Abstract. Background: A carcinoma is the underlying cause of superior vena cava syndrome (SVCS) in 95-97% of patients. The aim of our study is to retrospectively analyse the outcome of patients after local radiotherapy compared to literature data. Patients and Methods: In 35 consecutively registered patients, irradiated because of SVCS, different primary carcinomas (lung, breast, head-and-neck, Non-Hodgkin’s lymphoma) were ascertained. Distant metastases had already been diagnosed in 33 patients. Chemotherapy had previously been given in seven patients. Results: In 30 patients, radiotherapy obtained a reduction of symptoms within 5-9 days. However, in seven patients, radiotherapy had to be stopped early because of local progress and tumor induced complications. Local recurrences were observed in six patients. The 1-year overall survival rate was 15.6%. Survival rate depended significantly on the performance status (p<0.004). Conclusion: Based on literature data our results are comparable regarding the incidence, the radio-oncological procedure and the response to treatment. These data confirm that radiotherapy is the standard treatment in most patients suffering from SVCS. However, it should be determined if endovascular stenting, which is more frequently considered in the last few years in patients with a tumor induced SVCS, may be a useful option as a simultaneous or sequentially given treatment to optimize the palliative effect.

The superior vena cava syndrome is characterized by the obstruction of the superior vena cava, resulting in an increase in the venous pressure in the upper extremities, neck, and head region. The patients’ symptoms include facial/cervical edema, swelling of the thoracic/cervical veins, cough, dysphagia, dyspnoea, hoarseness and chest pain (1-8). In 95-97% of cases, the underlying cause is a malignant disease (lung cancer 52-82%, lymphoma 5-18%, germ cell tumors 6%, metastatic cancer 5-9%) (1, 3-11). Depending on tumor histology, which should be ascertained as soon as ever clinically possible (2, 7, 9, 11), radiotherapy and/or chemotherapy are still considered to be the standard treatment (1, 5, 7, 10-16). Furthermore, publications recommending endovascular stents as first-line therapy prior to any antitumor therapy in superior vena cava syndrome have become more frequent (11, 17-22).

The aim of our retrospective study was to analyse the outcome in our own patients, who were irradiated because of superior vena cava syndrome, to compare these results with literature data, and to give a prospective view on strategies for patients admitted to radiotherapy, whilst also considering the data regarding endovascular stenting.

Patients and Methods

From January 1997 to December 2003, 35 cancer patients (29 men and six women, 39-80 years of age, median 54 years) with a superior vena cava syndrome were consecutively registered and treated at the Department of Radiotherapy and Radiation Oncology of the Johann Wolfgang Goethe – University Hospital, Frankfurt/Main, Germany. In 31.4% (n=11), the superior vena cava syndrome was the first symptom of cancer, whereas in 24 patients (68.6%) the diagnosis of cancer had already been ascertained. Visceral (lung, liver, CNS) and osseous metastases were known in 33 patients (94.3%). Histological evaluation revealed a small cell lung cancer (SCLC) in twelve patients (34.2%) and a non-small cell lung carcinoma (NSCLC) in 20 patients (57.1%), whereas a further three patients had a breast carcinoma, a carcinoma of the oropharynx and a Non-Hodgkin’s lymphoma, respectively. In seven patients (SCLC n=4, NSCLC n=2, lymphoma n=1), the superior vena cava syndrome had already but ineffectively been treated by chemotherapy.
The radiological diagnosis (i.e. computer tomography of the chest) of the superior vena cava syndrome was obtained 26 days (range 0-175 days) before first admittance to our department. At this time, the Karnofsky performance status was 90-100% in 8 patients, 70-80% in 18 patients, and ≤ 60% in 9 patients (median 70%). 57.1% of patients (n = 20) suffered from dyspnoea, 25.7% (n = 9) and 20% (n = 7) from cough and dysphagia, and 8.6% (n = 3) from hoarseness, respectively. A dilatation of the cervical and thoracic veins was observed in 40% (n = 14).

In 62.9% of patients (n = 22), radiotherapy was applied within 24 hours after admittance, whereas in the remaining patients the beginning of treatment was started after histological diagnosis and/or completed staging (maximum delay: 96 hours). In contrast to 14 patients (40%) continuously treated with 2 Gy/day, the initial dose given to the mediastinum ± supraclavicular region (involved field) was 3 Gy/day, for the first 3-5 days in the remaining 21 patients (60%). Treatment was then continued with 2 Gy/day (± weekly). After conventional simulation (opposed beams), in all patients three-dimensional treatment planning was done. In six patients with lung cancer, a dose-modified chemotherapy was simultaneously given.

