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Left Orbital Metastasis as the First Clinical Manifestation of Lung Adenocarcinoma

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Abstract: ***Lung adenocarcinoma is the most common subtype of lung cancer that metastasis to other site. Orbital metastasis from primary lung tumor is a rare entity, with incidence approximately 7%. The rareness of presentations would invariably lead to a delay in the correct diagnosis, thereby increasing the risk of loss of vision, which decreases patient's quality of life. Herein, we report a case, a 64 years old man who presented with left orbital swelling, pain, and blur of vision and was firstly diagnosed with glaucoma. In the next visit to hospital, patient had chest pain, cough, low back pain, tingling and weakness in his both lower extremities. Detailed examination and investigations revealed a mass in the right lung and left retro bulbar that metastasis to brain, liver, costae, and vertebrae. The patient had left orbital exenteration and microscopic examination found the tumor consists of proliferation of neoplastic cells with cribriform and tubular pattern infiltrating the choroid and retina. We also found the neoplastic cells infiltrate to intraneural and intravassa. This patient had mutation epidermal growth factor receptor (EGFR), deletions in exon 19. The patient had a targeted therapy with tyrosine kinase inhibitor (gefitinib).***

Keywords: orbit, metastasis, lung, adenocarcinoma

1. Introduction

Lung adenocarcinoma is the most common subtype of lung cancer that metastasis to other site. Orbital metastasis is quite rare, occurring in only about 7% of cases.[1,2,3] Delays in diagnosis this malignancy will increasing the risk of loss of vision of the patient thereby decreasing their quality of life. Lung adenocarcinoma most commonly metastasize to bone (39%), brain (25%), liver (16%) and adrenal gland (13%).[2] Patients with lung cancer with distant metastases will receive either systemic therapy chemotherapy, target therapy or combination.[2]

Here, we will report a case of a 64-years-old man, who came with an initial swollen complaint on the left orbit, pain, blurred vision and was diagnosed with glaucoma. After further examination, the patient was found to have mass in the right lung and left retro bulbar oculi with metastasis to the brain, liver, ribs, and vertebrae.

2. Case

A 64-years-old man complained of a swollen, red, and painful left eye. The left eye blurred progressively until he could not see at all. This patient was diagnosed with glaucoma with central retinal vein occlusion and retinal detachment. Two months later the patient complained of right chest pain, cough lower back pain, tingling and weakness in both limbs. The patient is a gold mining worker for 10 years, and then he becomes a driver for 20 years. He has smoking history 1 pack per day for 30 years, and has stopped since 10 years ago.

Physical examination revealed proptosis, palpebral edema and hyperemia, conjunctival chemosis and corneal edema on the left eye (figure 1). Decrease vocal fremitus, dullness, and decreased breath sound was found on the right anterior thorax at level fifth to sixth intercostal spaces. Hepatomegaly and pathological reflexes on both limbs were also found.

Thorax CT scan with contrast shows a right subhilar tumor. There were multiple nodules in the liver which have ring enhancement post contrast and also destruction on the left posterolateral 7th costae (figure 2A, 2B). Head and orbital CT scans with contrast shows intraconal mass of left retro bulbar oculi infiltrated into musculus rectus, optic nerve, and left maxillary sinus that causes proptosis and retinal detachment of left oculi (figure 3A). There were multiple mass in left occipital lobe, right and left parietal, and left temporal suspicious for metastatic process (figure 3B). Cerebral edema with midline shift to the right, and soft tissue swelling on left periorbita. Lumbosacral MRI with contrast (figure 4) shows mild compression on anterior corpus vertebrae L1 and L2, multiple lesion with undefined margin on the corpus vertebrae L1, L3, L4, S1, and S2 supporting the vertebral metastasis.

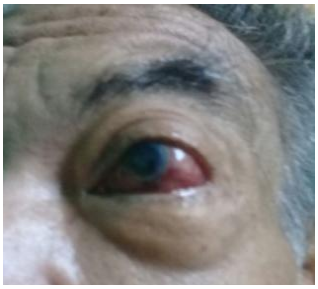

Figure 1: Proptosis, palpebral edema and hyperemia, conjunctival chemosis and corneal edema on the left eye.

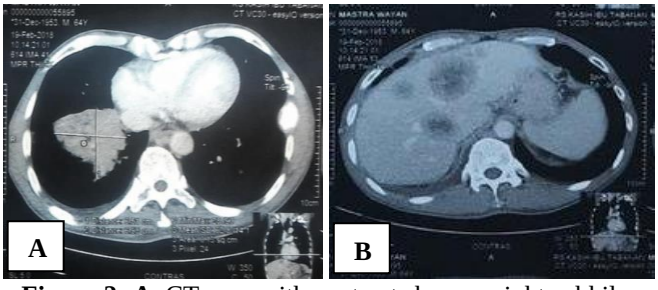

Figure 2: A. CT scan with contrast shows a right subhilar tumor, with enhanced post contrast pneumonic reaction with

multiple nodule satellites in both lungs. **B.** There were multiple nodules in the liver which have ring enhancement post contrast.

