AXIS Medical Education

Hemophilia A:

Strategies for Improving Long-Term Holistic Management, Adherence and Quality of Life

This transcript has been edited for style and clarity and includes all slides from the presentation.

This activity is provided by

AXIS Medical Education

This activity is supported by an educational grant from Genentech, a member of the Roche Group.

Case Consultation with Faculty Experts

Miguel Escobar, MD, Cindy Leissinger, MD and Guy Young, MD

Case Study

- 17-year-old man with severe hemophilia A
- Has been on prophylaxis with standard half-life FVIII since age of 5, given 3X per week with minimal breakthrough bleeding
- He has right ankle arthropathy from playing soccer in middle school
- In preparation to start college, his parents recently let him manage his own prophylaxis but he has missed an average of 2-4 doses per month and has had 2 spontaneous joint bleeds in the previous 6 months

Discussion:

1. What approaches can be used to improve adherence in this patient?
2. Can the use of an extended half-life factor be an option for the patient?
3. Can emicizumab be an option for prophylaxis?

AXIS Medical Education

Miguel Escobar, MD: I would like to discuss a virtual case.

This is a young man, a 17-year-old male with severe hemophilia A, has been on prophylaxis with a standard half-life factor VIII, very early; you know, his parents most likely were giving it 3 times a week, and minimal breakthrough bleeding. Seems like in middle school he was playing soccer and had some joint bleed, and so has maybe mild arthropathy of the right ankle.

But now he is in that stage where he's ready to go to college, and they are having that discussion with the parents how is he going to do it. And they've given him the responsibility, saying now you manage your prophylaxis which is actually what we recommended for our patients to kind of let them do that. But it seems like now when he comes to clinic he's missed maybe 2 to 4 doses per month and has already had 2 bleeds in the last 6 months, which is something that we see when they are doing that transition from the parents to the patient.

Now, the question here is, and I think some of these issues we have discussed. What approaches can be used to again improve adherence in this exact population, can the extended half-life products maybe be an option, or maybe something like emicizumab also could be an option for this kid. So, Guy, what do you think?

Guy Young, MD: Yes, so I think part of it depends on if he's going to continue to play soccer or not. Cindy mentioned earlier that people who are really active in sports, we rely on the peak of factors where we can put them in the normal range at least for some period of hours when they're doing that activity, and if he's going to want to do that I would stick with factor therapy, and depending on how often he plays either an extended half-life or a standard half-life, or based on what you showed on the PROPEL study even potentially an extended half-life factor given every other day, given in a more frequent regimen.

If he's like no, I'm going to college and I'm going to focus on studies, and I'll be active a little bit but I'm not really going to play sports, then I would definitely start thinking about emicizumab. Because in this case, it seems like he's missing doses. He's not missing all his doses, he's missing some, and to me the

hint there is that this is just taking too long and some days I just don't have time for this.

