Managing Hodgkin Lymphoma Expert Interview Series

An Update on the Current State of Hodgkin Lymphoma Care in China

George Davatelis, PhD – Moderator/Writer
with
Raymond Hin Suen Liang, MD
Department of Medicine
University of Hong Kong
Queen Mary Hospital
Hong Kong SAR, China

Editor's Note:
The treatment of patients with Hodgkin Lymphoma (HL) is one of the major success stories in oncology. Currently between 70–90% of treatment-naïve patients are cured of their malignancy depending on clinical stage and risk factors.[1] In patients with refractory or relapsed disease, high-dose chemotherapy (HDCT) followed by autologous hematopoietic stem cell transplant (HSCT) is the standard of care, and can lead to a cure in ~50% of patients.[2] However, current combined modality treatment regimens for first diagnosed HL patients can induce severe, life-threatening treatment-related side effects, which include secondary cancers and cardiovascular disease. Despite success in both treatment-naïve patients and patients with refractory or relapsed disease, new treatment options are needed. On behalf of *ManagingHodgkinLymphoma.com* (MHLC), George Davatelis, PhD, spoke with Raymond Liang, MD, of the Department of Medicine at the University of Hong Kong, Queen Mary Hospital in Hong Kong SAR, China, to discuss the latest advances and current state of HL treatment in Asia.

MHLC: *Compared with the West, Hodgkin lymphoma in Eastern Asian countries is characterized by a lower incident rate but a higher proportion of mixed cellular histology.[3] Can you tell us a little bit about this and what the standard of care is for Hodgkin lymphoma in Asia?*

Dr. Raymond Liang: I think the data is quite definite that we see a lower incidence of Hodgkin lymphoma in Eastern Asia, but I believe that in more developed areas the incidence is rising. There is a question of whether the lower incidence is due to underdiagnosis, but in general, I think the diagnosis of Hodgkin lymphoma is not too difficult, so I do not think it would account for the lower incidence that we have observed. On the other hand, the so-called higher proportion of mixed cellularity, I do have some reservation because the definition of mixed cellularity may not be as firmly established in some places, and it depends on the pathologists. We do need good pathologists, experienced pathologists to handle lymphomas, and in some places this

may not be readily available. So, when we talk about Eastern Asia in general, I think there are some variations in the quality of the pathology that we are talking about.

Once the diagnosis is made, the treatment is pretty standard. The ABVD (adriamycin, bleomycin, vinblastine and dacarbazine)[4] regimen is still widely used and adopted in Asia, while the German protocol of using BEACOPP (bleomycin, etoposide, adriamycin, cyclophosphamide, Oncovin, procarbazine and prednisone)[4] is seldom used in Asia in general because I think people do worry about the higher toxicity that we are facing, and in some parts of Asia, they may not be well prepared for such degree of toxicities.

MHLC: *What are the treatment challenges in treating Hodgkin lymphoma in Asia and how do you think they differ from other areas such as the EU or the US?*

Dr. Raymond Liang: I think how to get tissue for diagnosis is a challenge. Sometimes whether the expertise is available, whether there is a CT-guided core biopsy and then, as I mentioned earlier, the importance of an experienced pathologist. In general, in East Asia because of the incidence of nasopharyngeal cancer which is quite treatable with radiotherapy, most places have good facilities for radiotherapy, so that is usually not an issue. But whether they are familiar with the modern trend of radiotherapy in lymphoma, I think that is the question. And then, I think the other issue that we worry about is for the relapsed cases. Although a great majority of Hodgkin lymphoma can be cured with first-line therapy, there are still patients who relapse and some of these patients may benefit from an autologous and sometimes allogeneic stem cell transplant. But unfortunately this is the kind of service that may not be available in every place in Asia. Also, access to new drugs is also a challenge because of availability.

MHLC: *Do you see any unique opportunities in treating Hodgkin's in Asia?*

Dr. Raymond Liang: We understand that there has been a low incidence of Hodgkin lymphoma in Eastern Asia, and there appears to be a rising trend, so this may give us an opportunity to study the etiological factors causing Hodgkin lymphoma and the interactions between the genetic factors and environmental factors, but in general, I think the treatment of lymphomas in Asia should be quite similar to the other areas in the world.

