal enhancement. Since there is no established chemotherapy for LM from parotid carcinoma, craniospinal irradiation is considered the most effective treatment option.
Conclusion: Leptomeningeal metastases from poorly differentiated parotid carcinoma are rare but should be considered in patients with severe secondary headaches and a history of parotid cancer. Early diagnosis through clinical, imaging, and CSF analysis is crucial, as delayed diagnosis can be fatal.

Keywords: leptomeningal metastases; poorly differentiated parotid carcinoma; diagnose

INTRODUCTION

Leptomeningeal metastase (LM) is a complication of malignant tumors that metastasize to leptomeninges and subarachnoid space. The prevalence of LM in solid cancer patient is approximately 10-15%, but very rare in parotid carcinoma, a head and neck carcinoma.[1,2] The incidence remains uncertain because of the clinical diagnosis is still challenging.

Secondary headache is a critical sign and symptom of cerebral involvement of LM. Forty-five percent LM patients suffered of secondary headache. Its secondary headache is acute bilateral diffuse accompanied by cranial nerve and spinal involvement.[3] Posterior fossa involvement can develop dizziness and coordination problems. However, a head and neck carcinoma causes 80% cancer pain that appear similar with headache. About 30-50% cancer pain occur during therapy and the incidence increase up to 70-90% on the next stage.[4]

Leptomeningeal Metastases should be proven by imaging and cerebrospinal fluid cytology. T1-weighted magnetic resonance imaging (MRI) with gadolinium contrast is the gold standard imaging method to diagnosis LM. MRI is reported to have a sensitivity and specificity about 75%.[5] Cranial meningeal-only involvement can be detected to approximately 40-43%, spinal meningeal-only involvement is about 10-23% and cranial-spinal meningeal involvement is up to 24-26%.[6] Cerebrospinal fluid (CSF) cytology has a sensitivity of 55% on the first puncture and can be reached up to 85% when done thrice.[5]

Based on data, diagnostic approach of headache is the “cornerstone” of the next diagnostic steps and management for LM. We report a case of a 27-year-old women to diagnostic approach of leptomeningeal metastases and its management.

CASE REPORT

A 27-year-old woman came to the emergency department complaining of severe secondary headache and dizziness followed by vomiting. She was feeling throbbing pain at the entire of her head. Her headache was getting worst in ten days and disturbance her sleep. She also had experienced of temporary blurry vision. The physical examination found slightly peripheral facial nerve palsy, ataxic gait, right dysmetria, right intention, and postural tremor. She was hospitalized, and her secondary headache was relieved after a high dose of dexamethasone intravenous (10 mg twice a day) and acetaminophen injection.

One year prior, she experienced cancer pain at left parotid mass that radiated in the left side of the scalp. The cancer pain was getting worst day by day. Acetaminophen was slightly decreased her complaint. Its relieve after using morphine sulfate 10 mg twice a day. She was diagnosed with poorly differentiated parotid carcinoma and had multiple lesion in the liver. She had completed 4 of 6 cycles of chemotherapy. Her chemoteraphy regimen was cisplatin, doxorubicin hydrochloride (Adriamycin), and fluorouracil (CAF). Cancer pain disappeared approximately 2 weeks after the first cycle.

In the emergency department, computed tomography (CT) scans of the head showed vasogenic edema with enhancement of leptomeningeal at the right cerebellum hemisphere and solid lesion in the left parotid gland decreased by 46 % (Figure 1).

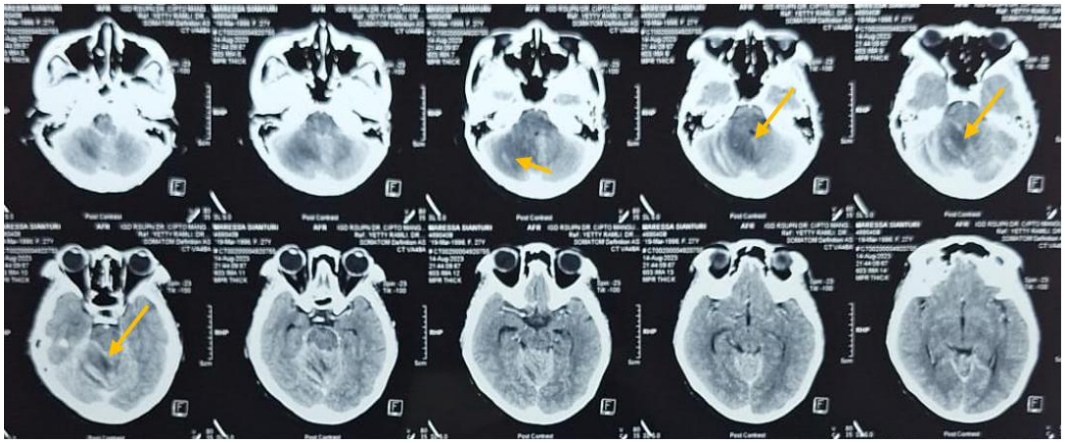

Figure 1. CT scans axial cut shows vasogenic edema with enhancement of leptomeninge