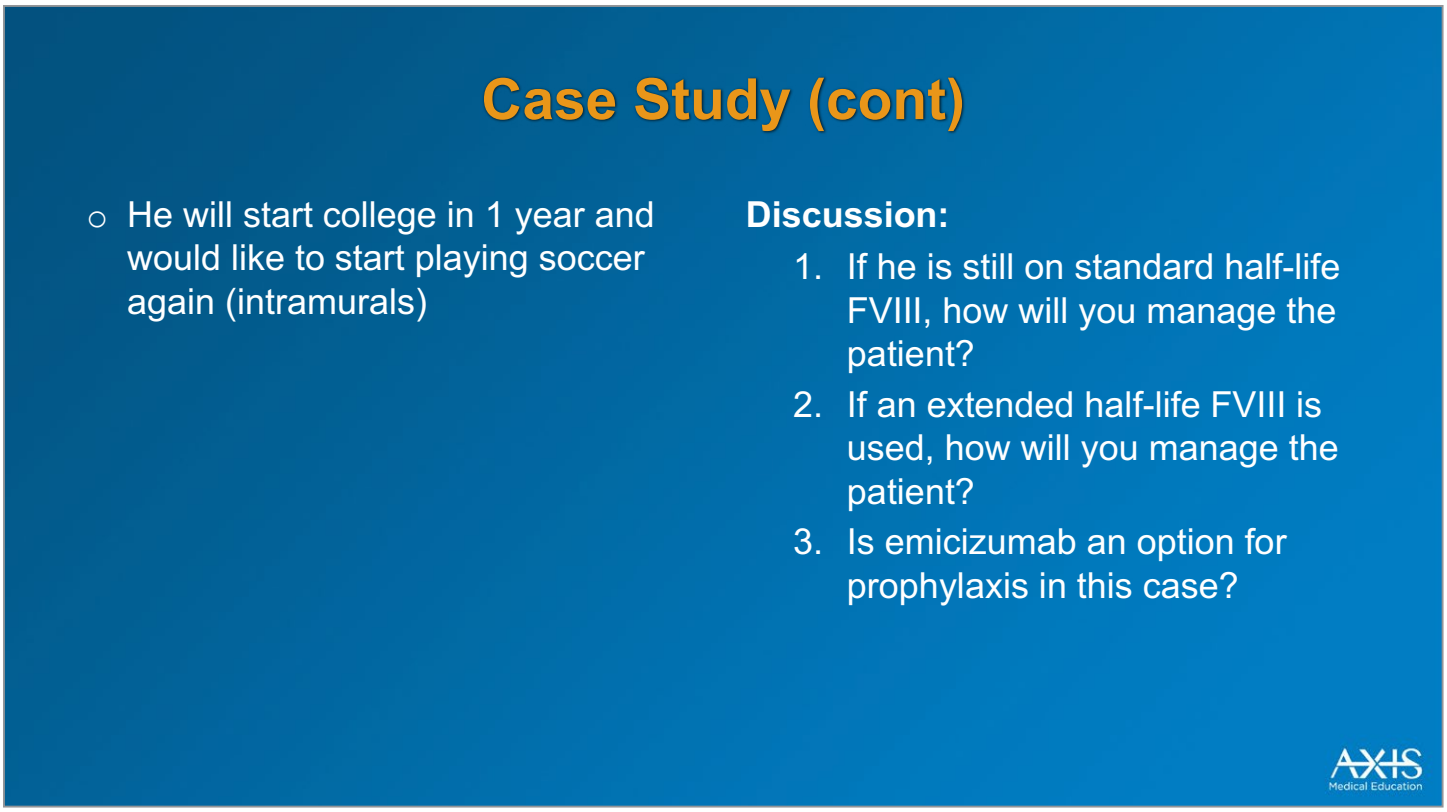
So switching to a non-factor therapy that you can give any time – not necessarily in the morning – once every 2 weeks takes away the time element and the effort element. And when I see this kind of story of adherence, this is kind of telling me that it's the time and effort that's the problem, and some days I just can't get around to doing it.

So I think it really depends on what his goals are, and this is where the shared decision-making comes in. We talk about well what are your goals, what do you plan to do in college, and then really have a mature conversation to say depending on your goals we have different treatment options. And if your goal is this we should go in this direction, if your goal is that we can go in that direction.

So I think that's the kind of discussion I would have. And I think that once we understand the goals and we give him the options, and we choose the one that meets his goals the best, hopefully at that point with somebody who is mature enough to go to college they'll listen, and they can follow through and have better adherence.

Escobar: Great. Cindy?

Cindy Leissinger, MD: Pretty much exactly what Guy discussed, that's how we would handle this as well.



Escobar: Okay. So, yes, let's say that he does plan to play some soccer, maybe not play in regards to very intense, but do some playing around in terms of intramurals, playing weekends, playing nights, things like that. Now, I guess if he wants to stay on the standard half-life, will that be an option for him, or if you consider maybe the extended, like Guy said, maybe using it every other day?

Leissinger: I personally would recommend switching to the extended half-life. He's missing about a dose a week, on average, a few doses a month from his probably 3 times a week regimen, so if we could go to an extended half-life if he wants to play actively on weekends, he can take a dose Saturday morning, and the perhaps another dose during the week.

The other thing is we'd want to follow him. Once we make these changes, we'd like to see him back in a few months to see how he's doing. So I think extended half-life I would prefer and recommend over standard half-life.

Escobar: Okay. Now, we talked about PKs. Will you consider doing a PK on him, at least maybe doing a trough and levels like that if he stays, let's say, on the standard or extended?

Leissinger: We'd certainly consider doing that, yes.

