Epidemiology of Plasma Cell Leukemia in the Czech Republic

Epidemiologie plazmocelulární leukemie v České republice

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Summary

Background: Plasma cell leukemia (PCL) is a rare but most aggressive form of monoclonal gammopathies. PCL is characterized by the presence of clonal plasma cells in peripheral blood. There are two forms of PCL – primary which presents *de novo* in patients with no evidence of previous multiple myeloma and secondary which is a leukemic transformation of relapsed or refractory disease in patients with previously recognized multiple myeloma. ***Materials and methods:*** This is the first study to provide information on PCL epidemiology in the Czech population using The Czech National Cancer Registry (CNCR) as the basic source of data for the population-based evaluation of PCL epidemiology. ***Results:*** According to CNCR data, there were on average six newly diagnosed cases of PCL and four deaths caused by PCL each year in the Czech Republic in the period 2000–2015. PCL incidence in the Czech Republic was reported at 0.57 per million in 2000–2015. We suppose that most reported cases of PCL are primary PCL because secondary PCL is a relapse of a previously reported myeloma and, in most cases, is not coded as an independent diagnosis in the CNCR. ***Conclusion:*** Data from registries such as the CNCR can provide useful information on epidemiology of various diseases. These data, however, have several limitations, such as diagnostic criteria and proper coding of not only the disease itself, but also its various forms. These limitations have to be taken into account during the process of results interpretation.

Key words

plasma cell leukemia – epidemiology – Czech National Cancer Registry (CNCR) – Czech Republic

Souhrn

Východiska: Plazmocelulární leukemie (PCL) je vzácná, ale velmi agresivní forma monoklonální gamapatie. PCL je charakterizována přítomností klonálních plazmatických buněk v periferní krvi. PCL existuje ve dvou formách, přičemž primární PCL vzniká *de novo* u pacientů bez jakéhokoliv záznamu o předchozím mnohočetném myelomu, zatímco sekundární PCL vzniká leukemickou transformací při relapsu nebo refrakterním onemocnění u pacientů s dříve diagnostikovaným mnohočetným myelomem. ***Materiál a metody:*** Prezentovaná publikace je první studií poskytující informace o epidemiologii PCL v české populaci využívající Národní onkologický registr (NOR) jako základní zdroj populačního hodnocení epidemiologie PCL. ***Výsledky:*** Dle dat NOR je v období 2000–2015 každoročně průměrně diagnostikováno šest nových případů PCL a z důvodu PCL dochází ke čtyřem úmrtím ročně. Incidence PCL v České republice je v tomto období 0,57 případu na milion obyvatel. U většiny zaznamenaných případů PCL jde pravděpodobně o primární PCL, protože sekundární PCL, která je relapsem dříve zaznamenaného myelomu, není obvykle v datech NOR kódována jako samostatná diagnóza. ***Závěr:*** Data z populačních registrů jako je NOR mohou poskytovat užitečné informace o epidemiologii různých onemocnění. Tento typ dat má nicméně určité limitace, jako jsou např. problémy vyplývající z diagnostických kritérií onemocnění, jejich změn v čase a korektního kódování nejenom vlastních onemocnění, ale i jejich různých forem. Tyto limitace musí být vzaty do úvahy během interpretace výsledků epidemiologických analýz.

Klíčová slova

plazmocelulární leukemie – epidemiologie – Národní onkologický registr (NOR) – Česká republika

