Pancytopenia and oesophageal thrush after irradiation and palliative chemotherapy of adenocarcinoma of the lung (NSCLC)

Objectives:

1. Palliative treatment of adenocarcinoma of the lung
2. Upper influence stowage and radiogenic esophagitis as a possible complication of mediastinal tumors
3. Challenges of drug delivery through PEG probes

▶ Evaluation

The adenocarcinoma of the lung is one of most common forms of non-small cell lung cancer, like squamous carcinoma. Unlike squamous cell cancer non smokers frequently have the adenocarcinoma.

The treatment approach in advanced stages is usually palliative. The following case describes the complications after an emergency irradiation and subsequent chemotherapy. The supportive and necessary medication could have been optimized and the use of individual drugs is discussed after a preliminary visit and a conversation with the patient. It was possible to change the treatment regimen and the patient could receive a monotherapy in outpatient department. This case also highlights the importance of a functioning, interdisciplinary cooperation in the treatment team to the clinical outcome and quality of life of seriously ill patients.

▶ Literature

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Link H, Bokemeyer C, Feyer P: Supportivtherapie bei malignen Erkrankungen, 2006, Deutscher Ärzte-Verlag

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Patient: female, 69 years, height: 162 cm, weight: 66 kg, BSA 1,7 m²

Subjective data	The patient had difficulties in speaking. She complaind of pressure and tightness in the chest and abdomen and existing breathing difficulties. Due to the previously received radiation and chemotherapy, she felt weakened considerably. Getting up and exercise was difficult for her. Until the day before she was isolated in a single room. Due to having continued difficulties in swallowing, a gastric tube was placed. The current transition from parenteral to enteral nutrition was accompanied by recurring nausea and mild diarrhea. The new painkillers appeared less effective than the previous one, resulting in recurrent pain. She felt depressed, suffered from restlessness, anxiety and tightness. She tossed about a lot and often lay awake at night. In 2006, the patient was diagnosed with cervical cancer. This was followed by surgery and followed by chemotherapy and radiation. 6 weeks ago she visited physician due to severe dysphagia and dry cough. In the 8 weeks before, she had lost 8 kg. The patient did not smoke, drink alcohol and, in her own words, had a healthy lifestyle.
Objective data	The patient was in poor general condition (Karnofsky 60%). The hospitalization was required due to weeks of existing esophageal dysphagia. As the only tumor manifestation a large mass in the upper mediastinum was found. This extends from the right side of the neck to the middle mediastinum. The lesion is located very close to to the large vessels and esophagus, and threatens to close them. The impending closure of the vena cava, which returns all of the blood from the head and neck and upper extremities through the mediastinum to the heart, causes a backflow of venous blood in the brain. This is known as the upper vena symptoms and is a clinical emergency which requires immediate treatment. Physicians performed emergency-irradiation of the mediastinum in 10 fractions. The tumor mass decreased in the extent, so that the function of the mediastinal vessels could be restored. However, the irradiation caused a radiation-induced esophagitis with deterioration of the current difficulties at swallowing. The patient had to be switched to the parenteral nutrition and intravenous administration of medication. In the further course of treatment the patient received the first cycle of palliative chemotherapy consisting of carboplatin/vinorelbine. This resulted in long-lasting pancytopenia (see control parameters). Isolation of the patient and a demolition of the current cycle of chemotherapy on day 8 was necessary. From day 5 after start of the cycle the daily administration of G-CSF and an empirical antibiotic therapy began. In addition, the patient received four red blood cell and platelet concentrates. Currently, the situation has stabilized somewhat. With the recent therapies we achieved a decrease in tumor mass by more than 25% (minor remission). However, the patient was diagnosed, by gastroscopy, a thrush of the esophagus and the other a narrowing of the existing stenosis at the upper esophagus. Due to the expected persistent food supply difficulties the patient was given a gastrostomy tube and the transition to enteral nutrition started.

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Diagnosis:
Non-small cell lung cancer (NSCLC), large cell histology, poorly differentiated adenocarcinoma, stage IIIb, T4N3M0

Updated: esophageal thrush

Known medical history:
- hypertension
- gastric ulcer in 1998
- gastroesophageal reflux disease
- cervical cancer in 2006, after surgery and adjuvant radiotherapy and chemotherapy (cisplatin / 5-FU) in complete remission

Prescriptions

Prescriptions	**Treatment goals**
Tilidine / naloxone drops 100 mg 1-1-1	Alleviation of tumor-related pain
Codeine 30 mg 0-0-0-1	Relief of the cough stimulus
Ciprofloxacin 200 mg i.v. 1-0-1	Antibiotic prophylaxis during cell lows
Pantoprazole 40 mg i.v. 1-0-1	Prevention of reflux esophagitis
Propranolol 25 mg 1-0-1	Treatment of arterial hypertension
Metoclopramide 20 drops. b. Bed	Relief medication for nausea
Inhalation: Salbutamol 1.25 mg 1-1-1-1 Ipratropium bromide 0.5 mg 1-1-1-1 Dexpanthenol Inhalation Solution 5% 1-0-1 (own recipe)	Facilitate breathing by expanding the airways and support the regeneration of the bronchial mucosa Decrease in tumor growth and improving the quality of life
Tumor-Specific Treatment Carboplatin AUC 6 i.v., d1 Vinorelbine 25 mg / m² iv d1, 8 repeat d 22 Discontinuation on day 8! Granisetron 1 mg i.v. d 1 Dexamethasone 8 mg i.v. d 1	Antiemetic prophylaxis before administration of the cytostatics

Analysis and Plan
Effectiveness of tumor therapy

Analysis / assessment	**Plan / Consulting**
• Chemotherapy Despite daily doses of G-CSF with a total of 17 days the patient had a long-term and severe pancytopenia with consequent increased risk of infection and bleeding. The observed prolonged bone marrow	The non-small cell lung cancer is one of the fast-growing tumors.

