

Neglected conditions

Neuroendocrine tumours: The day after the third annual Worldwide NET (neuroendocrine tumour) Cancer Awareness Day, Kelsall¹ pointed out the multiplication of disease recognition days in a *CMAJ* editorial and called for “articles on neglected conditions that may benefit from increased attention.”

Despite the recent rise in incidence of this rare malignancy, patients with neuroendocrine tumours experience diagnostic delays of up to seven years after presentation of initial symptoms. This delay may be due to rarity, non-specific symptoms, unknown risk factors or a lack of awareness among primary care and specialized physicians.^{2,3} In Ontario, patients with neuroendocrine tumours visited primary care physicians a median of 14 times before receiving a diagnosis.^{3,4} The combination of slow progression and hormonal production in advanced neuroendocrine tumours produces debilitating symptoms, which lead to substantial deterioration of quality of life.

Neuroendocrine tumours represent a rare “chronic cancer” that forces patients to cope with steady debilitation. Beyond fragmented care, patient support is compromised because little information on prognosis and treatment is available to physicians. Large-scale analyses of epidemiology, behaviour, and health care delivery and utilization surrounding neuroendocrine tumours are paramount to patients and physicians in terms of timely diagnosis and delivery of effective therapies.

Neuroendocrine tumours must cease to be a diagnosis of exclusion that is established after years of investigation. We strongly believe that research is desperately needed to create targeted programs to raise awareness in the medical community and to improve outcomes and physician and patient experience. A comprehensive review of the current knowledge surrounding neuroendocrine tumours is the first step. It is often said that when hearing hoofbeats, one should think horses,

not zebras ... but sometimes one is not far from the Serengeti and has to know about zebras.

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References

1. Kelsall D. With a disease for every day, who will care for the orphans? *CMAJ* 2013;185:1475.
2. Moldin IM, Champaneria MC, Chan AKC, et al. A three-decade analysis of 3911 small intestinal neuroendocrine tumors: the rapid pace of no progress. *Am J Gastroenterol* 2007;102:1464-73.
3. Singh S, Saskin R, Lin N, et al. 2012 Neuroendocrine Tumor Symposium abstracts: patterns of care of neuroendocrine cancer in Ontario: health services delivery. Vancouver (WA): North American Neuroendocrine Tumor Society; 2012. Available: www.nanets.net/nanets_cd/2012/pdfs/C33singhresources-abstract3.pdf 2012 (accessed 2013 Dec. 3).
4. Singh S, Saskin R, Lin N, et al. 2012 Neuroendocrine Tumor Symposium abstracts: epidemiology of neuroendocrine tumors in Ontario: a 15-year population-based study. Vancouver (WA): North American Neuroendocrine Tumor Society; 2012. Available: www.nanets.net/nanets_cd/2012/pdfs/C32singhepi-abstract1.pdf (accessed 2013 Dec. 3).

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Sickle cell disease: In response to the *CMAJ* editorial on neglected diseases,¹ I would like to draw attention to sickle cell disease.

Now is an exciting time to be involved in both the research of sickle cell disease and the care of individuals with the disease. With changes in patterns of immigration, this condition is becoming more prevalent across all regions of Canada. In recent years, a dramatic increase in the understanding of the associated pathophysiology and genetics has led to excellent childhood interventions that have a substantial impact on morbidity and mortality. With the use of penicillin prophylaxis and childhood immunization, sickle cell disease has become a lifelong disorder rather than an indicator of early childhood death. Blood transfusions have effectively combatted the high prevalence of stroke in children with sickle cell disease, thereby reducing disabilities.

These successes bring new challenges. All medical practitioners in Canada — regardless of their geographic location and working environment (e.g., emergency department, family medical office, hospital) — must be aware of sickle cell disease and be willing and competent to participate in the management of affected individuals. This single gene blood disorder is now considered a phenotypically variable, multisystem disease caused by chronic ischemia-reperfusion injury and vascular endothelial remodelling. As such, it is an ideal disease to facilitate research across various medical specialties and a breadth of basic science realms in an era of collaboration and discovery. Its genetic basis also permits next generation genomics to further enable future progress and understanding.

The Canadian Haemoglobinopathy Association is composed of a multidisciplinary group of health care providers dedicated to the advancement of sickle cell disease in Canada. We will issue the first Canadian standards for the care of affected patients in Canada. This is an opportunity to educate the wider health care community about this chronic multisystem blood disorder. I encourage *CMAJ* to join us in this work.

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Reference

1. Kelsall D. With a disease for every day, who will care for the orphans? *CMAJ* 2013;185:1475.

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Cardiac tumours: I would like to commend Kelsall's¹ initiative to disseminate knowledge on rare diseases. The initiative will certainly help identify, stimulate, coordinate and support research, which could benefit patients who have any one of the nearly 6800 known rare diseases.

