Cancer treatment in the extreme elderly: case study of a 100-year-old lymphoma patient

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Practice points

- Research into the treatment of elderly cancer patients is rare.
- The presence of significant comorbidities may preclude aggressive treatment due to a perceived imbalance between risks and benefits.
- Comprehensive geriatric assessment helps identify patient's fitness for active therapy and influence treatment choice and intensity.
- We report a case of a female patient with lymphoma who was treated into her 100th year.
- Active treatment is possible in the extreme elderly cancer population with geriatric assessment a useful adjunct in determining the appropriate treatment protocol in relation to efficacy, intensity and adverse effect profile.

Limited data are available on the treatment of older adults with cancer. Comorbidities may preclude the administration of effective therapies, particularly in the extreme elderly. Comprehensive geriatric assessment can identify specific weaknesses of the patient and predict unexpected toxicities, thus enabling an optimized treatment strategy in this population. We report a case of the successful management of a 99-year-old female lymphoma patient with a strong wish for active treatment to improve quality of life and prolong survival past her 100th birthday. This case demonstrates that cancer treatment in the extreme elderly is possible and highlights the need for a formalized treatment plan based on geriatric assessment, frank discussion with patients and families, and defined goals of therapy.

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Older adults experience the majority of cancer diagnoses and deaths, and constitute the majority of cancer survivors. They are under represented in clinical trials, and trials designed specifically for the elderly are rare [1]. Hence, clinicians have a limited evidence base on how to treat this important group of patients. When developing treatment strategies clinicians are forced to extrapolate from trials conducted in younger, healthier populations. Whether all older patients are able to tolerate and benefit from cancer therapy is uncertain [1,2]. In addition to the lack of specific clinical trial data, there are other factors that may influence treatment in the elderly patient with cancer [3]. Older clients commonly have significant comorbidities which may preclude the administration of effective therapies at the appropriate dose intensity. Physicians may also be reluctant to prescribe aggressive treatments in this population due to the perceived imbalance between risks and benefits. This dilemma is even more pronounced in the extreme elderly patient.

KEYWORDS

- centenarian
- comprehensive geriatric assessment
- extreme elderly
- lymphoma
- rituximab

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Because chronological age alone is a poor descriptor of heterogeneity in the aging process, a systematic and evidence-based way of describing the heterogeneity is needed to guide oncology treatment decisions. A comprehensive geriatric assessment (CGA) can fill this knowledge gap [4]. Geriatric assessment is valuable in oncology due to its ability to detect impairment not identified in routine history or physical examination, predict severe treatment-related toxicity, forecast overall survival in a variety of tumors and treatment settings and influence treatment choice and intensity [4].

We wish to report a case of a 99-year-old woman diagnosed with follicular lymphoma transformed to diffuse large B-cell lymphoma (DLBCL) who continued treatment into her 101st year.

Case presentation

A 99-year-old Caucasian woman was transferred to our regional cancer center, from a low care nursing home, for investigation of unilateral right lower limb swelling of a few months duration. She had suffered a significant decline in mobility and independence over the 2 weeks prior to admission due to the painful condition. Obvious right inguinal swelling was present. She had no B-symptoms. CT subsequently showed extensive para-aortic and right iliac chain lymphadenopathy causing compression of the right external vein. A nonocclusive thrombus of the right external iliac vein was confirmed on ultrasound. Core biopsy of the right iliac lymph node demonstrated follicular lymphoma with focal transformation to DLBCL. CD20 B-cells were strongly positive. The patient clearly communicated her wish to have minimal investigations and appropriate treatment to improve her symptoms. As the goal of therapy was clearly defined as palliative, complete staging with bone marrow biopsy and positron emission tomography scan was not performed. Her performance status was poor with an ECOG score of three.

Her prior medical history was significant for ischemic heart disease, paroxysmal atrial fibrillation, hypertension, Type 2 diabetes mellitus, mild renal impairment, urinary incontinence, osteoporosis with previous minimal trauma vertebral compression fracture, osteoarthritis, depression and an untreated right frontal squamous cell carcinoma. Regular medications were diltiazem, flecainide, citalopram, gabapentin, ibuprofen and buprenorphine patches.

This case was discussed at our multidisciplinary lymphoma meeting where results of her CGA were considered. Further discussions were held with the patient and her immediate family. As she was symptomatic from her disease, the patient strongly re-expressed her wish for active intervention to improve quality of life. She also hoped that therapy would extend her survival by months and allow her to reach her 100th birthday. Possible outcomes and complications from palliative chemoimmunotherapy were outlined and a treatment plan formulated with a low threshold for ceasing active treatment if she developed any adverse events impacting on her quality of life. A 'not for resuscitation' plan was completed with patient and family.

