

## DERLEME / REVIEW ARTICLE

# The Transmission Risk of Prion-like Proteins in Adenotonsillar Surgery: 'Iatrogenic' Variant Creutzfeldt-Jakob Disease (vCJD)

C. Altındağ

## Adenotonsiller Cerrahide Prion-benzeri Proteinlerin Bulaşma Riski: 'Iatrojenik' Varyant Creutzfeldt-Jacob Hastalığı (vCJD)

Bovine spongiform ensefalopati (BSE) ve varyant Creutzfeldt-Jacob hastalığı (vCJD) 1980'lerden beri birçok ülkede görülen dejeneratif hastalıklardandır. BSE ve insanlarda görülen vCJD'nin etken ajanı olarak prion-benzeri proteinler suçlanmaktadır. Bu etkenlerin cerrahi aletler ile iatrojenik geçişi tespit edildiğinden ve tonsil gibi lenfoepitelyal dokularda prionların varlığı ile adenotonsiller cerrahi, iatrojenik vCJD açısından bir sorun oluşturmaktadır. Şu ana kadar adenotonsiller cerrahinin tek başına neden olduğu bir vCJD olgusu görülmemiştir. Ancak teorik olarak tek kullanımlık (disposable) setler ile kıyaslandığında; aynı cerrahi setlerin kullanımı, prion geçişi açısından bir risk oluşturur. Bu nedenle ameliyathane aletleri sterilizasyon koşullarında uygun, güncel değişiklikler yapılmalıdır. -Son yıllarda Birleşik Krallık'daki (UK) vCJD olguları sayısının artışı nedeni ile, tek kullanımlık cerrahi aletlerin adenotonsillektomi için tercih edilmesi bu ülkede tartışma konusu olmuştur. Ocak 2001'den başlayarak; İngiltere'de tek kullanımlık setler rutin olarak tercih edilmişse de komplikasyonlar (bir ölüm olgusu dahil) nedeni ile, Aralık 2001'den itibaren tek kullanımlık setlerin kullanımı, uygun setlerin temini sağlanıncaya kadar askıya alınmıştır. - Ülkemizde BSE ve vCJD olgusu şu ana kadar tespit edilmemiş olsa da (en düşük riskli bölgedeki diğer ülkeler gibi) adenotonsillektomi cerrahisi sırasında presemptomatik hastalardan prion geçişi riski olabileceği gözardı edilmemelidir.

Adenotonsillektomi için doğru endikasyonları tercih etmek ve cerrahi alet sterilizasyon yöntem değişikliklerine gereken önemi vermek, herşeyden önce bu hastalığın iatrojenik yoldan olası geçiş riskini ortadan kaldırmada en iyi önlem olacaktır. Bu derleme konuyu, yazarın NHS-ENT klinikleri deneyimi ışığında yansıtmaktadır (Londra, UK/ 2001-2002).

**Anahtar Sözcükler:** Prion, adenotonsiller cerrahi, cerrahi aletler, varyant Creutzfeldt-Jacob hastalığı.

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Cem Altındağ, MD  
Consultant ENT Surgeon, Istanbul

## Abstract

Bovine spongiform encephalopathy (BSE) and variant Creutzfeldt-Jacob disease (vCJD) are degenerative disorders, which have occurred in several countries since 1980s. Prion-like proteins are blamed as responsible infectious agents for BSE and also for vCJD, in humans. As iatrogenic transmission by surgical instruments was shown, adenotonsillar surgery has been a concern because of the presence of prion-like proteins in lymphoepithelial tissue such as tonsils. To date, no cases of iatrogenic vCJD has been demonstrated during adenotonsillar surgery. However, theoretically, it contains a possible risk to choose re-usable instruments rather than using disposable ones for adenotonsillectomy. Therefore, the sterilization facilities should be upgraded in the operation rooms of the hospitals. -In the recent years, use of disposable instruments in adenotonsillectomy has been controversial in the UK, due to increase in vCJD cases. Despite use of disposable sets had started in January 2001, these instruments were withdrawn by the UK Government-Health Authority, because of postoperative complications (including one death) as of December 2001, until more suitable single-use instruments are provided for the ENT surgeons. - We should be aware of the potential transmission of prion-like proteins from the presymptomatic patients, particularly in adenotonsillar surgery, although no case of BSE or vCJD in Turkey have been shown (like the other lowest-risk countries in Europe). Overall, defining the right indications for adenotonsillectomy and modifying the sterilization methods; would be the best prevention in order to eliminate the possible risk of transmission of the disease, via iatrogenic route. This review reflects the issue in the light of NHS-ENT clinic experience of the author in London UK, 2001-2002.