She was hospitalized and underwent nasopharynx MRI examination. Nasopharynx MRI showed enhancement at leptomeningeal of right-left cerebellum hemisphere, mainly in the right, suspected metastases. We also found no enhancement lesion in the right hemisphere cerebellum that urged pons, narrowing of the fourth ventricle accompanied by dilatation of the right-left lateral ventricles and third ventricle, suspected of metastases (Figure 2).

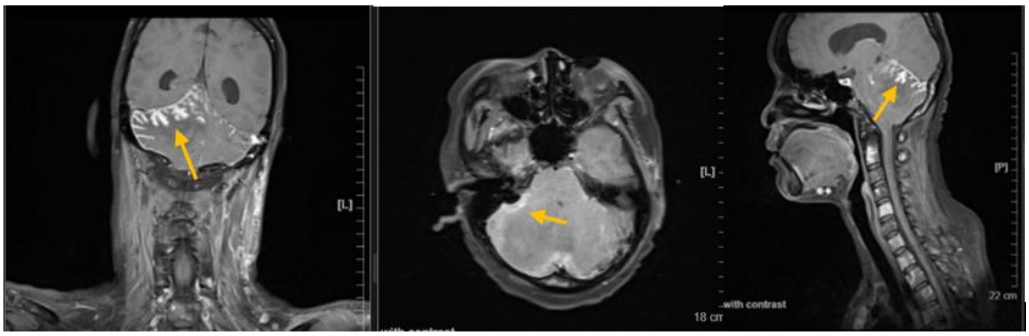

Figure 2. Nasopharynx MRI shows enhancement at leptomeningeal of right-left cerebellum hemisphere (*left to right: Coronal cut, axial cut, sagital cut)*

Lumbar puncture with CSF analysis was performed. We obtained increased of protein and low level of CSF glucose. CSF Cytology showed positive, poorly differentiated malignant tumor with a pleomorphic nucleus, rough chromatin, and a few cytoplasms in the nuclei (Figure 3). Our NeuroOncology Meeting decided that she was diagnosed with confirmed leptomeningeal metastases. She would continue her two-last cycle of chemotherapy and perform craniospinal irradiation. She got high dose dexamethason intravenous that was tappering off three until five days based on improvement of clinical status. Her karnofsky performance status score is 70. She can perform daily activity without headache.

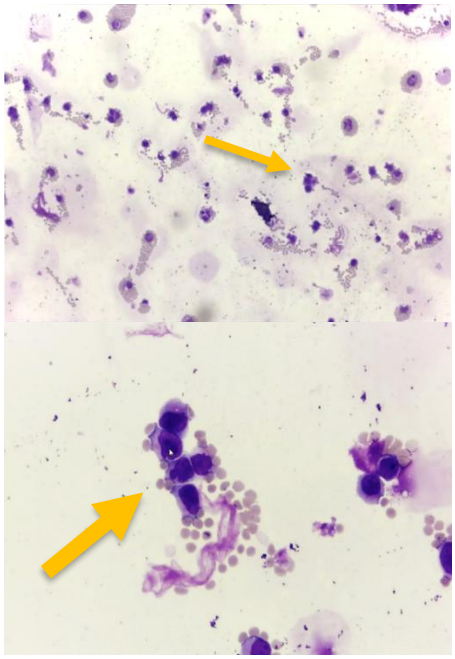

Figure 3. The cytology demonstrated positive, poorly differentiated malignant tumor

DISCUSSION

Clinical sign of symptom

Leptomeningeal metastases is uncommon complication in parotid carcinoma. However, the pathophysiology explains that tumor cell of head and neck cancer can undergo perineural migration from systemic metastases into

subarachnoid space.[7] Leptomeningeal metastastes have multifocal sign and symptom. They are cerebral, cranial nerve and spinal involvement.[8,9] Uniquely, the patient was just experienced of secondary headache followed by dizziness, without cranial nerve and spinal involvement. Secondary headache is the most symptom of cerebral involvement and must be differentiated from cancer pain of head and neck carcinoma. Secondary headache is considered because it is diffuse, bilateral and does not originate from the tumor. Its supported by data that her cancer pain was gone 2 weeks after the first cycles of chemoteraphy.

