

Research in infantile haemangioma: local perspectives

Two articles related to infantile haemangioma (IH) are published in this issue of the *Hong Kong Medical Journal*. The first was written by a group from Prince of Wales Hospital (PWH) focusing on the clinical and radiological features of IH.¹ The second was from the United Christian Hospital (UCH) describing the use of propranolol as treatment.² How much do these articles contribute to better understanding of IH in Hong Kong?

Both studies did not specify the denominators in their studies, that is, the total number of IH case records reviewed and the total number identified (included and excluded for analysis). Therefore the prevalence of IH could not be estimated. The commonly cited figures of 1 to 3% in textbooks were mostly derived from western populations and continue to be referred to even in Chinese populations.

The PWH group collected 58 cases over 10 years, while the study by the UCH group collected 12 cases in 1 year. The baseline characteristics of both groups were very different. Thus, case selection would have a very significant effect on the attributes of subjects eligible for analysis.

The PWH study was retrospective and based on electronic record retrieval using the key word "vascular anomaly" for searching in the Paediatric Haematology and Oncology Unit. The time covered was from 1998 to 2007. The criteria to further define and qualify the diagnosis of an otherwise bona fide "haemangioma" for inclusion in the analysis was not specified. In some patients, the diagnoses of haemangioma were not irrevocable and this might have a bearing on the interpretation of data, and not surprisingly some of the cases included for analysis were heterogeneous. Patient ages ranged from 2 months to 18 years, and their clinical features also varied; some had internal organ involvement as well. Treatment modalities also varied although no patient received propranolol. The overall features and clinical course in some of the cases in their series were suggestive of vascular malformations. In addition, their series included three cases of Kasabach-Merritt syndrome, now regarded an entity different from conventional IH.

Apart from the clinical features, the radiological features were described. While the presence of phleboliths in a haemangioma is an occasional finding (approximately 20% in their series), these are fairly common in long-standing low-flow vascular malformations. In this regard, phleboliths are not generally anticipated in rapidly changing vascular

lesions over months.

Therefore, in the absence of clearly described inclusion criteria for the cases described in the PWH study, the conjecture that the data might have been contaminated by non-IH cases cannot be excluded and requires careful interpretation in that context.

The UCH study was also retrospective and involved electronic record retrieving using the key word "haemangioma/facial haemangioma" for searching in the Paediatric Unit. The time covered was about 1 year (2008/2009). The cases included for analysis were more homogeneous, all the subjects were younger than 2 years and all except one had lesions limited to head/face. All the patients achieved partial or complete regression following treatment with propranolol, albeit four had laser therapy in addition. The UCH group may have the enthusiasm to share their joy at achieving such good results with propranolol treatment, and certainly the pre- and post-treatment clinical photos are very impressive, and so do the two cases of relapse after treatment, and regression induced upon re-initiation of treatment. Regrettably, the only conclusion to arrive at scientifically is that propranolol is useful in selected patients with IH. In fact, given the complicated nature of the subjects, even on expectant management treatment, outcomes in the PWH series were quite good (partial or complete regression in 34/39 or 87% of patients), whereas 15/19 (79%) achieved such results on active treatment. These findings underscore the importance of including a control group for any disease entity, which has a natural propensity to regress. Clearly, more robust study methodology has to be adopted to confirm the usefulness of propranolol in IH.

Whilst a randomised controlled trial is the well-known and well-accepted gold standard in the evidence-based medicine paradigm, it is very expensive, time-consuming, and technically more demanding to undertake. The research group may consider adopting a much simpler way to look into the research question, by conducting a case control study and present the results in a Kaplan Meier curve, whilst applying relevant statistical methods to test the null hypothesis.

Having a research-oriented approach is also important when using new therapies, which are reported in the literature but not yet widely accepted as the standard of treatment. Propranolol was used around the time when the results of the French

group were published in the *New England Journal of Medicine*, at which time propranolol was still not regarded as standard first-line treatment (and even now it is not universally accepted).^{3,4} Mere verbal informed consent cannot replace a properly designed research protocol and endorsement by the institutional review board/ethics committee. Had such an approach been adopted by the UCH group, their evidence would have been much more robust.

Nevertheless, the experience and suggested

protocol derived from both groups will be useful to local doctors involving in clinical management of children with IH. Moreover, I believe that propranolol will eventually be listed as one of the standard first-line treatments for IH.

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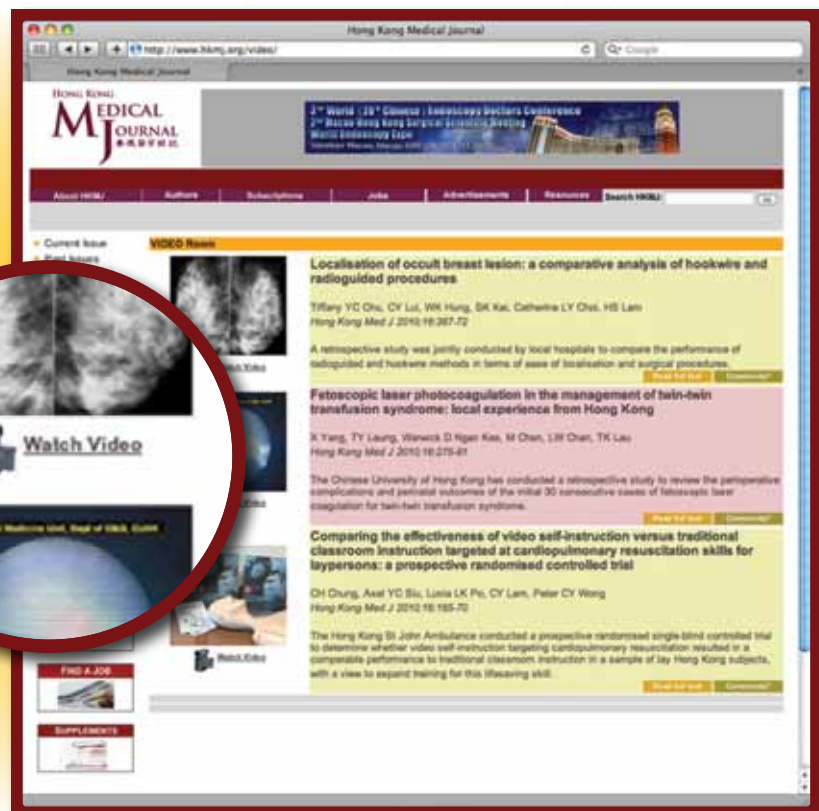
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