



Neoplastic meningitis: a rare presentation of bronchial adenocarcinoma

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Abstract

Following chronic daily headache, neoplastic meningitis was diagnosed in a non-smoking 44-year-old man. A bronchial adenocarcinoma was found to be the primary tumor. He was treated with erlotinib. Meningitis as the first manifestation of a malignancy is very rare.

Key words: Neoplastic meningitis; carcinomatous meningitis; meningitis carcinomatosa; bronchial adenocarcinoma.

Introduction

Neoplastic or carcinomatous meningitis is a rare complication that occurs in 3% to 8% of patients with a malignancy (1, 2). Leptomeningeal metastasis can occur in all solid malignant tumors and hematologic malignancies. Carcinomatous meningitis as the initial presentation of a malignant tumor however is very rare. We describe a previously healthy 44-year-old man who presented with chronic headache. Carcinomatous meningitis secondary to a bronchial adenocarcinoma was diagnosed.

Case report

A 44-year-old man consulted because of chronic daily headache since 2 months associated with mild nausea, weight loss (4 kg over 2 months) and occasional word-finding difficulties. His medical history was unremarkable. He had never smoked. Clinical neurological examination revealed some slight neck stiffness. There was no focal neurological deficit. Brain MRI showed diffuse leptomeningeal contrast-enhancement and a parenchymal lesion supra-orbital in the left inferior frontal gyrus (Fig. 1 + 3). Our differential diagnosis was neurosarcoidosis, carcino-

matous meningitis or tuberculous meningitis. A tuberculin skin test and sputum examination for tubercle bacilli were negative. Cerebrospinal fluid (CSF) was macroscopically pale yellow and slightly turbid. Analysis of CSF showed an increased protein content of 122 mg/dl, a low glucose of 25 mg/dl, a lactate of 4.6 mmol/l and a lymphocytic pleocytosis of 34 leukocytes/mm³ including lymphocytes, histiocytes and monocytes. There were also groups of larger atypical cells with a remarkably increased, partly irregular, core (Fig. 2). Some of these nuclei also had an enlarged nucleolus. These tumor cells were immunoreactive with cytokeratin-7 and pancytokeratin antibodies. This immunocytochemical profile was compatible with a metastasis of an (adeno-)carcinoma because of expression of these keratin markers. A bacterial culture of CSF was sterile. Chest X-ray and CT-images revealed a stellate tumor in the superior segment of the right lower lobe. A whole body FDG-PET scan also suggested a malignant tumor in the lower lobe of the right lung; furthermore there was a hypermetabolic focus at the level of L1 vertebral body and at the iliac crest of the right hip. Histological examination of lung tissue, obtained via transthoracic biopsy, confirmed the diagnosis of a bronchial adenocarcinoma. A mutation in the epidermal growth factor receptor (EGFR) gene was detected. Headache and nausea appeared very resistant to therapy and were eventually partially alleviated by treatment with ketorolac, dehydrobenzperidol and methylprednisolone. Chemotherapy was started with oral erlotinib 150 mg a day orally. A new chest CT, 2 months after the first one, showed a good response with a marked decrease in volume of the tumor. At the time of writing this report, about 6 months after his first neurological assessment, the patient is still alive.

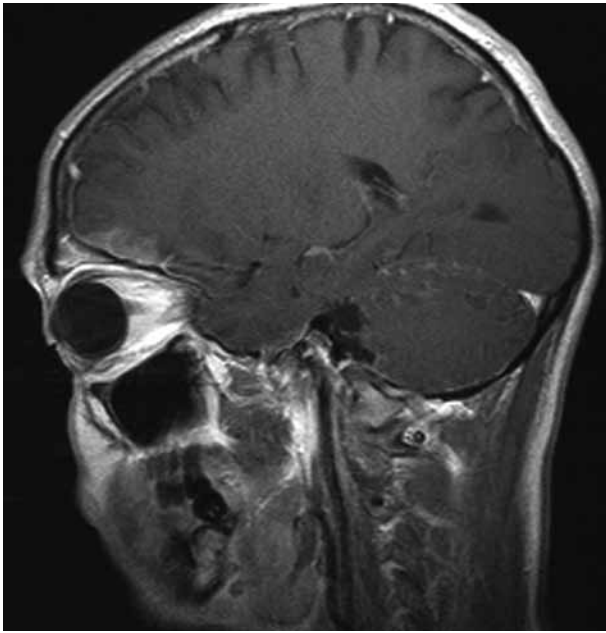


FIG. 1. — Sagittal Gd-enhanced T1-weighted MR images of the brain reveal diffuse leptomeningeal enhancement. Additionally, there is a focal area of enhancement in the left orbitalfrontal cortex, indicating invasion of the brain parenchyma.