MHLC: *Do you believe that European or US trials in Hodgkin's are really relevant to Asian clinical practice?*

Dr. Raymond Liang: I think the Western experience should be in general quite applicable to Asian patients except that I think we have to be cautious in the problem of correct diagnosis. As I mentioned earlier, I think if you add in some of the patients

wrongly diagnosed as lymphoma then of course the experience may be different, but in general I think if the diagnosis is correct, the experience in Western clinical trials should be quite applicable and relevant to Asian clinical practice.

MHLC: *We are seeing great efficacy rates with the standard of care for Hodgkin lymphoma, but we are also seeing some fairly high-level treatment-related side effects, so can you tell us what the latest thinking is on your side of the world to address the toxicity issues?*

Dr. Raymond Liang: I think in general the more intensive treatment of BEACOPP regimen is not popular in Asia because of the toxicity issue, and most people are still using the ABVD chemotherapy. And since most of the patients are quite young, acute cardial toxicity is not a major issue in general, but there are still cases of severe bleomycin toxicities that we are seeing. I think that needs to be addressed and the clinician should be aware of this potentially serious or even fatal toxicity of the treatment. Also, while Hodgkin lymphoma is quite curable nowadays, many of these patients will live for many years, and the long-term toxicities of second malignancies and also cardiovascular toxicities should be addressed, and the trend of using less radiotherapy is a very important issue.

MHLC: *Could give us just a top line thought of what you think of the new agents, and if any of them look extremely promising in your view?*

Dr. Raymond Liang: I think for Hodgkin lymphoma, the antibody-drug conjugate brentuximab vedotin is a major advance. I think it still needs to be explored whether this agent has a role in frontline therapy or whether this will still be just used for relapsed cases. In Hong Kong, we face the problem of this drug being quite expensive and it is still not reimbursed by the public funding, and also, there are many places in Asia where this drug is still not available. I think it is a valuable drug for relapsed cases and we should think of ways to make it more readily available to the needy patients.

MHCL: *You have written papers about the increasing incidence of Hodgkin lymphoma in Chinese people that have emigrated to British Columbia.*[3] *How do you believe both genetic and environmental components influence the pathogenesis of Hodgkin's?*

Dr. Raymond Liang: I think there are probably interactions between our genetic makeup and also the environment that we are living in, and in more developed places in Asia, we are seeing an increasing incidence of Hodgkin lymphoma. So definitely, there is a strong environmental influence into the cause of Hodgkin lymphoma, and in our studies of the Chinese immigrants to British Columbia, we need more long-term studies because the effect of the environment needs time to take its effect, and we need to observe their

second- and third-generations before we can see more definite pattern whether they have a high incidence of Hodgkin lymphoma compared with their parents.

MHLC: *Demographic changes around the world are resulting in a higher number of older patients being diagnosed with HL. What is your standard of care now for the older patients that you are seeing?*

Dr. Raymond Liang: Yes. I think we noticed that there is a second peak where you see some elderly patients suffering from Hodgkin lymphoma. Fortunately, this number is still relatively small, and I say luckily because these patients often cannot tolerate the present intensity of chemotherapy. I think this is a challenge. If we are seeing more and more of these elderly patients with Hodgkin's, we will need a different strategy. The question is whether we can have some less toxic regimens for this group of patient achieving similar efficacies like ABVD.

MHLC: *Do you see any of those new agents possibly filling a void for the older patients simply because of toxicity issues with the standard of care?*

Dr. Raymond Liang: Yes, I think the antibody drug conjugate is an attractive agent that we may be able to use in elderly patients. I think we need further clinical studies on whether these new agents like brentuximab can be used in frontline so that these elderly patients may have less toxic treatment and see whether it may improve the clinical outcome of these elderly patients.

MHLC: *What are your thoughts on the educational needs of the clinicians in your country and in the rest of Asia? Where do you see a need for more education?*

Dr. Raymond Liang: I think there are two areas that I am thinking of. One, the area that I have mentioned earlier is the pathology. I think the pathology in lymphoma including Hodgkin lymphoma is a rapidly evolving field. The new classifications, new entities, differential diagnosis, and also, we are seeing the same patients who have had composite lymphoma, say Hodgkin's plus mediastinal B-cell lymphomas. Second, I think the new treatments are suddenly challenging and exciting. I think that we need more information about these new agents.

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