ORIENTEERING

Palliative Care in Rheumatic Diseases: a First Approach

STEFFEN SIMON, Institute of Palliative Care, Oldenburg, Germany, and King's College London, School of Medicine, Department of Palliative Care, Policy and Rehabilitation, London, England, UK, MICHAEL SCHWARZ-EYWILL, Palliative Care Centre Oldenburg, Department of Internal Medicine and Rheumatology, Evangelisches Krankenhaus, Oldenburg, Germany, CLAUDIA BAUSEWEIN, King's College London, School of Medicine, Department of Palliative Care, Policy and Rehabilitation, London, England, UK

BACKGROUND

In the last decades, major advances have been made in the treatment of rheumatic diseases. The development of new and evidence-based therapies, backed up by research, greatly improved the prognosis and reduced the mortality of several rheumatic diseases (1). The introduction of the so-called biologicals (immunomodulating therapy, e.g., tumour necrosis factor antibodies) made it possible for the first time to achieve remission in patients suffering from advanced rheumatic diseases. Nevertheless, this success should not obscure the fact that the vasculitides, the connective tissue diseases, and severe courses of rheumatoid arthritis (RA) are still life-threatening diseases and, even nowadays, patients may die early from them.

Since its foundation by Dame Cicely Saunders in the 1960s, palliative care deals with terminal illness and still focuses on the management of malignant disease. Even in 2004, 95% of patients treated in specialized palliative care units in the U.K. suffered from cancer (2). For a long time, amyotrophic lateral sclerosis (ALS) was the only nononcological disease to be considered for palliative care. Patients suffering from other nonmalignant disease such as heart or kidney failure, or chronic obstructive pulmonary disease have only had access to palliative care since the late 1990s (3). However, patients with advanced rheumatologic disease in a palliative situation hardly ever have access to palliative care. Nevertheless, they should also benefit from the advances and therapeutic options of palliative medicine.

The aim of this article is to describe and discuss three typical patients with advanced rheumatic diseases fulfilling the criteria for palliative care, and to discuss palliative issues in rheumatic disease.

CASE REPORTS

Patient I

A 45-year-old, mobile woman reported a history of epigastric pain for seven months. She also complained of loss of appetite resulting in weight loss, and of polymyalgia. Large vessel vasculitis was diagnosed (Takayasu's arteritis, according to American College of Rheumatology [ACR] criteria). Further investigations showed mesenteric involvement (superior mesenteric artery and celiac trunk), and treatment with cyclophosphamide and steroids was started. The course of the disease was characterized by a dramatic and fulminant decline, without recovery after treatment with immunosuppressants. Abdominal pain increased in intensity, and the patient suffered from nausea and vomiting several times a day, which could only be treated symptomatically. Two months after diagnosis, she was admitted to hospital with acute abdominal pain. The laparotomy revealed a total gangrene of the small bowel and right colon, necessitating bowel resection. The previous therapy with immunosuppressants was stopped. Meanwhile, the patient was bedridden and immobile. She suffered from psychological distress with severe anxiety regarding her own condition and the future care of her family. Psychosocial and spiritual support was provided regularly for the patient and her family by a psychologist, the chaplain, and the care team. The support helped to reduce her distress. Despite parenteral nutrition, the patient developed cachexia and her general condition declined. Furthermore, she suffered several times from pneumonia and sepsis, and needed ventilation. After seven months in hospital, the patient could be discharged. She was free of symptoms but needed care from her relatives and support from a home care service. Two months later, the patient developed a candida sepsis leading to fatal multiorgan failure. She died in hospital.

Patient II

A 63-year-old man, initially treated for left-ventricular heart failure, developed a progressive, particularly right-sided muscle weakness and anasarca. A secondary vasculitis in association with Waldenström's syndrome was diagnosed. Although therapy with cyclophosphamide and steroids had been started immediately, the patient became tetraplegic from polyneuromyopathia.

Journal of Palliative Care 24:4/2008; 270–273

The further course was characterized by a progressive decline punctuated by recurrent cardiac decompensations necessitating cardiopulmonary resuscitation. Furthermore, the patient suffered from refractory anemia, renal insufficiency, recurrent pneumonia, and therapy-resistent diarrhea. Because of the development of a progressive dysphagia, a feeding tube was placed. Although therapy with high-dose immunosuppressants was started, the patient did not recover and, therefore, disease-specific therapy was stopped. The patient struggled with his prognosis and completely denied his condition. He was reluctant to discuss advance care planing. Communication about end-of-life issues was further complicated by a difficult relationship between the patient and his relatives. Long conversations were necessary regarding his wishes and options for his care. Finally, he was able to be discharged from hospital after his general condition improved. However, 12 hours later, he returned with left-ventricular heart failure and died from it soon afterwards.