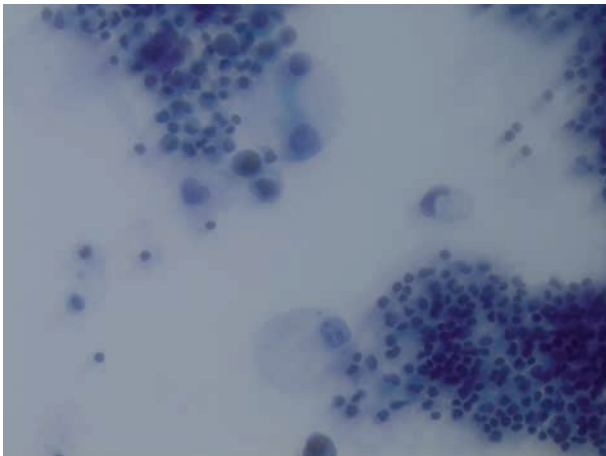


FIG. 2. — CSF Pap stain cytology showing a few large atypical cells with abundant cytoplasm, the one on the right with a 'signet ring' appearance, among a large number of normal lymphocytes ($\times 40$). Cells are concentrated because a Cytospin slide centrifuge was used.

Discussion

Although carcinomatous meningitis usually complicates an advanced oncological disease stage, about 6% of these patients present at initial diagnosis of cancer (2-4). The incidence of carcinomatous meningitis is dependent on the primary tumor localization and is highest for lung and breast cancer

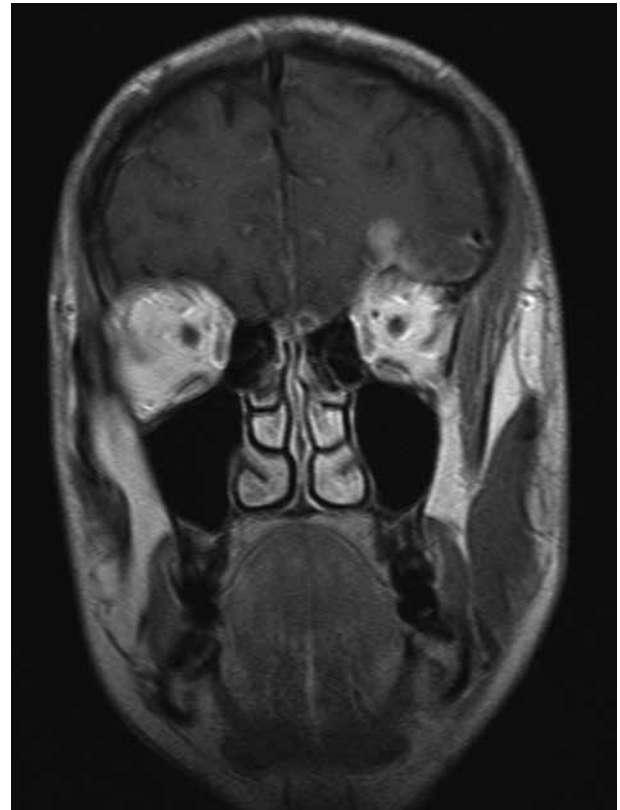


FIG. 3. — Coronal Gd-enhanced T1-weighted MR images of the brain reveal diffuse leptomeningeal enhancement. Additionally, there is a focal area of enhancement in the left orbitalfrontal cortex, indicating invasion of the brain parenchyma.

Table 1

Incidence of neoplastic meningitis in various different solid tumors (data from Gleissner *et al.*, 2006)

Primary tumor	Incidence of neoplastic meningitis
small-cell lung cancer	6%
breast cancer	3%
unknown primary tumor	3%
melanoma	1.5%
non-small cell lung cancer	1%
gastrointestinal tumor	0.015-0.25%

(Table 1). Frequent symptoms of carcinomatous meningitis are headache, alteration of mentation, ataxia (in 50%) and cranial nerve lesions (in 40%) (1). About half of patients with leptomeningeal metastasis have parenchymal involvement (3). This was also the case in our patient. Gadolinium-enhanced brain MRI typically shows leptomeningeal contrast-enhancement, which can extend into the

sulci. The sensitivity of MRI for neoplastic meningitis is 66% to 71% (5, 6). Cytological examination of CSF is crucial in the diagnosis of carcinomatous meningitis (5-7). Sensitivity of an initial lumbar puncture to detect malignant cells in CSF is only 54%. The yield of CSF cytology can be increased by obtaining at least 10 ml of CSF and repeated lumbar punctures. A second lumbar puncture may increase the yield to 82% and a third would increase the yield further to 90% (2). Pleocytosis in CSF is detectable in about 60% (1). The prognosis of carcinomatous meningitis is poor with a median survival of 2.5 to 6 months in solid tumors (1, 3, 6). Untreated, most patients die within 1 to 9 weeks (median survival 3 weeks) (1). Treatment options are chemotherapy (systemic or intra-CSF), radiotherapy or a combination of both (2). Erlotinib is a tyrosine-kinase inhibitor that acts on EGFR. Recently there are some publications which have described a beneficial effect on brain metastases and carcinomatous meningitis in patients with non-small cell lung cancer (8-10). In line with these data, our patient was treated with erlotinib.

We found in the literature only one similar case report of a patient with carcinomatous meningitis as the first presentation of a bronchial adenocarcinoma. That patient, reported by Paramez, *et al.* was treated with cisplatin-based chemotherapy and died after 3 days treatment (4). A gallbladder carcinoma and a gastric carcinoma which presented with neoplastic meningitis have also been reported (11, 12).

In conclusion, we would like to suggest that the possibility of neoplastic meningitis should be considered in cases of a (chronic) meningitis of unknown etiology, even in patients who are not known with a malignant tumor. Clinicians should have a low threshold to obtain cytological examination of CSF. Repeated lumbar punctures may be necessary.

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