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Introduction

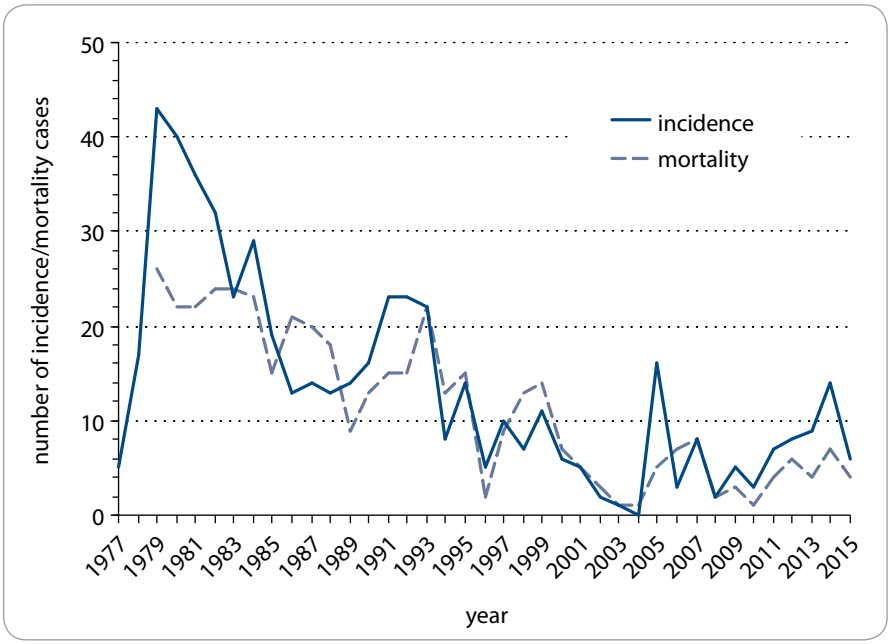
The importance of cancer epidemiology has been growing steadily, partly due to the growing cancer burden worldwide. The Czech Republic is no exception in this regard; in fact, it is one of the countries with the highest burden of several cancer types. Tens of thousands of cancer patients are newly diagnosed in the Czech Republic each year, and hundreds of thousands of them are followed up due to a history of cancer in the past [1]. This work aims to describe the epidemiological situation as well as epidemiological trends of plasma cell leukemia (PCL), which is a rare but the most aggressive form of monoclonal gammopathies. PCL is defined by the presence of more than 20% of plasma cells in the peripheral blood or the absolute plasma cell count > 2 × 109/L [2]. PCL is classified as primary (pPCL) when it presents *de novo* in patients with no evidence of previous multiple myeloma (MM) and as secondary (sPCL) when it is observed as a leukemic transformation of relapsed or refractory disease in patients with previously recognized MM [3]. About 60–70% of PCL are pPCL, whereas the remaining 30–40% are sPCL [4].

Materials and Methods

High-quality data play a key role in the evaluation of cancer epidemiology; in particular, the following two data sources [5] are used for this purpose in the Czech Republic.

First, data on demographic structure of the population of the Czech Republic are processed by the Czech Statistical Office (CZSO) as part of its monitoring activities. These data cover demographic characteristics of the population, such as the total population size, age structure, life expectancy etc. [6,7]. Population-based data on cancer mortality are stored in a database of causes of death, which is also processed by the CZSO in accordance with international methodology and based on data from death certificates (ICD-10 classification).

Second, the Czech National Cancer Registry (CNCR) is the main source of data on cancer epidemiology. Nowadays, the CNCR is an integral part of comprehensive cancer care, covering 100% of the Czech population and containing more than 2.3 million cancer cases recorded between 1977 and 2015. According to CNCR data, the lifetime risk of developing cancer is approximately 1/3 in the Czech population. However, PCL is a very rare disease that only accounts for 0.02% of these records. In general, the registration of malignant tumors is enshrined in the Czech legislation and is obligatory. The CNCR is also the source of data for the assessment of basic performance indicators of cancer care, particularly for the assessment of patient survival. The Czech Society for Oncology has used CNCR data to develop an information system that predicts not only the population burden of cancer, but also treatment burden for future periods. Predictions of the population burden of cancer are based on modelling of the development of demographic structure and cancer incidence in the population. On the other hand, predictions of prevalence of cancer patients to be treated in the near future are based on survival models. The methodology and applied prediction scenarios are described in Dusek et al. [1].



Graph 1. Trends in plasma cell leukemia incidence and mortality – absolute numbers [7].

Results

International comparison of PCL epidemiology

Due to relatively low incidence and prevalence rates of PCL, international epidemiological data are not available in commonly used databases, such as the GLOBOCAN database (http://gco.iarc.fr/). Epidemiological estimates are therefore based on isolated studies. PCL is usually diagnosed in 2–4% of MM patients [8,3–10]; this is consistent with our results from the CNCR (1977–2015), where the ratio of PCL to MM patients is 3 : 100.

Epidemiology of MM in the Czech Republic

For the purpose of analysis of CNCR data, neoplasms with diagnosis C90.1 (according to the International Statistical Classification of Diseases and Related Health Problems – 10th Revision, ICD-10) and neoplasms with morphology code 9733/3 (according to the International Classification of Diseases for Oncology – 3rd Edition, ICD-O-3) were included in the group of PCL. Nevertheless, available data do not distinguish between pPCL and sPCL; most cases of sPCL are therefore probably included under MM in CNCR data and cannot be distinguished as an independent diagnosis.

Trends in PCL incidence and mortality in the Czech Republic over more than three decades are shown in Graph 1. Both incidence and mortality rates decreased until approximately the year

2000 and have stabilized since then. The average annual incidence was 19 patients in the period 1997–1999, and 6 patients in the period 2000–2015. This downward trend can be probably attributed to diagnostics and coding issues of this rare diagnosis. In absolute numbers, the incidence in 2015 was 6 persons (0.57 per million population), namely 5 men and 1 woman. In terms of mortality, 4 persons (0.38 per million population) died from PCL in 2015, all of them were men. The overall epidemiological situation regarding PCL in the Czech Republic is summarized in Tab. 1. Data from the CNCR have shown that 4.5% of PCL cases (14.7% in the period 2000–2015) were preceded by another cancer in the same patient.