Patient III

A 65-year-old woman reported a history of myalgia and pruritic erythema for several weeks before presentation. She also complained of progressive proximal muscle weakness. The diagnosis of a dermatomyositis was made histologically, without evidence of a malignant disease. Therapy was started with azathioprine and steroids. The patient became tetraplegic due to progressive muscle weakness, leading to immobility. In the following weeks, she suffered from pneumonia, candida esophagitis, capillary-leak syndrome, marked hypersialosis, and reactive depression. The development of a progressive dysphagia necessitated feeding tube placement. Although therapy with immunosuppressants was altered several times, the patient did not recover and the therapy was stopped after three months. She developed a mild depression which was treated with antidepressants. Support from the psychologist helped her to cope better with her situation. Continuous communication with the patient's relatives was helpful for the further care. After stabilization, the patient was discharged to a nursing home. Follow up after five months revealed unchanged tetraplegia and recurrent complications caused by infections, suggesting a poor prognosis.

RHEUMATIC DISEASES AND PALLIATIVE CARE

According to the WHO definition of palliative care (4), patients suffering from the following inflammatory-rheumatic diseases should be considered for palliative care management, especially in advanced stages of the disease or with a fulminant course:

- vasculitides
- connective tissue diseases
- dermatomyositis
- special courses of a disease:
  a) the malignant course of rheumatoid arthritis (RA)
  b) development of a progressive pulmonary fibrosis in the context of an autoimmune disease

The vasculitides are a heterogenous group of diseases that cause inflammatory, necrotic infiltration of the blood vessels. First, the vasculitis may affect only one blood vessel or region. But commonly, it is an inflammatory systemic disease affecting several organs. The group of primary systemic vasculitides consists of the following (according to the Chapel Hill Consensus Conference, 1992): giant-cell arteritis, Takayasu's arteritis, polyarteritis nodosa (PAN), Kawasaki disease, Wegener's syndrome, Churg-Strauss syndrome (CSS), microscopic polyangiitis (MPA), Henoch-Schönlein purpura, essential cryoglobulinemia vasculitis, and cutaneous leukocytoclastic angiitis. Secondary vasculitis either develops in connection with another illness, such as rheumatoid arthritis, or is induced by drugs.

The term connective tissue diseases (or collagen diseases) describes a group of systemic tissue diseases with multiple autoimmune phenomena. Particularly the inner organs, but also joints, muscles, and the skin are affected. The group of connective tissue diseases consists mainly of the following: systemic lupus erythematosus (SLE), progressive systemic sclerosis (PSS), mixed connective tissue disease, and Sjörgen's syndrome. In addition dermatomyositis should be added.

Rheumatic arthritis (RA) is a chronic, systemic, inflammatory disease causing polyarthritis. Extra-articular organ manifestations especially are responsible for malignant courses of the disease and are, therefore, of interest to palliative care.

Finally, progessive pulmonary fibrosis can develop in connection with all rheumatic systemic diseases, particularly with primary systemic scleroderma, rheumatoid arthritis, vasculitides, and connective tissue diseases.

The prognosis and fulminant courses of vasculitides, connective tissue diseases, and rheumatoid arthritis are summarized in Table 1.

DISCUSSION

This is the first report discussing the palliative care needs of patients with advanced rheumatic disease towards the end of life. Despite the fact that the group reported on is very small, there is a clear need for the palliative care approach in this group, as patients are suffering from uncontrolled symptoms and severe psychosocial

Table 1 / PROGNOSIS AND FULMINANT COURSES OF RHEUMATIC DISEASE

	Vasculitides	Connective tissue diseases	Rheumatoid Arthritis
Prognosis (5-year survival rate)	PAN, MPA, CCS >80% (5) Takayasu's arteritis 93% (6) Wegener's syndrome 76% (7)	SLE 80%–90% (8) dermatomyositis 63% (9)	SMR* 2.26 (10)
Percentage of fulminant courses (Percentage of patients dying early to total deaths)	58% (1)	unknown	unknown

*standardized mortality ratio (SMR): ratio of observed deaths to expected deaths in a population in a region

distress towards death, comparable to patients with advanced cancer.