Palliative treatment was commenced as an inpatient on 1 May 2015 with rituximab 375 mg/m² intravenous (iv.) and vinblastine 6 mg/m² iv. both given on day 1. Rituximab monotherapy was to be given on days 8, 15 and 22, with maintenance rituximab 375 mg/m² then to be given at 3 monthly intervals. Hydrocortisone 100 mg iv. premedication was administered prior to each rituximab infusion. Subcutaneous enoxaparin 1.5 mg/kg daily was also started. Performance status had improved to ECOG 2 at the time of discharge, 5 days after commencing therapy. A good early clinical response with marked reduction in swelling and pain in the right leg was noted when she returned as a day patient for day 8 rituximab. Enoxaparin was changed to rivaroxaban after 2 weeks. Treatment was well tolerated with no adverse effects. Anticoagulation was ceased after several months due to bleeding from her facial squamous cell carcinoma. She was deemed not suitable for surgery or radiotherapy and managed conservatively. A total of three doses of rituximab maintenance were administered, with the last dose given 2 days after her 100th birthday, which she celebrated in February 2016. At her last clinic visit her mobility had decreased and there was deterioration in her memory. She had been transferred to a high care nursing facility. There were no clinical signs of lymphoma progression. She died on 11 April 2016 with the cause listed as bronchial pneumonia. Patient consent for the publication of this case was obtained prior to commencement of treatment.

Discussion

Life expectancy has dramatically expanded and the number of nonagenarians and

centenarians with malignant disease has significantly increased [5,6]. However, cancer in the very elderly is relatively uncommon as a disease and as a cause of death, being characterized by a slow pattern of growth and a modest life-threatening potential [6]. Some epidemiological data on cancer in centenarian patients are available, but studies on management are scarce [6]. Older adults respond differently to cancer treatments than younger patients. This has been attributed to a number of factors including: age-associated physiological changes, such as changes in organ function, a higher incidence of comorbidities and concomitant medication use which could interact with cancer treatments [1]. They are therefore more sensitive to toxicity and the adverse effects resulting from treatment. The great heterogeneity in the health of the elderly makes chronological age an inadequate characterization of their health status.

In the treatment of the elderly with lymphoma the object should be to identify specific weaknesses of the patient and thus predict potential unexpected toxicities which may endanger outcome. This information enables an optimized treatment strategy to be proposed, with an efficacy/toxicity ratio that is acceptable to both hematologist and patient [7]. Patients may be divided into two groups: fit patients who should be treated with standard treatment (e.g., R-CHOP) and unfit patients who need to be treated with caution. Unfit patients may be treated with reduced doses (e.g., R-mini-CHOP, R-COP) or rituximab alone [7].

Prior to considering treatment in our patient a number of assessments were conducted. No cognitive impairment was found. Charlson Comorbidity Index (CCI), a classification of comorbid conditions which may alter mortality risk, was calculated as three [8]. For assessment of self-care activities, tasks of household management and independence status, the Katz Activity of Daily Living [9] and Lawton Instrumental Activity of Daily Living [10] were performed. She scored four on the Activity of Daily Living, with a range of zero (patient very dependent) to six (patient independent), indicating moderate impairment. On the Instrumental Activity of Daily Living she scored two, with a range of zero (low function, dependent) to eight (high function, independent), indicating low-to-moderate functionality. These results were considered, bearing in mind that functional impairment may be due

to malignant disease and not other comorbidities, when selecting an appropriate treatment regimen. Kobayashi *et al.* evaluated the correlation between comorbid medical status and clinical outcome among elderly patients with DLBCL [11]. A total of 80 patients from age 66–90 years were analyzed. CCI, without considering primary disease, was calculated for each patient and then they were divided in low CCI (zero or one) or high CCI (>2) groups. The low CCI group, into which our patient would fall after eliminating the score of two attributed to her primary lymphoma, was independently associated with a better outcome.

As the treatment intent in our patient was always palliation, a full pretreatment work-up was not performed. It was felt that additional tests such as bone marrow biopsy and positron emission tomography scan would be inconvenient and potentially painful, and not influence the proposed treatment plan. It was also decided, in consultation with the patient and family, not to perform further CT scans to monitor disease progress but to rely solely on clinical assessment. Due to her unfit status following CGA, our patient was treated primarily with rituximab immunotherapy. Vinblastine was chosen as the only chemotherapeutic agent due to the low propensity for myelosuppression and neurotoxicity in comparison with other potential agents. Subsequent vinblastine doses were not given to allow her primary treatment to be administered over a shorter timeframe. Steroids, other than hydrocortisone premedication, were not given as this may have worsened diabetic control and possibly induced limiting myopathy.

Treatment choice in the extreme elderly is difficult as studies of lymphoma in patients above 90 years are rare. Extermann *et al.* reviewed charts of 177 patients who were aged 90 years or older [5]. Only seven (4%) had a hematologic malignancy and only limited information was provided on chemotherapy or targeted therapy use [5]. A multicenter retrospective analysis was undertaken of patients diagnosed with lymphoma at the age of 90 or older in France over a 12-year period [12]. A total of 234 patients were identified of whom 133 had aggressive non-Hodgkin lymphoma with 113 (48.3%) having a diagnosis of DLBCL. Treatment data were analyzed for 104 patients with aggressive non-Hodgkin lymphoma which comprised no treatment or corticosteroids (33.6%), radiotherapy

or surgery alone (9.6%) single-agent therapy (13.5%), polychemotherapy without anthracyclines (33.6%) or polychemotherapy with anthracyclines (9.6%).

Conclusion

This case demonstrates that treatment of DLBCL can be achieved in the extremely elderly population with improvement in quality of life. Geriatric assessment should be considered as a useful adjunct when determining management options. The identification of potential weaknesses of the patient will aid the hematologist in selecting the appropriate protocol in relation to efficacy, dose intensity and potential adverse effects.

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Informed consent disclosure

The authors state that they have obtained verbal and written informed consent from the patient/patients for the inclusion of their medical and treatment history within this case report.

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