Very rare cancers – a problem neglected

Very rare cancers are often misunderstood, misdiagnosed, or poorly investigated, and there are usually few treatment options. The question is, how rare is very rare? The US Congress Orphan Drug Act 1983 defines 'rare' as "under 200 000 cases in the USA, or more than 200 000 cases but no reasonable expectation that the costs of developing a new drug for this condition will be recovered from its sales". This definition was created in relation to drug development and is now being used by information services, database, and registry organisers, but is not actually that helpful in this context. 'Very rare' cancers have entirely different problems, in terms of research, funding, and available information, to cancers such as leukaemia, head and neck cancer, and the Orphan Drug Act.

The lack of knowledge of very rare cancers among physicians and pathologists can have disastrous consequences for the patient. For example, lymphomatoid granulomatosis (less than 50 cases a year in the USA) is often misdiagnosed as T-cell lymphoma and is consequently mistreated. It is typical for patients to go for over a year without a proper diagnosis. Scientific workshops and focus groups are sometimes set up by experts in the field, or by the Office of Rare Diseases at NIH. But the situation is so frustrating to patients, that patient groups often end up taking charge and organising the scientific community themselves. The first international workshop on a very rare paraneoplastic disorder called Dancing Eye Syndrome (DES) (near Oxford, UK, February 22–24) was organised by parents of affected children. DES only affects about five new cases in the UK and about 20 in the USA each year. One paediatric neurologist who attended said that in over 20 years of seeing children with DES (about 20 cases altogether), this was the first time that she had been involved in this sort of forum. It allowed the participants to forge new collaborations and discuss avenues for further research.

The empowerment of patients has been greatly helped by the growth of the internet. Finding other patients in similar situations was just not possible before, especially for very rare diseases, where there might not be another patient in the same town, state, or even country.

Oncologists obviously have to devote most of their time to managing patients with common cancers and will understandably concentrate on publishing on these diseases. Physicians may only see a very rare cancer once or twice in their career, yet the importance of discussing and disseminating information on these cases should not be underestimated. The study of very rare cancers, especially paediatric and hereditary cancers such as retinoblastoma (about 200 cases a year in the USA), has led to the identification of numerous cancer genes and has had a huge impact on our understanding of cancer biology.

The Information Centre for Rare Diseases (Bergamo, Italy) was set up in 1992 for patients and medical personnel to obtain information, and as a resource for identifying potential eligible patients for clinical studies. The Information Centre has a database of rare diseases and a directory of clinical research centres in Europe, yet only 16% of those requesting information are physicians; most are patients or their families. A call for a national database and an organised structure in the UK in a recent editorial (*Clin Oncol* 2000; **12:** 231–32) stimulated little interest.

Because of the lack of information, case reports and case series are extremely valuable for those seeking information on rare disorders. However, many journals no longer publish case reports. Journals that receive a large number of papers every year, and therefore have a low acceptance rate, may decide not to publish papers on rare conditions, even if they have received favourable peer reviewers' reports, because they are deemed not to be of general interest to the readership. The advent of the internet has had an enormous impact on the way in which oncologists find and exchange information. So, the answer may be to publish on the web, but then we have a chicken and egg situation – the web-user, be it patient, family physician, or oncologist, needs to have a good idea what they are looking for in order to find it. One way forward would be to consider setting up an internationally recognised and well-advertised website of rare cancers, but this would only succeed if it became established as *the* source of information and the recognised forum for discussion.

In the USA, there seems to be no difficulty funding research into rare diseases, because of the commitment of the NIH. In Europe, however, lack of funds for clinical and basic research is seen as the single greatest barrier to treatment discoveries in the field. If some 'rare' cancers are not of interest to pharmaceutical companies, research funding bodies, etc, what chance do 'very rare' cancers have?

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