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	suppression is best explained by a pre-damage of the bone marrow following chemotherapy of cervical cancer in 2006. In a palliative therapy the administration of a further cycle of carboplatin / vinorelbine is unacceptable. It would be conceivable to continue the therapy as a monotherapy with vinorelbine or gemcitabine in order to reduce the tumor growth, to improve the symptoms and to meet the desires of the patient after a very mild chemotherapy. In the future, this should be avoided, despite chemotherapy required a new pancytopenia. Alternatively, it would possible to continue therapy in the sense of best supportive care, after consultation with the patient and the relatives.	Therefore the therapy should be continued as soon as possible. After consultation with the patient and family vinorelbine as monotherapy with the same dose in 3-weekly intervals is continued. In the subsequent cycles can be carried out with blood-adapted dose modifications, since a shifting of the therapy should be avoided because of the advanced situation.
	• Antimicrobial therapy As the leukocytes are already approximately in the normal range, administration of antibiotic prophylaxis is not necessary. Instead the thrush of the esophagus requires a prompt systemic therapy. The spread of the fungal infection must be avoided must with regard to continuation of the cytostatic therapy. Additionally, the patient should get a local antifungal prophylaxis in the form of a mouth and throat flushing to prevent the spread of infection in the mouth and throat.	Ciprofloxacin i.v. therapy is discontinued. Fluconazole 400 mg iv is prescribed as a systemic antifungal therapy 1-0-0. Furthermore, an additional amphotericin B - 4 x 1ml suspension is used to prevent the spread of infection on the mouth and throat. The use of the suspension was discussed with the patient. At least 4 times a day 1 ml suspension should be distributed in the mouth and throat until the entire surface is coated. The exposure time should be 1 minute or longer to prevent the spread.
	• Pain Management Tilidin/Naloxon-drops appear to be inadequate against the recurrent pressure pain. The half-life of the active metabolite nortilidine is 3-5 hours, so that even at high doses pain peaks experience may occur again and again.	The application of a pharmaceutical form with constant release kinetics is better and is not administered orally or through the probe. The patient receives a fentanyl matrix patches 25 micrograms / h. The patch is changed every 72 hours.
	• antitussive therapy The evening administration of	However, it should be checked whether the newly scheduled fen-

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	codeine-drops appear sufficient to relieve mainly the night time cough.	tanyl matrix patch causes a relief of symptoms. In this case, codeine can be discontinued eventually.
	• Inhalation therapy The existing inhalation of salbutamol and ipratropium bromide therapy, and Dexpanthenol inhalation solution is felt by the patient to be relieving and alleviates irritations.	The inhalation therapy should be continued unchanged.
	• Restlessness and sleep disorders Benzodiazepine or a benzodiazepine-like drug could be used for the treatment of agitation and sleep disorders. A pharmaceutical form can be easily swallowed with the saliva or possibly given slightly through probe should be chosen due to the background of massive swallowing problems. If additional symptoms of depression are noted in the patient, the use of an antidepressant, for example, citalopram may be considered. Additionally, she should be linked to the psycho-oncology services of the hospital.	The patient first receives lorazepam platelets 1mg 0-0-0-1 before going to bed. The platelets dissolve within seconds in the mouth and can be swallowed with the saliva. Alternatively, a tile can be dissolved in a little liquid and applied through the probe.
	• nausea and diarrhea The enteral food intake through a tube after parenteral nutrition can cause nausea and diarrhea. In the case of this patient, the change of diet will be accompanied from the hospital nutrition team. Consequently, when problems during the changeover occur, the nutrition team is consulted. The prescribed relief medication in the form of MCP Ratiopharm® drops (4 mg / ml, 1 ml or 18 drops) is under-dosed with 20 drops. The effective single adult dose is 10 mg. For the patient the dose of 45 drops per administration is needed. For persistent diarrhea, a mild antidiarrheal be found which should not further impair the gut motility, and can be possibly also administered through the gastric tube.	Adjustment of processing rate of the feeding pump isdone by the nutrition team. The use of Plantaginis ovatae seminis tegumentum is discussed with nutrition team, Because of the water-binding properties. Mucofalk bag is used for the symptomatic treatment of diarrhea. Mucofalk – dissolve 5g granules in 150ml water 1-0-1 After each application via the gastric tube it must be carefully rinsed with sufficient liquid to prevent blockage of probe by swelling granules. Doctors and nurses are informed about the correct dosage of MCP ratiopharm drops (4 mg / ml).

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Control parameters	Laboratory values: - Normal: creatinine, sodium, potassium, calcium, Quick value, ALAT, ASAT, GGT lowest point – 7 days after the beginning of the cycle: - hemoglobin: 6.4 g / dl (14 - 18 g / dl) - RBC 3.4 Mill / mm ³ (4.2-5.4 Mill / mm ³) - platelet 19000/mm ³ (150T - 400T/mm ³) - leukocytes 500/mm ³ (4.8 T - 10T/mm ³) 24 days after start of cycle - Hemoglobin: 11.4 g / dl (14 - 18 g / dl) - 3.5 million red cells / mm ³ (4.2-5.4 Mill / mm ³) - platelet 91000/mm ³ (150T - 400T/mm ³) - leukocytes 4700/mm ³ (4.8 T - 10T/mm ³)