Secondary headache was perceived at dermatome of C2-C3. The symptom of dizziness and coordination problems mean that the disease occur from posterior fossa. Leptomeningeal inflammation located in posterior fossa will produced pain at the level of C2-C3. Inflammatory mediator activate trigeminal nociceptor in pia artery, produced glutamate, P substance and calcitonin gene-related peptide (CGRP). The signal will be continued to trigeminal ganglion contained unmyelinated C-fiber and myelinated A-delta-fiber. It is projected to trigeminal spinal nucleus and somatosensory cortex via thalamus and hypothalamus. These fossa posterior nociceptor that projected via C2-C3 spinal branches called trigeminocervicocomplex (TCC).[10–12]

Secondary headache may occur because of increasing intracranial pressure due to vasogenic edema of tumor cell in cerebelli hemisphere. Intracranial pressure activate trigeminal nociceptor in meningeal via TCC. It was supported by relieve pain after high dose dexamethasone injection.[10–13]

Imaging of leptomeningeal metastase

CT scan should be restricted to emergency setting such as to rule out CSF obstruction or cerebral haemorrhage. Because of many technical limitation, CT has no rule to diagnosis of LM.[8]

MRI is the importance initial diagnostic method and follow up of patient with suspected or confirmed LM. The sequences should include three-dimensional (3D), pre-contrast

T1-weighted, two-dimensional (2D) or 3D fluid-attenuated inversion recovery (FLAIR), 2D diffusion-weighted imaging, 2D pre-contrast T2-weighted, postgadolinium 3D T1-weighted and post-gadolinium 3D FLAIR sequences. Meningeal enhancement is the characteristic of leptomeningeal involvement on MRI finding. Typical findings are contrast enhancement of cerebellar folia and sulci, basilar cisterns,cranial nerves, brain surface, surface of the lateral ventricles, lumbar nerve roots, and the cauda equina. MRI presentation is devided into five subtype. There are linear, nodular, linear + nodular, hydrocephalus and normal. Based on European Association of Neuro-Oncology (EANO), linear, nodular, and linear + nodular finding will be considered as a probable LM (with typical clinical signs) and possible LM (without typical clinical signs).[5,8,9]

Cerebrospinal Fluid Cytology

CSF analysis and cytolocy is the gold standard for diagnostic of LM. Lumbar punctures should be performed after neuroimaging. Its important to avoid risk of herniation due to major brain metastases of complications from local bulky diasease. In the CSF analysis, we will find increased opening pressure (>200 mm H_2O), increased leukocyte counts (>4 per mm^3), elevated protein (>500 mg/l), and decreased glucose (<600 mg/l). Moreover, lumbar puncture will give more information from cytology examination. 60,5-83% tumor cell have been detected in CSF cytology.

Confirmed diagnosis will established when CSF cytology show positive of malignant cells according with its primary tumor.[8] In this case, we found positive, poorly differentiated carcinoma appropriate with prior biopsy of parotid mass.

Steroid therapy

High dose dexamethasone intravenous (10 mg twice a day) relieve her secondary headache in 6 hours. Maksimal improvement can be seen during 24-72 hours after injection. Dexamethasone is drug of choice for secondary headache due to perifocal edema and leptomeningeal inflammation. Is can decrease blood brain barrier permeability and has minimal mineralocorticoid effects.

Tumor cells release prostaglandin, tumor necrosis factor-alfa (TNF-Alpha), endothelin, interleukin-1 (IL-1), interleukin-6 (IL-6), tumor growth factor-beta (TGF-beta) dan Platelet-derived growth factor (PDGF). Tumor growth causes compression, ischemia, and proteolysis that increase more inflammatory mediators. Vasogenic edema is caused by loosen tight junction result from interaction between vascular endothel and inflammatory mediators. Steroid has role anti-inflammatory effects such as inhibit kolagenase expression, decrease pro inflammatory cytokine, stimulate lipocortin and tumor cells apoptosis.[13]

Acetaminophen

Acetaminophen induces analgesia by its metabolite N-acylphenolamine (AM404) acts on the transient receptor potential vanilloid 1 (TRPV1) and cannabinoid 1 receptors in the brain. Central effect of acetaminophen should be given by caution since masked effect of secondary headache due to increase intracranial pressure.[14]

Craniospinal irradiation

Based on National Comprehensive Cancer Network, craniospinal irradiation is considered for the patient with karnofsky performance status score 70 and minor neurological deficit. There is no choice chemotherapy for LM from parotid carcinoma. Monitoring of blood counts should be performed weekly since given risk of hematologic toxicity.[8,15]

CONCLUSION

In conclusion, leptomeningeal metastases from poorly differentiated parotid carcinoma is a very rare. The diagnosis can be difficult due to “non-classical symptom” of LM. However, carefully differentiate of secondary headache and cancer pain, give an esensial keyword of intracranial process. Combination imaging and cerebrospinal fluid examination can provide definitive diagnosis. Appropiate treatment will improve quality of life.

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