Young: Yes, I would say I think it's worthwhile to do it. Knowing his peak and trough and then being able to apply that to his intramural soccer, and even showing it to him and saying here's where you are when you're given your factor. And if you're here you can play soccer, and while you still might suffer a soccer injury, it's not going to be a hemophilia, per se, injury. And here's where you are on the other days where we don't want you to be playing soccer. So let's figure out when you're playing.

If it's intramural like you said, Miguel, once or twice a week, I agree with Cindy, an extended half-life factor it makes sense. Doing the PK may actually reinforce adherence. It may be almost just for that reason to then show them on the graph what it looks like, and I think that might be a reason alone to do the PK.

Escobar: Okay. Now, I heard I think from both of you that maybe if he wants to start playing sport, emicizumab might not be maybe the best recommendation. Is there any data on emicizumab, let's say, with sports, with really very active individuals, or is this something that maybe is based on your experience that you've seen patients having breakthrough bleeding while on emicizumab? Cindy?

Leissinger: I would say that I don't know of any specific data around this, but we certainly take care of patients who have mild hemophilia with baseline levels around 10%, 12%, which is kind of what we believe emicizumab may give, sort of that equivalent protection or that equivalent hemostasis.

And if patients are engaged in activities where trauma is possible – twisting their ankle stepping in a hole, hitting their head – we would certainly want them to have better protection than what we would anticipate they're getting with emicizumab. So my thinking is sort of based around our experiences with patients with mild hemophilia, so that kind of drives that decision.

Certainly with activities that may not involve risk, whether it's working out in the gym or whatever, I think emicizumab certainly would be adequate for that, in my opinion.

Escobar: Alright, what do you think, Guy?

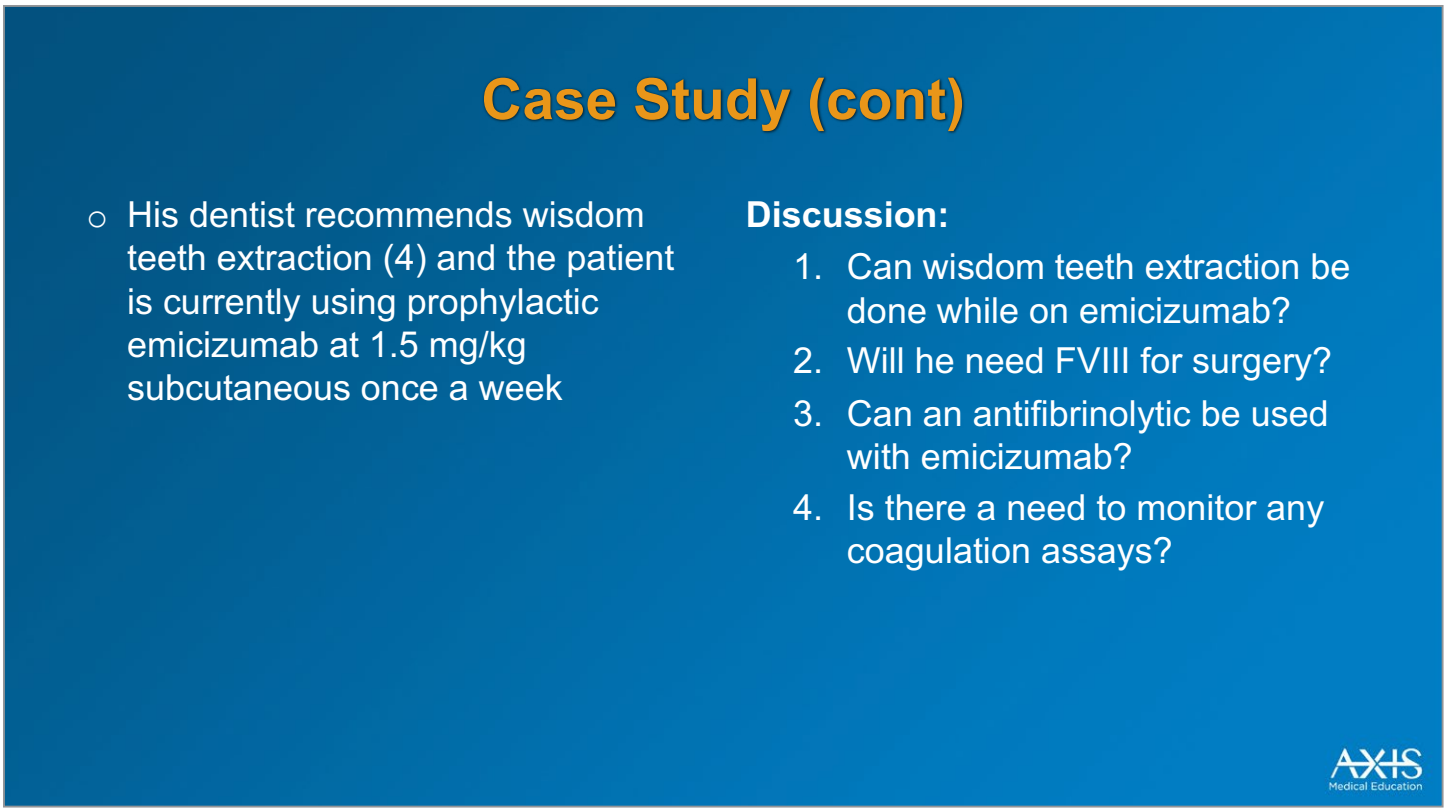
Young: Look, I think emicizumab is a great drug, and I do prescribe it quite a bit. I've talked about the younger children in particular that we've really shifted our practice quite a bit. However, I am seeing breakthrough bleeding with trauma activities, and actually we have a lot of kids in Southern California that do play soccer, I had an 8-year-old recently come in with a pretty bad knee bleed. And the family was definitely adherent with his emicizumab, we even drew a factor level, a human chromogenic factor VIII level to show us that we knew he was.

