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Alveolar soft part sarcoma: a report of 15 cases

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Abstract

The aim of this study was to evaluate the presentation, course and treatment outcome of 15 patients with this rare type of sarcoma. The files of the patients were retrospectively analysed. Overall survival was calculated according to the Kaplan–Meier method. There were 15 patients, 8 male and 7 female. The mean age at diagnosis was 29 years for men and 24 years for women. The median survival was 48 months with an overall 5-year survival of 38%. 5 patients had haematogenic metastases at the time of diagnosis. For the remaining 10 patients with localised disease, the median survival was 48 months and the 5-year survival 48%. The median disease-free survival for these patients was 12 months with a 5-year disease free survival of 40%. After the occurrence of haematogenic metastases, patients survived a median period of 8 months (range 0–45 months). 5 patients are still free of disease after a median period of 234 months (12–295 months). Alveolar soft part sarcoma is found especially in young adults. When diagnosed, it is often metastasised with a poor prognosis. However, when radically resected, long-term survival is possible. © 2002 Published by Elsevier Science Ltd.

Keywords: Alveolar soft part sarcoma; Surgery; Survival

1. Introduction

Alveolar soft part sarcoma is a rare tumour, representing 0.5–0.9% of all soft-tissue sarcomas in adults and 0.8–1.8% of those in children [1]. Published series on presentation, course and treatment outcome are scarce [1–8]. Remarkable is the young age of patients at diagnosis in comparison with other sarcomas [1]. Although alveolar soft part sarcoma is considered indolent with metastases that often appear rather late and tend to grow slowly in the majority of patients, in the long run it is mostly said to be a fatal disease [2].

1.1. Pathology and histogenesis

Alveolar soft part sarcoma shows a characteristic light microscopic appearance [9]. It consists of nests of 5–100 large, loosely arranged, polygonal cells, surrounded by capillaries, resembling alveoli. The tumour cells are rich in cytoplasm, containing periodic acid Schiff (PAS)-positive and diastase-resistant granules and typical crystals. The nuclei are round or oval, have an irregular chromatin pattern and their nucleolus is clear. Mitoses are infrequent.

The histogenesis of alveolar soft part sarcoma remains unclear. In most immunohistochemical studies, expression of muscle-associated proteins like actin, desmin and MyoD1 is found [10,11], however there are conflicting data [9,12,13]. The typical crystals are also seen in muscle spindles in healthy persons in electron-microscopic studies [11,14]. Therefore, the origin of alveolar soft part sarcoma is nowadays considered as myogenic [9,11,15,16]; however, there is no general consensus.

2. Patients and methods

From our registry (1663 sarcomas), we found 15 patients (0.9%) with alveolar soft part sarcoma who were treated at The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital between 1977 and 2000. We collected the files and describe their presentation, course and treatment outcome.

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Survival was determined from date of diagnosis to the date of death or the date of the last follow-up. Disease-free and overall survivals were calculated according to the Kaplan–Meier method. Statistical analyses were performed with Statistical Package for the Social Sciences software (SPSS, Chicago, IL, USA). The results were compared with data from literature.

3. Results

3.1. Characteristics

The study group consisted of 8 men (mean age 29 years) and 7 women (mean age 24 years). The mean age at diagnosis was 27 years (range 1–52 years). The primary site was the lower extremity ($n=8$), buttock ($n=2$), abdominal wall ($n=2$), breast ($n=1$), axilla ($n=1$) and temple ($n=1$). The site of localisation was on the left in 10 cases and on the right in 5 cases. The mean maximal diameter was 10 cm (range 3–20 cm). One patient presented with haemoptysis, the other patients with a painless mass. In 2 cases, the mass, localised in the lower extremity, caused impairment of motility.

3.2. Local treatment

9 patients underwent resection of their primary tumour (Table 1: patients 2–10). In 3 cases, a re-excision was performed, resulting in clear margins in all patients. One patient developed a local recurrence, 3 years after primary treatment. Because of involved margins after resection, radiotherapy was given at that time. She is still alive without disease 25 years after initial diagnosis.

3.3. Adjuvant therapy after surgery

7 of 9 patients with localised disease received adjuvant radiotherapy. Radiotherapy was omitted in patient 6 (Table 1), because the first histology report stated a benign myoblastoma granulare. Patient 7 (Table 1) underwent an upper leg amputation. Radiotherapy in this patient was considered to be of no additional use. 3 patients (numbers 2, 4 and 5) were given adjuvant chemotherapy in a trial setting, consisting of a combination of doxorubicin with ifosfamide.

3.4. Survival

The median follow-up was 170 months (range 2–370 months). One patient was lost to follow-up with evidence of systemic disease 12 months after date of diagnosis. Patient characteristics and follow-up data are listed in Table 1. The median survival of the whole group was 48 months with an overall 5-year survival of 38% (Fig. 1). The 5-year survival for the 10 patients with localised disease at presentation was 48%. The remaining 5 patients already had metastases at the time of diagnosis and survived 1, 22, 39, 48 and 111 months, respectively. 5 patients developed metastases during follow-up after a tumour-free interval of 1, 2, 3, 8 and 12 months with survival after diagnosis of metastases of 0, 4, 8, 36 and 45 months (median 8 months). So far, 5 patients are free of disease and alive after 12, 12, 234, 242 and 295 months, respectively.