I would like to draw attention to tumours of the heart. Primary cardiac

tumours represent only 25% of all cardiac tumours. The most prevalent are metastatic cardiac tumours and pseudo-tumors. Estimated frequency of primary tumours of the heart ranges from 0.0017% to 0.33%.² Seventy-five percent of primary cardiac tumours are benign. Myxomas account for nearly half of them. Primary malignant cardiac tumours are predominantly sarcomas.²

Since noninvasive diagnostic modalities have become more sensitive, there has been marked increase in the number of patients who receive diagnoses.

Presenting symptoms, treatment options and prognosis are largely controlled by the anatomic location of the tumour. Tumours of the heart are known to be great mimickers.^{2,3} Most patients with malignant cardiac tumour die within one year of initial diagnosis, either because of the often asymptomatic presentation of cardiac tumours until advanced disease or because of a low index of suspicion on the part of the physician. The survival rates for extracardiac malignancies have improved substantially. Meanwhile, the prognosis in cardiac malignancies is still dismal. Median survival for patients with cardiac sarcomas is 6 months, and 93 months for those with noncardiac sarcomas. Patients with primary cardiac sarcomas who undergo surgical resection have a median survival of 12 months. Patients who undergo only palliative chemotherapy have a median survival of one month.⁴

Management options for cardiac tumours include surgery, neoadjuvant and adjuvant chemotherapy. Surgical resection is the treatment of choice.⁵ In the case of inoperable disease (i.e., unresectable tumour, presence of metastases) palliative chemotherapy should be offered, although in some cases, palliative surgical debulking may be undertaken to relieve rapidly progressing symptoms. Younger patients with no metastatic disease may be considered suitable candidates for orthotopic heart transplant.⁴

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References

1. Kelsall D. With a disease for every day, who will care for the orphans? *CMAJ* 2013;185:1475.
2. Butany J, Nair V, Naseemuddin A, et al. Cardiac tumours: diagnosis and management. *Lancet Oncol* 2005;6:219-28.
3. Neragi-Miandoab S, Kim J, Vlahakes GJ. Malignant tumours of the heart: a review of tumour type, diagnosis and therapy. *Clin Oncol (R Coll Radiol)* 2007;19:748-56.
4. Leja MJ, Shah DJ, Reardon MJ. Primary cardiac tumors. *Tex Heart Inst J* 2011;38:261-2.
5. Leja M, Reardon MJ. Cardiac sarcomas: Therapeutic options? *Future Cardiol* 2011;7:595-7.

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Oculopharyngeal muscular dystrophy: Oculopharyngeal muscular dystrophy (OPMD, OMIM 164300) fits the description of a neglected condition as described in the *CMAJ* editorial by Kelsall.¹

This condition has escaped attention in many medical school and resident teaching curricula despite having an unusually high prevalence in those with Quebec French-Canadian ancestry. This is due to a founder effect. A mutant trinucleotide repeat expansion allele was introduced by three emigrant French sisters in 1648.² The most common disease manifestations are dysphagia, ptosis and limb weakness, with symptoms usually appearing in the fifth decade. The disease often goes undiagnosed when referral for dysphagia, which can be severe, is made. A label of myasthenia gravis is occasionally incorrectly applied as well. Treatment can be difficult, but is available for both dysphagia and ptosis. Counselling patients on the hereditary nature of this condition (autosomal dominant) frequently results in identification of additional affected family members.

Greater awareness would improve diagnosis and mitigate the unnecessary investigation that frequently occurs, including repeated upper endoscopy. A Scottish study showed a 3-to-20-year delay from symptom onset to diagnosis, with a quarter of patients with dysphagia having undergone a decade of investigation and treatment for pharyngeal problems.³ The findings are congruent with the experience shared by many who manage these patients. Because patients of Quebec French-Canadian ancestry represent one of the world's most prevalent OPMD carrier groups, this disease should receive more attention in our country.

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References

1. Kelsall D. With a disease for every day, who will care for the orphans? *CMAJ* 2013;185:1475.
2. Brais B, Rouleau GA, Bouchard J-P, et al. Oculopharyngeal muscular dystrophy. *Semin Neurol* 1999;19:59-66.
3. Agarwal PK, Mansfield DC, Mechan D, et al. Delayed diagnosis of oculopharyngeal muscular dystrophy in Scotland. *Br J Ophthalmol* 2012; 96:281-3.

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Some letters have been abbreviated for print. See www.cmaj.ca for full versions and competing interests.

CORRECTION

Author's affiliation in Mar. 4, 2014, issue

In the *CMAJ* article "The association between ownership of common household devices and obesity and diabetes in high, middle and low income countries," the affiliation for Roya Kelishadi should be "Isfahan Cardiovascular Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran.

Reference

1. Lear SA, Koon K, Gasevic D, et al. The association between ownership of common household devices and obesity and diabetes in high, middle and low income countries. *CMAJ* 2014;186:258-66.

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