So I am seeing that. And what I'm learning from these experiences is that – and this is an 8-year-old, right, not even a teenager at that super-high level – is we do see breakthrough bleeds with trauma with emicizumab. And so in a situation like this, I think this is where you really do need to think twice about whether this is the best option for the patient.

As far as data on activity with emicizumab, I haven't really seen anything. I think it's going to be important to try to collect it, although it's difficult to collect it. And people talk, well, we can do Fitbits and things like that. Well, a Fitbit doesn't really tell you about whether you stepped funny while playing soccer, or whether you twisted your… I mean, there is no Fitbit for that, and really that's the kind of injuries we're seeing.

So I think it's going to be really, really hard to collect the kind of data that's going to give us that reassurance. And so I think really all of this decision-making with activity is really going to be based on our experiences and shared experienced, that's why these kind of discussions are so great to hear from the two of you, as well, where we can sort of collectively with a group experience learn about how to best use the options we have. Because right now we have the option of factor therapy, we have the option of emicizumab, in the future we'll have other options, and I think these types of discussions is how we'll learn how to use them best.

Escobar: Right. Yes, I think I have pretty much the same experience as you both have alluded here.



Escobar: So let's say that patient is on emicizumab, he's taking it the dose subQ once a week, and he needs wisdom teeth extraction. I know there's not a lot of data in surgery in the studies, and there have been studies that were some patients that needed to have surgeries.

What has been your recommendation or your practice, let's say, when somebody's on emicizumab is doing well and needs wisdom teeth extraction? Do you, first of all, recommend the surgery on emicizumab; well, he needs factor VIII, can you add anti-fibrinolytics and let it be given, and is there anything to monitor for this patient? Guy?

Young: Yes, the HAVEN studies did have a large experience mostly published in abstracts. I can share that there is a surgery paper that will finally be published, it's taken a bit too long, but there's a surgery paper that is going to be published soon about the HAVEN 1 through 4 surgical experience.

With respect to this case, there were, if I remember correctly, 64 dental procedures. Now, there are different types of dental procedures, and a wisdom tooth is one of the more intense ones, so I don't know how many of those were wisdom tooth procedures.

But what I'll say is that out of those, two-thirds of those patients per their investigator on the trial, did not get any factor before their dental procedure. 20% roughly – about 22%, I think – had bleeding after the surgery that needed factor. Twenty-two patients got factor before the procedure. And guess what, exactly the same number, 22%, needed factor after the procedure.

What I take from that data is that for dental procedures, whether you give factor before or not doesn't seem to make a difference. So I've taken the approach of I'm not going to give them the extra dose of factor. A lot of these are done in surgery centers, and it's not that it's that hard to get a dose of factor in, but it does add one layer of complication. And then I tell them to monitor themselves, and then if they do bleed they can get a dose of factor after, and nothing terrible generally is going to happen.