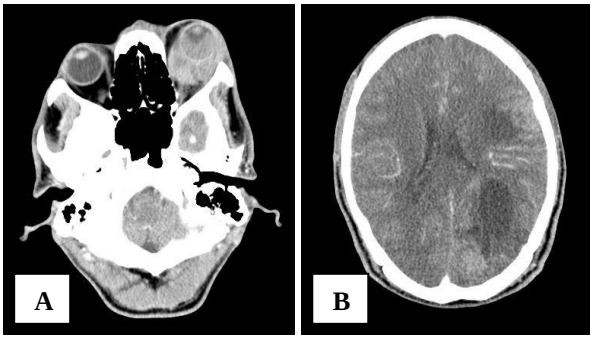

Figure 3: A. Orbital CT scan with contrast shows intraconal mass of retrobulbar oculi **B.** Head CT scan with contrast shows multiple mass in left occipital lobe, right and left parietal, and left temporal suspicious metastatic process.

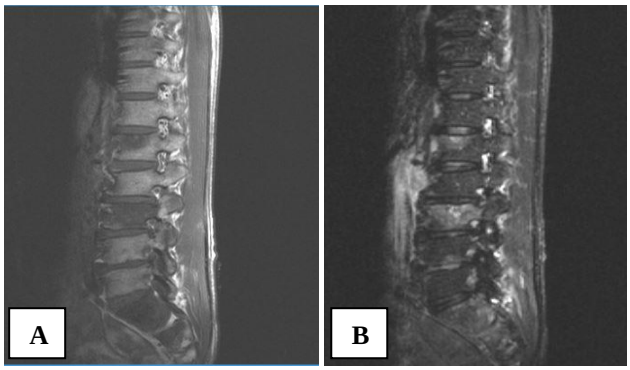

Figure 4: Lumbosacral MRI with contrast on **A.** T1WI dan **B.** T2WI shows mild compression on anterior corpus vertebrae L1 and L2, multiple lesion with undefined margin on the corpus vertebrae L1, L3, L4, S1, and S2 supporting the vertebral metastasis

Bronchoscopic examination revealed elliptical narrowing on the inferior right lobe bronchus (except B6) due to pushing from extralumen, infiltrative and easily bleeding mucosa. The cytology of bronchial washing obtains group of neoplastic cells that form acini, morula like, and dispersed single cells. The nuclei round-oval, arranged in crowding overlapping, coarse chromatin with small nucleoli, irregular nuclear membrane, N/C ratio increased, cytoplasm basophilic. Cytomorphology consistent with adenocarcinoma.

Left orbital exenteration has been done. On a macroscopic examination (figure 5) there is a mass in the posterior part of the eyeball, the size is 2.5 × 1.5 × 1.3 cm. Microscopic examination with Hematoxillin and Eosin staining, (figure 6A, 6B) obtained tumor mass consist of proliferative neoplastic epithelial cell forming cribriform and tubular pattern which infiltrating the choroid, desmoplastic connective tissue, fat and skeletal muscle. The morphology of the cells are cuboid-oval, eosinophilic cytoplasm, N/C ratio increased, vesicular chromatin, nucleoli single-multiple prominent, nuclear pleomorphism moderate-severe. We also found perineural, intraneural, and intravasa invasion. Based on clinical and histopathological findings, this case was concluded as Adenocarcinoma with moderately differentiation, tend to be lung origin. Resection margin of optic nerve contains carcinoma cells. The distance of the tumour to inferior resection margin is 8 mm, to medial is 5 mm, to the lateral is 3 mm, the superior margin did not contain carcinoma cells.

Figure 5: A. Macroscopic examination revealed a mass in the posterior part of the eyeball (arrows).

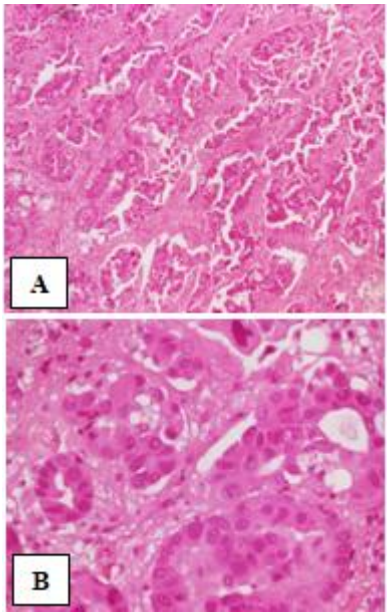

Figure 6: A, B. Microscopic examination obtained tumor mass consist of proliferative neoplastic epithelial cell forming cribriform and tubular pattern which infiltrative in the desmoplastic connective tissue, fat and skeletal muscle. The morphology of the cells are cuboid-oval, eosinophilic cytoplasm, N/C ratio increased, vesicular chromatin, nucleoli single-multiple prominent, nuclear pleomorphism moderate-severe (A. H&E x100, B. H&E x400).