**Key Words:** Prion, adenotonsillar surgery, surgical instruments, variant Creutzfeldt-Jacob disease.

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## Introduction

Prion diseases can be classified as non-human & human prion diseases. Non-human prion diseases consist as BSE (bovine spongiform encephalopathy) (Public term: 'mad cow disease'), scrapie, transmissible mink encephalopathy, chronic wasting disease of aptive mule deer. Human prion diseases are as follows; vCJD, CJD, Kuru (a Cannibal disease), fatal familial insomnia, Gertsman-Straussler-Scheinker disease.<sup>1</sup> BSE reflects the disease of cattle which makes outbreaks, particularly in the UK, Portugal and France. Also vCJD is the variant disease of BSE, in Humans. Both of these diseases are fatal. Prion-like proteins have been responsible for these diseases. The term 'prion' firstly was used by Prusiner in 1982,<sup>2</sup> then 'prion disease' term has been preferred in the literature. Research have revealed that; prion proteins are accumulated abnormally (PrPc) and are changed into the disease-specific isomer (PrPsc).<sup>3</sup> BSE & vCJD have the same prion chain. BSE seems responsible for vCJD by consuming beef products or zoonotic transmission.<sup>4</sup> First vCJD case was seen in the UK, 1996.<sup>5</sup> To date, 125 vCJD cases were diagnosed and died in the UK (6 cases in France, 1 case; in USA, Ireland and Italy). Every year the number of the cases have been increased.<sup>5,6</sup> According to EU Commission, scientific steering committee reports in 2001; UK and Portugal were the two countries comprising the incidence rate of >100 indigineous cases per million cattle aged over 24 months. Lower level-countries (10-100/million) are as follows, Ireland, Switzerland, Belgium, Spain, Germany, France, Slovakia, Italy and the Netherlands. Also; Denmark, Greece, Finland, Austria's levels are between 1-7/million. The committee has addressed the other 14 countries including Turkey, at the lowest level (<1/million) for BSE.<sup>4</sup> Some countries like USA, have strict regulations regarding blood transfusions for the foreigners who had been settled in the UK or in EU area for a certain amount of time.

WHO also recommended some selection criteria for donors, since 1997.<sup>5,6</sup>

On the other hand, there has not been found any evidence of transmission for prions regarding blood products.<sup>7</sup> In the UK, all cattle over 30 months is being controlled for BSE. Moreover, EU Commission for food safety made a decision for banning specified risk materials (SRM) since October 2000.<sup>5</sup>

Best prevention from prions is to avoid from beef and beef products (burger or sausages). No evidence of prion transmission to humans has been shown for milk and milk products.<sup>5</sup>

## vCJD & Iatrogenic vCJD

vCJD can be diagnosed on some clinical criteria such as progressive demans, followed by cerebellar ataxia, EEG findings.<sup>8</sup> But, the main confirmation is provided only by brain tissue biopsy. In the early incubation period, the value of a tonsil biopsy has gained some popularity in the living patient to confirm vCJD since 1998.<sup>9,10</sup> No significant morbidity has been shown with tonsil biopsy. The details and precautions for tonsil biopsy have been described by Frosh and Layaaraj.<sup>10</sup> Western blot testing have been observed more sensitive rather than immunohistologic testing for the patients. To date, no specific blood test is available for diagnosing or screening the disease for presymptomatic patients, despite current advanced research.<sup>11</sup> MRI findings have been demonstrated to diagnose the vCJD. Some researchers have revealed that 'pulvinar / putamen signal intensity' ratio can be used to diagnose vCJD.<sup>12,13</sup>

