

ANSWERING REVIEWERS

1 Revisor

The manuscript is, in general, well written and of interest. There are some use of English errors, which I have corrected (see attached .doc), and some sentences need to be rephrased, which I have marked. Also, I feel that some aspects of the paper need to be cleared:

1.- How is the fact that the surgery was a liver transplantation important to the development of Tapia's syndrome in this case? This is important having in mind that the Journal is oriented to both liver transplantation surgeons AND clinical hepatology (i.e. internists, gastroenterologists...) specialists

This question is answered in the discussion, page 12:

Liver transplantation is usually a long lasting surgical procedure, which could contribute, along with other factors to the development of Tapia's syndrome. This fact should be taken into account by all clinicians involved in the liver transplantation care: liver surgeons, anesthetists, intensivists, hepatologists, gastroenterologists, etc.

2.- Maybe including only bilateral cases could make the case seem how exceptional the case portrayed is. All in all, I think the case reported is special enough, and the revision illustrative, to be shared with the medical community, being not sure of whether the audience of this journal is the appropriate for doing so.

All clinicians involved in liver transplantation are regular readers of hepatology journals. Even though the initial etiopathology is probably a consequence of the intubation process, the signs and symptoms are usually seen by hepatologists/gastroenterologists, intensivists and surgeons from liver transplant units who follow these patients. All of them ususally asist to the liver transplant committees, where clinical evolution of new candidates or already liver transplanted patients are

discussed. So it is important to divulgate the symptoms to those specialists implicated in the liver transplant process.

2 Revisor

This is a very interesting case report and a good literature review about the topic.

3 Revisor

A very interesting case report - unique for a patient undergoing liver transplantation but I suspect that the procedure is not as important as the cuff pressure of the endotracheal tube. Some mention of the measurement of cuff pressure during inflation and maintenance should be mentioned.

In page 7 , when describing the case we have added some measurements as suggested.

An 8.0 endotracheal tube was placed. The cuff was inflated with 3 ml of air and verified with a manual manometry to reach a filling pneumotamponade of 20 cm water. Surgery lasted 375 minutes.

4 Revisor

Title: Isolated bilateral Tapia's syndrome after Liver Transplantation: a case report and review of the literature The authors described a case of bilateral Tapia's syndrome in HIV/HCV liver transplant recipient which was due to prolonged intubation and/or frequent attempts at intubation and extubation. It is very rare problem but the authors did literature search and did good educational discussion of the problem. I wonder if the authors can elaborate at the rule of HIV and antiviral medications in the etiology of this case!since it is known that HIV and antiHIV medications can cause neurotoxicity

The patient was taken Atripla, a combination of Favirenz (Sustiva), Emtricitabina (Emtriva) and Tenofovir (Viread), some years prior to liver transplantation without any sign or symptom of neurotoxicity. So we can not speculate about the rol of these drugs as contributors to the development of Tapia's syndrome. We think that the most important contributors in our case were desnutrition with lack of adipose tissue of the patient, the prolonged intubation associated to a liver tranplant process and the several manipulations of the upper respiratory track .

In page 7 , when describing the case I have added the BMI to underline the importance of desnutrition as one of the contributors in our case

Editorial Revisor

Comment: I feel that the manuscript submitted by Dr. Bilbao and colleagues is, in general, well written and of interest. There are some use of English errors, which, and some sentences need to be rephrased, which I have marked in the commented Word Document I attach to the authors.

Responses: I appreciate the english correction

I have rephrased the sentences in the Revised manuscript in red color and I have deleted the sentence to be substituted:

1.- ~~dysphasia~~ **dysphagia**

2.- **We found only five published studies of bilateral Tapia's syndrome.** ~~similar to the current one and~~ **However this is** the first case reported in the literature in a liver transplanted patient.

3.- It is characterized by the unilateral paralysis of the tongue and the vocal cord caused by **extracranial injury to the hypoglossal nerve [XII] and the recurrent laryngeal branch of the vagal nerve [X] at the base of the tongue and the pyriform fossa) [1-6]** . **Although the Tapia's syndrome refers to the extracranial lesion of the hypoglossal and recurrent laryngeal nerves, some authors also describe a central type of Tapia's syndrome, referring to those patients with the**

same symptoms, but whose damage has occurred in the nucleus ambiguus, the nucleus of the hypoglossal nerve, and the pyramidal tract in the Central Nervous System. It has been described two types of this syndrome: central (due to an intramedullary lesion of the nucleus ambiguus, the nucleus of the hypoglossal nerve, and the pyramidal tract)(injury of Central Nervous Syndromes is usually not included in Tapia's syndrome) and peripheral (due to concomitant extracranial injury of the hypoglossal nerve [XII] and the recurrent laryngeal branch of the vagus nerve [X] at the base of the tongue and the pyriform fossa) [1-6]. We describe one case of bilateral Tapia's syndrome in a liver transplant patient, which is not previously reported in the literature.

4.- At that time, the nasogastric tube was preferred to the percutaneous gastrostomy to avoid invasive procedures in a patient with a complex postoperative (How come was a percutaneous gastrostomy via PRG not performed?)

5.- We carried out a literature research in the Medline database through the PUBMED search service. Medline/Pubmed search (REPHRASE)

6.- Two cases were attributed to a central cause (metastatic hemangiosarcoma in the medulla oblongata [2] and infiltration of a large B-cell lymphoma [14]) (Are these cases of Tapia's?),

As the clinical symptoms are the same, I have included the two cases specifying that the origin is central.

7.- At least 4 patients [8,17,23] required percutaneous endoscopic gastrostomy and 2 a naso-gastric tube insertion [20,42] to ensure nutritional requirements while the oro-esophageal route was unable to be used. and to prevent the risk of bronchoaspiration (naso-gastric and percutaneous gastric placed feeding tube do not prevent bronchoaspiration).

8.- . The caquexia of the patient and some degree of lypodistrophy due the HIV coinfection at time of transplant could also play a role. The fact that the

~~patient being caquectic (REPHRASE: Cachexia) and having some degree of~~
~~hypodistrophy due to HIV may have also played a role.~~ Liver transplantation is usually a long lasting surgical procedure, which could contribute, along with other factors to the development of Tapia's syndrome. This fact should be taken into account by all clinicians involved in the liver transplantation care: liver surgeons, anesthetists, intensivists, hepatologists, gastroenterologists, etc.

Comment

Any case, I am not sure of whether a paper covering a case of a surgery/anesthesiology complication not specific to liver surgery fits the content and the audience of your Journal, which includes, if does not consist in its majority, of clinical hepatologists.

Response

As I answered to Revisor 1, even though the initial etiopathology is probably a consequence of the intubation process, the signs and symptoms presented by the patients are usually seen by hepatologists/gastroenterologists, intensivists and surgeons from liver transplant units who follow them. All these specialists usually assist to the liver transplant committees, where clinical evolution of new candidates or already liver transplanted patients are discussed. So it is important to divulgate the symptoms to those implicated in the liver transplant process. And all the specialists involved in liver transplantation are regular readers of hepatology journals.