According to the literature, the prognosis for all rheumatic diseases is nowadays much better than 30 years ago and the survival rate of patients with vasculitis has improved in the last 20 years (1,6). However, the percentage of fulminant courses has increased (1) and there is still a relevant percentage of patients with limited life expectancy (Table 1). The term "fulminant course" describes a trajectory of illness leading to the patients' death within the first year of diagnosis. Bourgarit et al. (1) showed in their study of 60 patients with a fulminant course of vasculitis that these patients had a median survival time of just three months. The main characteristic of all three patients described in this article was the fulminant and dramatic trajectory of illness, with two patients dying ten and four months after the diagnosis had been established, or 20 and eight months after onset of the first symptoms, respectively. In all reported cases, inner organ manifestations were regarded as risk factors predicting a fulminating and fatal course, e.g., the patient described in the first case report had inflammatory modification of the mesenteric vessels which caused intestinal infarction and tissue necrosis necessitating intestinal resection. Organ manifestations are partly disease-specific (1). The degree of involvement may be similar to the degree of metastasis in cancer.

Further fulminating and fatal courses have been described in the literature (11,12). Most patients with rheumatoid arthritis die of heart failure, primarily due to chronic cardiac insufficiency (13). Therefore, the course of illness might be similar to the group of organ system failure as described in the trajectories model of Lynn (14). The incidence of fulminating courses can only be calculated for vasculitides (1). The relatively high rate of fulminant courses must be interpreted with caution because of the single-site study. Other data is not available.

The first step in the management of this subgroup is to recognize and identify those rheumatologic patients whose course of disease makes palliative care necessary. Nearly all rheumatic diseases are incurable and progressive, defining them as chronic illnesses, but not necessarily as diseases that should be treated under aspects of palliative care. The aim of therapy should be altered from cure to palliation only if the rheumatic disease has progressed to an advanced stage or has taken a fulminant course. This is a gradual process and the introduction of the general palliative care approach should be considered while active treatment is still ongoing. As a consequence of the rapid progression of the disease, these patients suffer in the same way as patients with advanced cancer from severe physical impairment and various symptoms such as pain, nausea, or weight loss. According to our experience, rapidly progressive muscle weakness and fatigue lead to immobility which, in turn, leads to further complications and various problems, e.g., an increased susceptibility to infection, decubital ulcers, and progressive muscular atrophy. These symptoms are described regularly in the literature, but they are not evaluated with respect to prevalence, prognosis, and quality of life in patients with advanced stage of disease (15–18). Furthermore, these patients develop multiple complications, either due to the disease itself (e.g., intestinal infarction in vasculitis) or indirectly caused by therapy or immobility (e.g., increased susceptibility to infection) (19).

When unrelieved symptoms, psychosocial distress of patients and carers, or questions around advance care planning become the main focus, patients with rheumatic disease should have access to specialist palliative care. This includes a holistic assessment of patients' needs and an exploration of patients' future preferences for care, as well as documenting advance directives. Facilitated advance care planning through the provision of timely appropriate information can positively enhance rather than diminish patients' hope (20).

At this stage, the aim of maintaining and restoring the patient's quality of life through relief of suffering and symptom control (as mentioned in the definition of the WHO) is essential (4). It is more difficult to predict upcoming death for patients with chronic, nonmalignant disease than it is for patients with cancer (21). This uncertainty may be

caused by the impossibility of predicting a typical trajectory of illness, for example, rheumatological disease is characterized by a progressive decline punctuated by recurrent periods of exacerbation (22). The patient's prognosis can be readily assessed, especially in patients with progressive chronic illnesses, by asking oneself the following question, mentioned by Murray et al.: "Would I be surprised if my patient were to die in the next 12 months?" (23). If the answer is "no", patients should receive patient-centred treatment and palliative care. This applies to patients with advanced and complicated rheumatologic disease as well as to other nonmalignant disease. Recurrent hospital admissions and severe complications could be other indicators to identify the need for palliative care.

As a consequence of the lack of knowledge in the literature regarding the palliative care needs of patients with rheumatic diseases, there are potential areas for further research:

- definition of end-stage rheumatic disease and identification of potential cases with palliative care needs using defined criteria;
- evaluating palliative care needs of patients with rheumatic diseases and their relatives;
- prevalence of symptoms of these patients with different rheumatic diseases;
- therapeutic strategies for symptom control; and
- better understanding of illness trajectories and timing of palliative supportive services.

SUMMARY

Currently, the main goal in rheumatic research is to achieve remission, even in highly active stages of the disease. However, there is a lack of understanding of how to manage patients when some rheumatic diseases such as vasculitis, connective tissue disease, or rheumatoid arthritis develop fulminant, progressive, and complicated courses. There is a clear role for palliative care to enhance patients' quality of life, but hardly any data exist regarding the prevalence and management of symptoms, and the special needs of these patients and their relatives. Rheumatologists, and palliative and primary care physicians should become more aware of this patient group so as to offer them the care they need. Further research is necessary in this field.

Date received, March 13, 2008; date accepted, August 28, 2008.