CJD and vCJD are both degenerative and fatal disorders for humans. No exact treatment for this diseases was found yet, even though some researchers in various articles have reflected new research and controversial benefits for antioxidants, quinacrine, carboxylic acid and pentoxy phosphate for the patients of CJD and vCJD.<sup>14-19</sup>

vCJD differs from sporadic CJD by the early-beginning incubation period. Incubation period

may increase if there is a species barrier.<sup>20</sup> In general, vCJD have been observed in the twenties and thirties. Theoretically, the incubation period is thought that, it may be longer than a human life period.<sup>21</sup> Prions deposit in neural and lymphoreticular tissues (brain, retina and tonsil, spleen). The presence of prions in tonsil tissue, have been shown in the early incubation period of the presymptomatic patients.<sup>22</sup> Since this 'estimated' incubation period is long for vCJD in children, there is no doubt that; the number of cases may increase.<sup>23</sup> The presence of prions had also been demonstrated in surgical instruments from sporadic CJD patients.<sup>24</sup> So, the Health Authority in the UK has announced that, iatrogenic vCJD can be one of the potential transmission risk of the disease, particularly in children. Not only the surgical instruments could transmit the agent, but also the extracted pituitary hormones or stereotactic electrodes may be the sources of this iatrogenic risk.<sup>25,26</sup>

Prions are quite resistant agents that cannot be eliminated easily by the classic disinfection-sterilization methods. The techniques for the sterilization to eliminate prions, have been controversial. The ionizing and ultraviolet radiation also do not destroy prion-like proteins.<sup>27-32</sup> At present, NaOH combination of autoclaving at 134 C-more than 18 minutes- seems the only alternative for destroying the prions even the use of NaOH is harmful for the fragile instruments.<sup>29,31,32</sup> A detailed sterilization protocol has been developed for the surgical instruments by Rutala and Weber.<sup>32</sup>

In order to prevent the risk of transmission of vCJD for these reasons, The UK-Dept. of Health announced that all instruments used in adenotonsillar surgery should be disposable since

January 2001.<sup>33</sup> Following this advice, all adenotonsillectomies were being performed by using single-use instruments in all hospitals- during 2001- even though instruments/cautery were not quite comfortable (personal communication, Altindag C.).

By the end of 2001, some articles addressed the adverse effects and complications -mainly; sec-

ondary haemorrhagia- including one death regarding this disposable instruments and bipolar cautery.<sup>34,35,36</sup> Dept. of Health investigated the issue and suspended the use of disposable instruments as of December 2001, and advised the ENT surgeons that re-usable instruments should be used if any surgeon is uncomfortable with the disposable ones.<sup>37</sup> UK government also has planned to modify the old-sterilization facilities in the hospitals. At present, ultrasonic harmonic scalpel has gained popularity in tonsillectomy in some operating theatres of the private hospitals, despite the high cost. By using ultrasonic dissection, the bloodless field and the advantage of using less instruments during the operation may enable the surgeons and another patients a prion free field as well as creating a good post-operative haemostasis. However, there is no current research in the literature for plume whether it includes the prions or not. In some countries, ultrasonic dissection technique (or new coblation methods) may be preferred in tonsillectomy rather than cold dissection method, in the following years.

## **Conclusion**

In Turkey, although no cases of vCJD or sporadic CJD, BSE have been observed to date; the increase in the number of the cases of vCJD in the UK and, the presence of few cases in some countries of Europe have warned the rest of the other countries of the world for vCJD, in the recent years. UK has made it's own strategy regarding sterilization and use of disposable instrument issues for iatrogenic vCJD. Each country should take different precautions in various steps with regard to prevent the potential transmission risk of iatrogenic vCJD, particularly in adenotonsillar surgery and or neuro-surgical/ophthalmic instruments. Currently, the single-use instruments are not comfortable enough to perform the operations. Potential complications and the financial issues are another concerns for single-use instruments. Therefore, current sterilization techniques should be upgraded in the operat-

ing theatres. Adenotonsillar surgery and neurosurgical instruments should be taken into account, in terms of sterilization. High-risk and low-risk tissues and instruments for the prions may be defined for operating theatres. All hospitals may use a standard sterilization protocol, which our Country's Health Authority will offer it's own plan and advice by the cooperation of Hospital clinics. Use of disposable instruments in adenotonsillar surgery do not seem necessary for the lowest-risk European countries and Turkey. This issue is required attention as long as the number of research increases. Because, many questions are still in debate regarding the possible risk of prions during surgery, for the surgeon and the patients.

Overall, choosing the right indications for adenotonsillectomy appear the best method of reducing the risk of transmission for iatrogenic vCJD in all countries.

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**Correspondence: Cem Altındağ, MD**  
Eminalipaşa Cad. Beydağı Apt. 93/A/9  
Bostancı - İSTANBUL  
Phone: + 90 (0532) 322 06 09  
e-mail: caltindaguk@yahoo.co.uk

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