The proportion of men and women with PCL was approximately the same. We have confirmed that PCL is mostly diagnosed in older people – the median age was 66 years in men and 70 years in women, which is consistent with the median age of MM patients. Incidence rates were highest between the ages of 70 and 74 years in men and between the ages of 70 and 79 years in women (Graph 2). At the time of diagnosis, around 2% of all PCL patients were under the age of 45, and approximately 25% of all MM patients were under the age of 60. Age-specific incidence rates rise sharply from around the age of 45 (Graph 2) and thus demonstrate the growing risk of developing PCL in older age.

Graph 3 shows the comparison of PCL incidence in regions of the Czech Republic in the period 1977–2015. Prague (capitol of the Czech Republic) reported the highest incidence of PCL (2.09 cases per million per year), whereas the Olomouc Region and the South Moravian Region had the lowest incidence (both regions reported 0.52 cases per 1 million per year).

Tab. 1. Basic epidemiological characteristics of plasma cell leukemia in the Czech Republic [7].

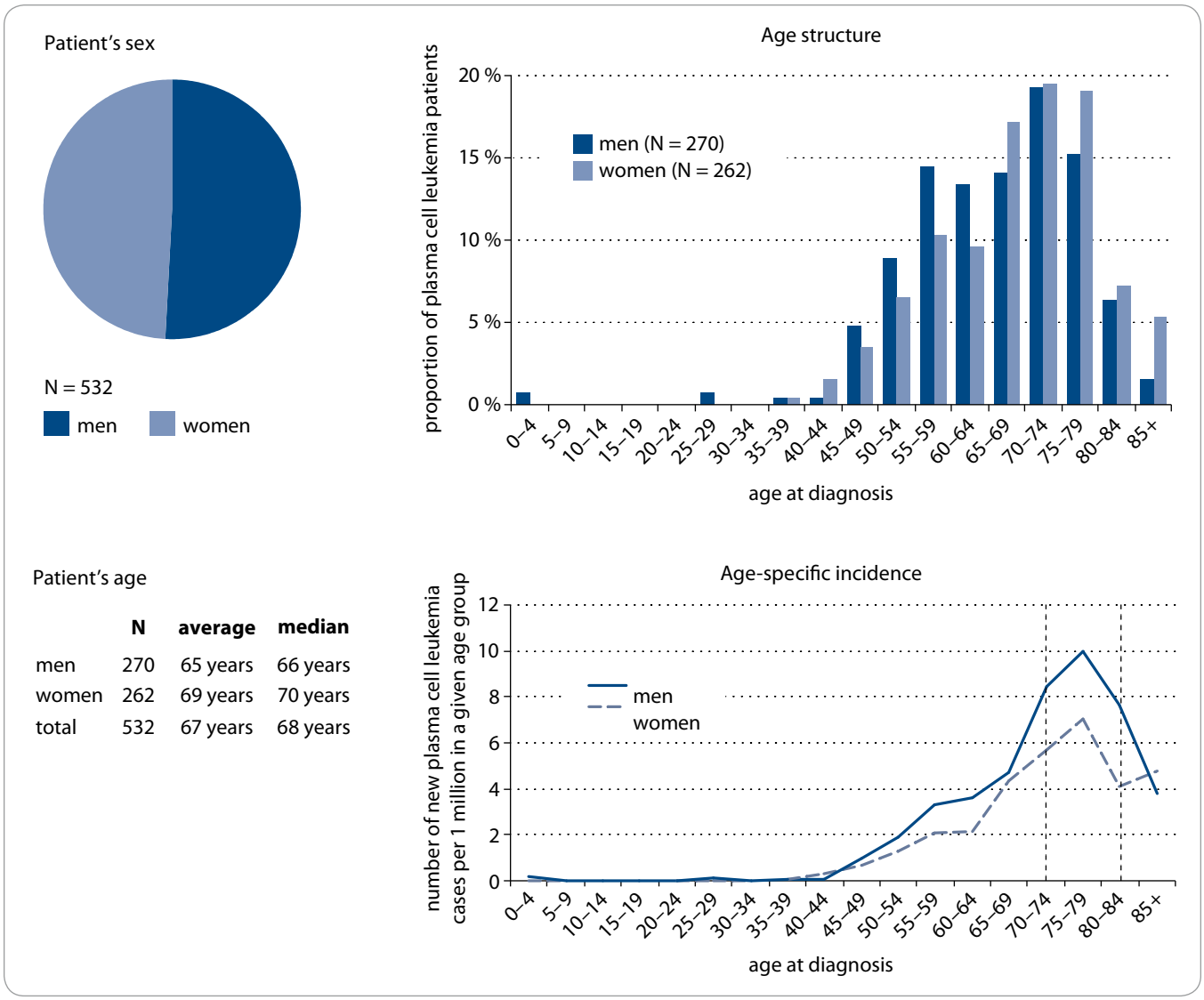
	Men	Women	Total
Incidence			
absolute number of newly diagnosed cases			
1977–2015	270	262	532
2000–2015	49	46	95
2015	5	1	6
number of new cases per 1 million population			
2000–2015	0.60	0.54	0.57
2015	0.97	0.19	0.57
trend in 2000–2015	+61%	–26%	+18%
typical age (median; 25–75th percentile; 1977–2015)	66; 58–74	70; 60–76	68; 59–75
men : women (1977–2015)	–	–	1.1 : 1
Mortality			
absolute number of deaths			
1977–2015	210	213	423
2000–2015	32	36	68
2015	4	0	4
number of deaths per 1 million population			
2000–2015	0.39	0.42	0.41
2015	0.77	0.00	0.38
trend in 2000–2015	–60%	–51%	–57%
proportion of mortality/incidence (2000–2015)	0.65	0.78	0.72