So that's been our approach. I know other people have really insisted on giving a dose of factor before, and I would certainly not fault anybody for saying, well, I think for a wisdom tooth I'm going to give a dose of factor before, even maybe a dose of factor after with anti-fibrinolytics.

So I think there are different approaches.

I think that the surgery data from the HAVEN 1 through 4 trials does suggest that you don't necessarily need to do it. So you can take it on a case-by-case basis. If somebody has no trouble infusing and it's not a big deal to do it, I guess there's no harm in doing it before. If it's a little more complicated to get that dose of factor in before, you might say, well, there is data that suggests I don't need to do it, so since it's really complicated I'm going to go without the factor, and if I need to do it after then we'll figure it out.

Escobar: Cindy, what has been your experience?

Leissinger: Again, I just sort of go back to how I might manage a patient with mild hemophilia who's having wisdom teeth, especially if it's extensive procedure, multiple teeth, impacted wisdom teeth. I would absolutely recommend for those that they take a dose of factor. So since I would do that in my milder patients, I would do it, as well, in those on emicizumab.

Yes, I think it's really important for that data to be published, Guy, so I look forward to seeing that. Because that's really been one of the questions even that our patients have going on emicizumab, and they understand that it's hard to monitor factor VIII measure, etc., once you're on emicizumab. And so I think it'll be really important to see that data.

But, yes, at this point in time, my practice is to give the dose of factor with anti-fibrinolytics.

Escobar: Good, yes. I think in our experience it's very similar. I usually try to talk to the dentist, if they tell me that they're very impacted, I might give him a dose of factor VIII before going in in addition to the emicizumab, and definitely the anti-fibrinolytic for them to take anywhere from 3 to 5 days, and all these patients have done well so far. So I think it'll be important, yes, to see that data.

And then definitely in a major surgery I think it's something that we have probably less experience, but we're starting to do probably more and more surgeries in patients that are on emicizumab. Now, for these mild surgeries I don't think there's need to monitor really anything. For the major surgeries where you are giving factor, then that I think is much different and probably factor VIII levels need to be measured for the replacements of the joints, etc.

Young: Can I just point out though, Miguel, that with the monitoring – and my other hat is the director of the clinical coag lab. Just so the audience is aware, if you have a patient on emicizumab, you cannot do the regular one-stage factor VIII assay to monitor, you will need to do a bovine chromogenic factor VIII assay; there are two different types of chromogenic assays. So just make sure that if you are going to do a major surgery and you're going to monitor factor VIII, that you've got the right test to do the monitoring.

Escobar: Yes, that's a very important point. Thank you, Guy, for clarifying that.

About AXIS Medical Education, Inc.

AXIS Medical Education, Inc. is a full-service continuing education company that designs and implements live, web-based, and print-based educational activities for healthcare professionals. AXIS provides convenient opportunities to engage learners based on their individual learning preferences through a full spectrum of educational offerings.

The executive leadership of AXIS combines 75 years of experience in adult learning theory, curriculum design/implementation/assessment, continuing education accreditation standards, and medical meeting planning and logistics. Our team has a deep understanding of the governing guidelines overseeing the medical education industry to ensure compliant delivery of all activities. AXIS employs an experienced team of medical and scientific experts, medical writers, project managers, meeting planners, and logistics professionals. This team is dedicated to meeting the unmet educational needs of healthcare professionals, with the goal of improving patient outcomes.

AXIS believes that partnerships are crucial in our mission to deliver timely, relevant, and high-quality medical education to healthcare professionals. To that end, AXIS partners with other organizations and accredited providers to offer added expertise and assist in expanding access to our educational interventions. AXIS also partners with numerous patient advocacy organizations to provide recommended patient education and caregiver resources in specific disease areas. AXIS finds value in these partnerships because they complement our core clinical curriculum with validated and relevant supplemental resources for busy clinicians and their patients.

The mission of AXIS is to enhance the knowledge, skills, competence, and performance of the interprofessional healthcare team to ensure patients receive quality care, resulting in improved patient outcomes. We engage healthcare professionals in fair-balanced, scientifically rigorous, expert-led certified educational activities designed to foster lifelong learning that is applicable to clinical practice and patient-centered care.

To learn more and to see our current educational offerings, visit us online at www.AXISMedEd.com.

AXIS
Medical Education