3.5. Treatment of patients with metastases

When metastasised, patients were treated with various schedules of chemotherapy, surgical metastasectomies

Table 1
Characteristics of patients with alveolar soft part sarcoma

Patient	Sex	Site	Age (years)	Maximal diameter (cm)	Survival (months)	S[a] (months)	Status
1.	m	Axilla	1	8	3	0	DOD
2.	m	Abdominal wall	52	5	12	–	NED
3.	f	Lower extremity	28	10	12	–	NED
4.	f	Lower extremity	32	5	242	–	NED
5.	m	Abdominal wall	32	11	234	–	NED
6.	f	Temple	18	3	295	–	NED
7.	m	Lower extremity	21	20	48	36	DOD
8.	m	Buttock	34	10	46	45	DOD
9.	m	Lower extremity	35	6	10	8	DOD
10.	f	Buttock	16	11	12	4	Lost
11.	m	Lower extremity[b]	44	17	39	–	DOD
12.	f	Lower extremity[b]	22	15	111	–	DOD
13.	m	Lower extremity[b]	17	8	22	–	DOD
14.	f	Lower extremity[b]	24	7	1	–	AWD
15.	f	Breast[b]	25	13	48	–	DOD

F-up, follow-up; m, male; f, female; DOD, dead of disease; NED, no evidence of disease; AWD, alive with disease.
[a] Survival after occurrence of metastases.
[b] Metastases at presentation.

and palliative procedures, mostly in the form of radiotherapy. Remarkable is the fact that the group of 5 patients who had systemic spread at the time of diagnosis, all pulmonary localised, showed a median survival of 39 months (range 1–111 months), while the group of 5 patients who developed metastases during follow-up showed a median survival of 8 months (range 8–45 months). In the latter group, the site of metastasis was lung ($n=3$), lung/brains ($n=1$) and lung/liver ($n=1$).

3.6. Three remarkable cases

Patient 1 (Table 1), a 9-month-old male baby, developed an axillary swelling after a smallpox vaccination. The tumour extended to the left shoulder and to the ventral and dorsal neck. The size was 6×8 cm. X-ray of the chest showed consolidation of the upper lobe of the left lung. After the diagnosis of alveolar soft part sarcoma, chemotherapy and radiotherapy were started. After an initial partial tumour response, the young boy died 3 months later from respiratory failure. Post-mortem examination showed that the tumour occupied the whole left hemi-thorax. There were also multiple metastases in the right lung.

Patient 6 (Table 1) was 18 years when a painless well vascularised swelling at the left temple with a diameter of 3×2 cm was resected. Histology revealed a benign myoblastoma granulare. Three years later she noticed that her spectacles became less comfortable to wear. Under the scar a smooth, fixed tumour of 3×2 cm could be palpated. At surgery, this tumour proved to be localised in the temporalis musculature and was resected. The pathologist classified it as an alveolar soft part sarcoma. Revision of the former resected specimen resulted in the same conclusion. Because of possible involved margins, radiotherapy was added. Twenty-two years later, she is doing well without signs of local recurrence or metastases.

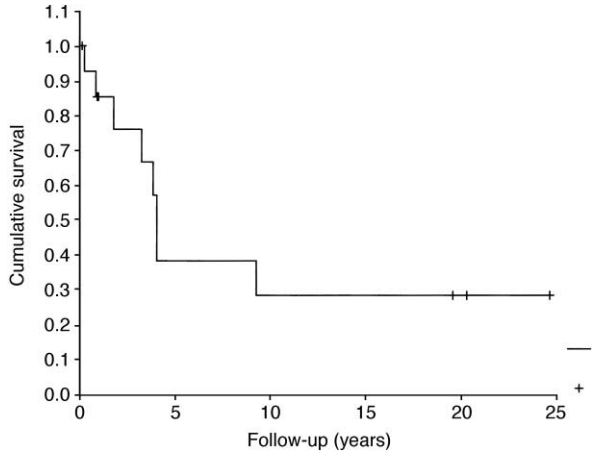

Fig. 1. Overall survival of 15 patients with alveolar soft part sarcoma.

Patient 12 (Table 1), a 22-year-old female, presented with haemoptysis. On chest X-ray, multiple lung metastases were seen. Patient reported the existence of a non-painful swelling with a maximal diameter of 15 cm on her left thigh near the quadriceps muscle for almost 1 year. Incision biopsy revealed an alveolar soft part sarcoma. After seven courses of doxorubicin, complete remission for almost 8 years was achieved. However, at that time, a metastasis was found between the liver and kidney which was surgically removed. Because of recurrent lung metastases several courses of chemotherapy, now in the form of etoposide and thereafter docetaxel, were given. Unfortunately, she was progressive and after 1 year she also developed brain metastases. Notwithstanding radiotherapy, she soon died, 9 years and 3 months after her initial diagnosis.