REFERENCES

1. Bourgarit A, Le Toumelin P, Pagnoux C, Cohen P, Mahr A, Le Guern V, et al. Deaths occuring the first year after treatment onset for polyarteritis nodosa, microscopic polyangiitis and Churg-Strauss syndrome. Medicine 2005 ; 84: 323–330.
2. Hospice and Palliative Care – Facts and Figures 2005. [www.hospiceinformation.info/factsandfigures.asp]
3. Lynn J. Caring at the end of our lives. NEJM 1996; 335: 201–202.
4. Sepúlveda C, Marlin A, Yoshida T, Ullrich A. Palliative care: the World Health Organisation's global perspective. J Pain Symptom Manage 2002; 24(2): 91–96.
5. Pagnoux C, Guillevin L. How can patient care be improved beyond medical treatment? Best Pract Res Clin Rheumatol 2005; 19: 337–344.
6. Park MC, Lee SW, Park YB, Chung NS, Lee SK. Clinical characteritistics and outcomes of Takayasu's arteritis: analysis of 108 patientens using standardized criteria for diagnosis, activity assessment, and angiographic classification. Scand J Rheumatol 2005; 34: 284–292.
7. Lane SE, Watts RA, Shepstone L, Scott DGI. Primary systemic vasculitis: clinical features and mortality. Q J Med 2005; 98: 97–111.
8. Uramoto KM, Michet CJ Jr, Thumboo J, Sunku J, O'Fallon WM, Gabriel SE. Trends in the incidence and mortality of systemic lupus erythematosus, 1950–1992. Arthritis Rheum 1999; 42: 46–50.
9. Airio A, Kautiainen H, Hakal M. Prognosis and mortality of polymyositis and dermatosmyositis patients. Clin Rheumatol 2006; 25: 234–239.
10. Wolfe F, Michaud K, Gefeller O, Choi HK. Predicting mortality in patients with rheuamtoid arthritis. Arthritis Rheum 2003; 48: 1530–1542.
11. Simon S, Schittko G, Bösenberg H, Holl-Ullrich K, Schwarz-Eywill M. Fulminant course of a Takayasu's arteritis and rare mesenteric arterial manifestation. Z Rheumatol 2006; 65(6): 520–526.
12. Nussaume O, Bouttier S, Duchatelle JP, Valere PE, Andreassian B. Mesenteric infarction in Takayasu's arteritis. Ann Vasc Surg 1990 ; 4: 117–121.
13. Boers M, Dijkmans, Gabriel S, Maradit-Kremers H, O'Dell J, Pincus T. Making an impact on mortality in rheumatoid arthritis. Arthritis Rheum 2004; 50: 1734–1739.
14. Lynn J. Perspectives on care at the close of life. Serving patients who may die soon and their families: the role of hospice and other services. JAMA 2001; 285(7): 925–32.
15. Engel JZ. Shortness of breath and chest pain with scleroderma. Tenn Med 1996; 89(10): 376–377.
16. Kozora E, Ellison MC, West S. Depression, fatigue and pain in systemic lupus erythematosus (SLE): relationship to the American College of Rheumatology SLE neuropychological battery. Arthritis Rheum 2006; 55(4): 628–635.
17. Herrick AL. Advances in palliative care for the patient with scleroderma. Curr Opin Rheumatol 1996; 8(6): 555–560.
18. Goldblatt F, Hill W, Ahern MJ, Smith MD. Shortness of breath in systemic lupus erythematosus: a diagnostic and therapeutic dilemma. Ann Rheum Dis 2002; 61(7): 588–590.
19. Pagnoux C, Mahr A, Cohen P, Guillevin L. Presentation and outcome of gastrointestinal involvment in systemic necrotizing vasculitides. Medicine 2005; 84: 115–128.
20. Davison SN, Simpson C. Hope and advance care planning in patients with end-stage renal disease: qualitative interview study. BMJ 2006; 333(7574): 886.
21. Lynn J. Learning to care for people with chronic illness facing the end of life. JAMA 2000; 284: 2508–2511.
22. Lynn J, Goldstein NE. Advance care planning for fatal chronic illness: avoiding commonplace errors and unwarranted suffering. Ann Intern Med 2003; 138: 812–818.
23. Murray SA, Boyd K, Sheikh A. Palliative care in chronic illness. BMJ 2005; 330: 611–612.

Disclosure
The authors declare that they have no competing interests. SS conceived the idea for the paper and drafted the manuscript; SS and MSE were the physicians caring for the patients presented in the case reports. CB was involved in discussions around the paper, helped search the literature, and revised earlier versions. All authors read and approved the final manuscript.