In addition to the descriptive statistics, survival-plots (Kaplan-Meier-method) and log-rank tests (23) were performed to evaluate differences between patients with regard to their Karnofsky-status and the incidence of the superior vena cava syndrome as first symptom of cancer. P-values less then 0.05 were considered significant (two-tailed). Follow-up data were available in all patients with the exception of two.

Results

After radiotherapy commenced, an evident reduction of symptoms was observed within the first 5-9 days of irradiation treatment in 30 patients (85.7%). Nevertheless, in seven patients (20.2%), radiotherapy had to be early stopped (median dose 34 Gy, 22-40 Gy), because of local progress, reduction of their performance status and tumor induced complications (thrombembolia). These patients died 6-45 days later (median: 27 days). A radiation dose of 31-56.4 Gy (median dose: 50 Gy) was applied in the other 28 patients (79.8%). Radiotherapy induced side-effects (erythema, dysphagia, cough) were mild (CTC I-II); in two patients in whom a chemotherapy was simultaneously given, severe dysphagia (CTC III) and leucopenia (CTC III) were observed, respectively.

Although in six patients (17.1%) local progression during radiotherapy or the follow-up was observed, in the other patients the follow-up was dominated by the treatment of known and/or newly diagnosed metastases. The survival curve of all patients revealed a median survival of 82 days (range 6-2061 days, 1-year overall survival rate: 15.6%) (Figure 1). Taking into consideration only those patients in whom radiotherapy was applied as initially planned, the median survival was 150 days (1-year overall survival rate: 20.8%). The median survival in patients with a good performance status (Karnofsky 90-100%) was 185 days (range 38-2061 days; 1-year overall survival rate: 40%) compared to 152 (range 27-677 days; 1-year overall survival rate: 17.6%) and 21 days (range 6-150 days) in patients with Karnofsky status 70-80% and 50-60%, respectively (p<0.004) (Figure 2). The difference in survival between patients in whom the superior cava syndrome was the first symptom of cancer compared to those in whom the diagnosis of cancer was already known was statistically not significant (p=0.35).

Discussion

Considering the literature data (published since 1990) of locally and/or systemically treated patients with a neoplastic superior vena cava syndrome, the incidence varies between 1.5-8.6 patients/year (4, 12, 14-18, 20, 22, 24-26) with the exception of three authors who observed 12.2, 15 and 17.8 patients/year, respectively (3, 5, 6). Therefore, in our study the yearly incidence of five patients, who also represent a typical distribution of underlying tumors, is comparable. Furthermore, except for those patients in whom chemotherapy was previously given, the median duration of clinical symptoms before radiological diagnosis, is 2-4 weeks (1, 3, 6, 16).

In accordance with our results, independent of tumor histology, a reduction of symptoms is observed in 74-95% of patients within 3-14 days after beginning radiotherapy (1, 4, 10, 13, 14, 16, 27); comparable data are reported in patients with SCLC (77-94%) (12, 16, 21) and NSCLC (60-90%) (15, 16, 21, 24). Non-responders were found in 10-20% (1, 13, 16). Side-effects of radiotherapy were often mild (CTC I-II) even in hypofractionated irradiation acting as effective retreatment of symptomatic superior vena cava syndrome (10); dysphagia and pulmonal reactions were observed in 5-22% (1, 2, 13, 16, 25, 27).

In 5-30% of patients recurrences of superior vena cava syndrome were observed occurring 1-16 months after radio-(chemo-)therapy (1, 12, 13, 21) correlating with our results. However, the local results are mainly given without radiological proof of the therapeutic effectiveness, because of the dominating problems of metastatic disease which determines further therapies as well as the patient's life. Independent of tumor histology, the 1-year survival published in literature data was 11-24%, which is also comparable to our results. In SCLC and NSCLC, the 1-year survival rates were 18-24% and 17-35% (1, 3, 8, 16), respectively.