Plasma cell leukemia definition – neoplasms with diagnosis C90.1 or neoplasms with morphology code 9733/3.

Discussion

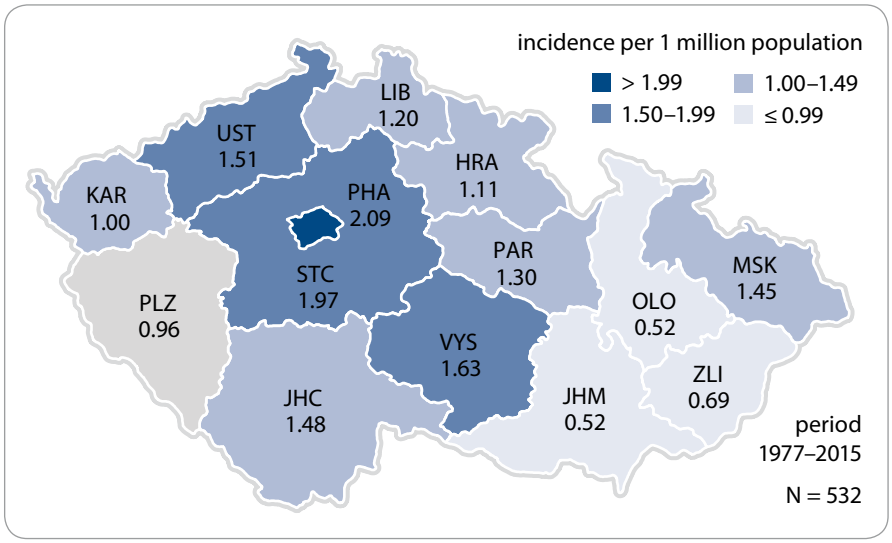
The epidemiology of rare diseases from CNCR data should be interpreted carefully, with awareness of data limitations. The quality of coding of rare diagnoses is closely related to diagnostics of the disease and the overall awareness of the disease. In general, there are two problems with PCL coding in a population-based registry, such as the CNCR. First, the disease is classified into two forms – pPCL, which occurs without previously identified MM stage, and sPCL, which develops from previously diagnosed and treated MM [11]. We suppose that most reported cases of PCL are pPCL because sPCL is a relapse of a previously reported myeloma and, in most cases, is not coded as an independent diagnosis in the CNCR. More recent data suggest that the incidence of sPCL has increased, now accounting for about 50% of the cases [12]; this might also influence the results. Second, the development of diagnostic criteria and laboratory techniques can influence the classification of PCL patients and therefore also the recorded epidemiology of the disease. The first diagnostic criteria were defined in 1974 [13] and amended in 1987 [14]. The current diagnostic criteria, which originated in the 1970s, might underestimate the prevalence of PCL, and their re-evaluation is therefore being considered [2].

Data from registries, such as the CNCR, can provide useful information on epidemiology of various diseases. These data, however, have several limitations, such as diagnostic criteria and proper coding of not only the disease itself, but also its various forms. These limitations have to be taken into account during the process of results interpretation.



	N	average	median
men	270	65 years	66 years
women	262	69 years	70 years
total	532	67 years	68 years

Graph 2. Age and sex of plasma cell leukemia patients in the period 1977–2015.



Graph 3. Regional incidence of plasma cell leukemia.

Conclusion

The aim of this work was to describe the epidemiological situation as well as epidemiological trends of plasma cell leukemia. In the Czech Republic, an average of 6 people were newly diagnosed with PCL and about 4 people died from it between 2000 and 2015 each year. The ratio of PCL to MM patients is 3 : 100, which is a result comparable to international data.

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