Fatal Myeloencephalitis Following Yellow Fever Vaccination in a Case with HIV Infection

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Abstract

A 53 year old physically healthy man, unaware of any immunocompromised condition developed rapidly fatal myelomeningoencephalitis following a live-attenuated yellow fever vaccination. He was found to have asymptomatic HIV infection with high viral loads and low CD_4 counts. This is the first reported case of such an incidence in the world literature. It is strongly suggested that in countries where HIV infection is endemic, an HIV blood test should be performed prior to the yellow fever vaccination and the vaccine should not be given to those immunocompromised persons.

Key word : Yellow Fever Vaccine, Myeloencephalitis, HIV Infection

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A CASE REPORT

A 53 year old Thai man was transferred from a hospital in Surin province to Vichaiyut Hospital on February 22, 2001 with a history of generalized seizures followed by unconsciousness.

One week prior to the admission, he had had a yellow fever vaccination at the Ministry of Public Health in preparation for a trip to the Middle East. Three days later, he experienced fever and malaise. He went to see a physician at a nearby clinic in his home town of Surin province and was treated for a common cold. Without any improvement, he developed a higher fever, severe myalgia, headache, nausea and vomiting.

One day prior to this admission, he experienced mental confusion and progressive agitation.

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He was then admitted to a private hospital in Surin province. CT scan of the brain showed diffuse brain edema without midline shift (Fig. 1). A lumbar puncture was performed and the spinal fluid revealed 286 white blood cells per mm^3. Differential count showed 80 per cent neutrophils and 20 per cent mononuclear cells. Protein content in the spinal fluid was 99.6 mg/dl and sugar was 135.9 mg/dl, Acid-fast and Gram's staining as well as Indian ink preparation were negative for any organism. He received supportive treatment for acute viral encephalitis but his condition deteriorated rapidly and he experienced generalized seizures followed by unconsciousness and irregular breathing. Endotracheal intubation was done to assist ventilation. He was then transferred to this hospital for further treatment.

The patient had been in very good health. He exercised about three hours daily. He did not smoke and stopped drinking alcohol about three years previously because of some abnormal liver enzymes related to alcohol.

Physical examination on admission revealed a 53 year old Thai man, sthenic build, with a high temperature of 39°C, pulse rate 88/min, respiratory rate 16/min and blood pressure of 130/80 mmHg. He was not anemic or jaundiced and no edema was noted. He was comatose with no response to verbal commands but still responded to deep pain stimuli as shown by movement of both arms. However, flaccid paralysis of both legs was also noted. Facial expression on the right side was weaker than the left side. Pupils were 1 mm in diameter with response to light. Stiffness of the neck and positive Kernig's sign were detected. Heart and lungs were normal. Abdominal examination revealed no abnormality, liver and spleen were not palpable.

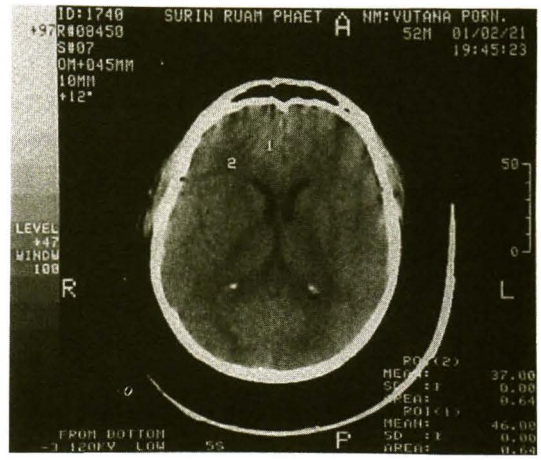

Fig. 1. CT scan of the brain on day 6 after vaccination showing diffuse brain edema without mid line shift.

Laboratory tests showed

Hct 40.0 per cent, Hb 13.0 mg per cent, WBC 10,800/mm^3, N 80 per cent, L 16 per cent, M 4 per cent, Blood sugar 130 mg/dl, BUN 21 mg/dl, SGOT 39 U/L, SGPT 21 U/L, Na 139 mmol/L, K 3.9 mmol/L, Cl 100 mmol/L, CO_2 24 mmol/L

Hemoculture was negative.

Lumbar puncture revealed open pressure of 200 mmH_2O, closed pressure 140 mmH_2O. The fluid was thick, turbid, yellowish in colour, specific gravity was 1.034, white blood cells were 152 mm^3 with 64 per cent neutrophils and 36 per cent mononuclear cells, RBC 2,597/mm^3. Protein content was 3,620 mg/dl and sugar was 150 mg/dl. Gram's stain, AFB stain and Indian ink stain of the spinal fluid were negative. Spinal fluid cultures for bacteria and fungus were negative. Antibodies for Varicellar Zoster IgM and Herpes simplex IgM Japanese Encephalitis IgM were undetected in the spinal fluid.

Since the clinical features were quite unusual and progressed rapidly, a blood specimen was tested for HIV antibody which was found to be positive. Subsequent HIV viral load of 264,434 log equivalence 5.42 log was found with low CD_4 of 108/mm^3.