4. Discussion

Alveolar soft part sarcoma is a rare tumour. It is most common in young women. The average age at diagnosis is 20 years for women and 30 years for men. Our group is consistent with these data from the literature. In adults, the tumour is often localised in the lower extremity, in children, the head and neck is the predominant site [1,2,17]. In our series, the majority of the tumours was found in the lower extremity (8/15). Remarkable are the earlier reports of the 2:1 preference for the right side of the body [3,18]; however, later studies could not confirm this statement [2,4,19]. On the contrary, in our series we find a preference for the left side of the body, suggesting that the site is irrelevant. Mostly presenting with few symptoms, the tumour can be easily overlooked. The mean maximal diameter in our series was 10 cm, indicating a late recognition. A relationship with trauma has never been found, but this is often mentioned to have taken place before the perception of a painless mass [20]. No aetiological factors are reported, except in a case report of an alveolar soft part sarcoma 20 years after radiation therapy [21]. Sometimes a murmur can be heard over this, in most instances, well vascularised tumour. Although alveolar soft part sarcoma is often considered indolent with metastases that often appear rather late and tend to grow slowly in the majority of patients, in the long run it is in most instances said to be a fatal disease [2].

Radical excision is the therapy of choice. Local recurrence is said to be unusual when radically resected. In our study, 1 patient developed local recurrent disease; therefore the recurrence rate was 11%, comparable to the series of Portera and colleagues [7]. However, the larger series of Zhang and colleagues ($n=51$) and Lieberman and colleagues ($n=91$) reported a recurrence rate of 50% [2,5]. There are no data available on survival after local recurrence.

The site of metastasis is usually the lung, bone or brains [3]. In our series, 5 (33%) patients were metastasised at time of diagnosis, all pulmonary localised, findings that are comparable with other studies [2,5]. 2 of these patients also developed brain metastases. From our 5 patients who developed haematogenic spread during follow-up, the site of metastasis was lung, liver and brains. The metastatic rate in our group was 56% (5/9) similar to the results of Zhang and colleagues [5] and Lieberman and colleagues [2] much higher than found by Portera and colleagues (16%), however [7]. Metastasectomies of the lung and brains have shown favourable results with prolonged survival in selected patients [2,19,22–25]. Only 1 patient in our series underwent metastasectomy for a solitary brain metastasis; however, 6 months later she presented with multiple cerebral recurrences. Lieberman and colleagues found 7% of the metastases in lymph nodes [3], which is to our knowledge the only report of lymphatic spread in literature. In our series, no lymphatic metastases were found. It has been reported that chemotherapy and radiotherapy are probably of no use [2]. However, Sherman and colleagues have queried this statement [26] and in our study a few patients benefited from chemotherapy, among them 1 long-term survivor.

Our 5-year overall survival rate was 38%, for localised disease this was 48%. Other 5-year survival rates vary between 45 and 88% depending on the selection of patients [2,4,5,7,8]. When metastasised at time of diagnosis, the median survival of our patients was 39 months, when metastasised during follow-up this was 8 months. We cannot explain this difference other than being a spurious result due to the small number of patients. Another explanation could be the fact that the in most instances X-ray of the chest was used to identify lung metastases. Nowadays, also in our hospital, both generally and spiral Computed Tomography (CT) scan of the thorax is a standard procedure for staging. Probably, when spiral CT scans were used in the cases when metastases occurred very soon after diagnosis, those patients were classified as already metastasised. Furthermore, in such cases, the described high median survival in patients with systemic spread would decrease and the found low median survival in patients with localised disease would increase. Data from the literature indicate a median survival for metastasised patients of 2 years [2]. Only 2 patients are reported with a survival of more than 20 years [7,27]. It is a remarkable finding that our study contains 2 such patients, all still alive without disease, at least 20 years after diagnosis.

The size of the primary tumour seems to correlate with survival; Evans found worse survival rates when the tumour diameter was more than 5 cm [3,6]. In our study, the mean largest diameter was 10 cm which could contribute to our worse survival in comparison to other reports. Jong and colleagues, however, could not demonstrate any correlation between survival and clinical presentation, histology grade, vascular invasion or p53 accumulation [28]. In addition, prognostic impact of sex and laterality of the primary site could be found [2]. We decided not to perform a statistical analysis for prognostic factors because of the limited number of patients.

5. Conclusions

Alveolar soft part sarcoma is most common in young adults. In contradiction to literature, in our patient group no female preponderance was found. The same was the case with the frequently reported preference for the right side of the body. The site of the primary tumour location was most commonly in the lower extremity. Presenting, in most instances, with few symptoms, tumour size at the time of diagnosis was frequently quite large. When diagnosed, a third of our patients already had haematogenic spread. In these instances, although some patients may survive a few years undergoing systemic treatment, the final outcome is always dismal. However, when radically operated, local recurrence is rare and long-term survival, over 20 years, is possible.

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