Considering prognostic factors, the extent of disease at the time of diagnosis is an important parameter (5) although our data could not confirm these results; in patients diagnosed with superior vena cava syndrome as the first symptom of their SCLC, the median survival was 9.5-16.1 months, whereas it was only three months in patients with recurrent or persistent tumors (3, 12, 26). Conflicting results were found regarding the prognostic impact of histology and previous treatment (3, 5, 14). Age obviously does not affect the prognosis (3). Furthermore, the
Fractionation of radiotherapy does not seem to have an impact on the local results as it is often believed (3, 10, 12, 14, 15) although a minimum dose of 20 Gy should be given (10). Regarding patients with SCLC, Chan et al. (12) stated that there is no need for initial hypofractionation, and favored conventional irradiation. On the other hand, if very large fractionation is preferred, Rodrigues et al. (25) recommended 3 x 8 Gy for rapid and effective reduction of symptoms. The patient’s performance status seems to be the most reliable prognostic factor (5, 14, 26). Confirmed by our results, Beck et al. (3) reported that depending on the Karnofsky status, (≥70%, <70%, ≤50%) the mean survival was 244, 71, and 17 days, respectively. Nevertheless, it has to be argued that all publications, considering the superior vena cava syndrome, present only retrospective results essentially containing clinical data, which are based on different patient, therapy, and tumor related characteristics.

Regarding both the observed results of treatment and the prognostic factors the radio-oncological procedure should be discussed. However, in contrast to curatively treated patients diagnosed with superior vena cava syndrome induced by small cell lung cancer without metastases (26), and although tumor histology initially influences the decision regarding chemo- or radiotherapy, literature data, as well as our data, demonstrate that the radiooncological strategies in palliative treatment of patients are based on clinical aspects. Some authors favored large fractionated protocols (2 x 6 Gy, 4 x 5 Gy, 2-3 x 8 Gy), because of the presumably low prognostic outcome of patients (14, 24, 25, 27), whereas in other studies, mean hypofractionation (10 x 3 Gy) (14, 15) or mixed protocols with initial hypofractionated radiotherapy (3-4 Gy), which were followed by conventional fractions (2 Gy, total dose 45-65 Gy) in patients demonstrating a good relief of symptoms (15, 16), were used. In our case, we obviously overestimated the prognosis in some patients; therefore, we now recommend mean hypofractionation (10-12 x 3 Gy) in most cases, whereas radiotherapy should be given only to patients with a good performance status (Karnofsky 90-100%) and controlled metastatic burden conventional.

In conclusion, the primary aim of therapy of the superior vena cava syndrome is a reduction of symptoms and the prevention of morbidity from local progressive disease for the rest of the patient’s life. The effectiveness of radiotherapy is demonstrated by literature data, as well as by our retrospective study. However, although there is little experience to date, in the last few years endovascular stenting, which is also a local procedure to reduce symptoms in tumor induced superior vena cava syndrome, has been recommended as first-line therapy prior to any antitumor therapy (11, 17, 18, 20, 21). Technical success was reported in 88-100% of patients followed by a, when compared to radiotherapy, quicker reduction of symptoms (within hours) in 80-95% of patients (17-19, 22). Although transient thrombosis occurred, major complications were seldom noted (17, 18, 22). Re-obstructions were observed in 13.6-17% of patients (19, 22). As stated in a review published by Rowell and Gleeson (21), endovascular stenting is considered more effective than radiotherapy and chemotherapy in tumor patients, with regard to reduction of symptoms. However, it has to be taken into consideration that in most patients, stent therapy was additionally followed by antitumoral effective irradiation and/or chemotherapy (18, 21, 22).
So far, there have been no trials comparing the effectiveness of radiotherapy, stenting and a combination treatment. Therefore, if stenting is to be an option in patients with superior vena cava syndrome, the optimal timing, supplementary to or after failure of radio-/chemotherapy, has to be individually determined. In our opinion, stenting directly followed by radiotherapy may be recommended in patients in whom the histological diagnosis is not yet known and in whom the necessity for a rapid reduction of symptoms is additionally given or in whom a reproducible positioning for irradiation purposes is not possible. This procedure will (i) provide the opportunity to establish the correct diagnosis before starting radiotherapy, (ii) improve the patient’s compliance regarding adherence to the following treatment protocol, and (iii) prevent side-effects by performing a well-balanced 3D-treatment planning without pressure of time. Depending on tumor histology, radiotherapy is still the treatment of choice in all other patients because of its local and antitumoral effect.

References