3. Discussion

Adenocarcinoma is the most common histologic type for lung cancer. Symptoms of lung cancer vary greatly from asymptomatic until symptoms that appear associated with the spread of the disease. Symptoms that often occur include progressive breathlessness, cough, chest pain, hoarseness and hemoptysis whereas symptoms that appear associated with spread of the disease is highly dependent on the organ where the malignancy metastasize[4] Orbital metastasis is a rare phenomenon that only occur in 3-7% of all cancers. In whites, orbital metastasis are reported most frequently from breast (39-48%), prostate and skin (melanoma) (12%), lung (8%), and kidney (7%-11%).[2] Symptoms that occur when

there is orbital metastasis include swelling of the eyelids, diplopia, proptosis, and blindness. These symptoms can appear before the symptoms of primary tumor, because lung cancer often does not provide specific symptoms until it reaches advanced stage.[1,2,4] This case reported a 64 years old man, complained of a swollen, red, and painful left eye at the beginning of his arrival to the hospital. He said his left eye blurred progressively, narrowing his visual field and finally he could not see at all. This patient was initially diagnosed with glaucoma accompanied by central retinal vein occlusion and retinal detachment. Two months later the patient complained of right chest pain, cough, lower back pain, tingling and weakness in both limbs.

Orbital metastasis can increase intraocular pressure that lead to glaucoma. Increased intraocular pressure may occur due to several mechanisms, such as effect of growing or infiltrative mass that suppresses the orbital structure. Progressive infiltration to the nerves exacerbate venous ischemia and result in neovascular glaucoma.[5] The mass on choroid can cause bullous retinal detachment, push lens and iris to anterior, and resulting in secondary closed-angle glaucoma. Metastasis in the iris causes secondary open-angle glaucoma when trabecular meshwork is closed by tumor cells. In this case, the mass was located in retrobulbar, infiltrate to the optic nerve and choroid, resulting in retinal detachment.

Smoking is a risk factor that associated with all types of carcinoma but more strongly associated with squamous cell carcinoma and small cell carcinoma. Lung cancer can occur in non-smoker patient in about 5-10 per 100,000 people per year and increased 20-30 times in smokers. Possible etiological factors for lung cancer among never-smokers include exposure to secondhand tobacco smoke, radon, various occupational agents, and emissions from indoor coal burning.[4] This patient was work as gold mining for 10 years, then as a driver for 20 years. He has smoking history one pack per day for 30 years, and has stopped since 10 years ago.

Complete anamnesis, thorough physical examination, supporting and histopathologic examination will achieve an accurate diagnosis. Subsequent investigations in this patient found a lobulated mass in the right subhillar with enhanced post contrast pneumonic reaction with multiple nodule satellites in both lungs. Radiologic examination also found multiple nodules in the liver and bone destruction on the left posterolateral costae, and also multiple masses in left occipital, left and right parietal and left temporal lobes, indicating the presence of metastases to the liver, bone and brain. Cytological examination from bronchial washing is consistent with Adenocarcinoma. Histopathological examination from left orbital exentration concludes a moderate differentiation adenocarcinoma, possibly from lung origin.

Management of lung cancer that metastasize to orbita includes chemotherapy, photocoagulation, cryosurgery, surgical resection, or radiotherapy. Radiotherapy may be administered with low-dose external radiation. In radio resistant case, surgical is required. Orbital areas have varying degree of resistance to radiation. Side effects that may arise from radiation are temporary or permanent lash loss, impaired lacrimal apparatus and lens. Sclera and cornea have high resistance to radiation.[6] Lung adenocarcinoma patients with epidermal growth factor receptor (EGFR) mutation, targeting therapies may be one of the therapeutic modalities. Administration of tyrosine kinase inhibitor (TKI), e.g. gefitinib can provide rapid response in lung adenocarcinoma with EGFR mutations.[2,7] This patient had EGFR mutation, deletion of exon 19 and was managed by orbital exenteration and targeted therapy gefitinib.

Patients with lung adenocarcinoma that metastasize and had EGFR mutations who receiving TKI therapy had 5-year survival rate 14.6%.[8] Overall prognosis in this case was poor.

4. Conclusion

Orbital metastasis from lung adenocarcinoma is a rare phenomenon and can cause symptoms including swelling of the eyelid, diplopia, proptosis, and blindness. Symptoms orbital metastasis can precede the symptoms of primary tumor in the lung causing delays in making the right diagnosis. Complete history, thorough physical examination, supporting examinations and histopathologic examination will achieve an accurate diagnosis. Management lung cancer with orbital metastasis include chemotherapy, photocoagulation, cryosurgery, surgical resection, radiotherapy, and target therapy. Overall, patients with metastatic pulmonary adenocarcinoma have a poor prognosis.

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