The diagnosis of myelomeningo- encephalitis post yellow fever vaccination was made along with HIV infection. Intravenous acyclovir was given and oral antiretroviral drugs namely lamivudine, didanosine and Indinavir were added *via* nasogastric tube. Dexamethasone 4 mg was given intravenously every 4 hours to relieve cerebral edema. Phenyltoin 120 mg orally was prescribed to control convulsions.

On the second day of admission, neurological signs deteriorated which indicated brain stem involvement as shown by eye disconjugation, facial diplegia and extensor plantar response bilaterally. On the third hospital day, he was in a deep coma, pupils were fixed and fully dilated, Doll's eye sign was negative and fundoscopy showed papilledema on both sides. He passed away on that day. Post mortem was not permitted.

DISCUSSION

This patient had been physically healthy yet he was an unrecognized immunocompromized person with HIV infection and low CD_4. He had a previous history of alcoholic liver disease. Three days after live-attenuated yellow fever vaccination, he developed flu-like symptoms followed by rapidly progressive neurological involvement as demonstrated by signs of myelitis, meningitis and encephalitis respectively. There was some evidence indicating unusually very severe neurological reactions namely CSF protein contents increased from 99.6 mg/dl to 3620 mg/dl within a day apart and very rapidly progressive neurological signs and symptoms without any response to the supportive treatment. Fatality came within ten days after the immunization. Neurological involvement undoubtedly can be clinically differentiated from that of AIDS with brain involvement.

Eventhough viral isolation or specific yellow fever viral antibody or antigen to definitely confirm the diagnosis of yellow fever myelomeningoencephalitis is not available here yet, other locally common viral infections of the brain were excluded by the negative FTA ABS IgM, Herpes Simplex IgM, Herpes Zoster IgM and Japanese encephalitis IgM. Bacterial and fungal cultures of the spinal fluids were negative. Based on the laboratory exclusions as well as the typical clinical features of previously reported cases[1-3] the authors believe that this immunocompromised patient was infected by live-attenuated yellow fever viruses.

Yellow fever vaccination is usually well tolerated yet minor reactions may be observed within a few days after immunization. About 6 days after immunization a few cases may present with low grade fever, headache and backache. No more than 17 cases of encephalitis have been reported over a period of 40 years and all occurred in children[4].

In reviewing the literature there are only 3 reports of 7 adults who experienced CNS involvement following yellow fever vaccination[4-6]. A healthy 29 year old man experienced CNS symptoms 3 days after vaccination[1] and this patient survived. Another 4 patients older than 63 years were reported to the US Center for Disease Control in 1998[2]. The onset of fever started between day 2-5 post vaccination which is similar to the present case. Only one of the four survived, three cases died on day 8, 21 and 30 post vaccination. HIV antibody was done with negative result in one case. Yellow fever virus was isolated from serum in one case, from spinal fluids in 2 cases and yellow fever antigen was detected from liver necropsy in another one case between day 7-10 post vaccination. These findings confirm the causal association between attenuated yellow fever viruses and clinical diseases which are similar to those infected with wild yellow fever virus infection.

In general practice live-attenuated viral vaccine is recommended not to be given to immunocompromized persons including pregnant women, very small children under six months of age[5] and old people. The presented case is the first report of post yellow fever vaccine encephalitis in Thailand and probably the first one found to be associated with HIV infection. It demonstrates a very important implication to all countries in which HIV infection is endemic. There are many asymptomatic persons or those unaware that they are HIV positive and such a tragic mistake may occur again and again. In countries with a strong human rights propaganda or where blood tests for HIV infection can not readily be done in those who need immunization by any live viral vaccines should be well informed of the severe fatal complications. In the CDC recommendation[6], besides infants and pregnant women, the yellow fever vaccine is contraindicated in those who are hypersensitive to eggs and those with immunocompromised hosts. However, the authors do not totally agree with the statement that persons with AIDS or HIV infection may be vaccinated if exposure to yellow fever can not be avoided. As for Thailand, based on this tragic experience, it is suggested that an HIV blood test should be done at least in sexually active and high risk persons prior to the yellow fever vaccination. The authors are against the idea of giving yellow fever vaccine to those proven to be HIV patients.

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ไขสันหลังและสมองอักเสบจนถึงเสียชีวิต หลังการฉีดวัคซีนป้องกันไข้เหลือง ในผู้ป่วย 1 รายที่ติดเชื้อเอ็ชไอวี

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รายงานผู้ป่วยชายไทย อายุ 53 ปี อยู่จังหวัดสุรินทร์ มีสุขภาพแข็งแรงดี จะไปเที่ยวตะวันออกกลาง จึงไปฉีดวัคซีนไข้เหลืองเมื่อ 1 สัปดาห์ก่อนมาโรงพยาบาล หลังจากนั้น 3 วัน มีไข้สูง ปวดตัวมาก คลื่นไส้ อาเจียน ต่อมาซึมไม่รู้ตัว กระสับกระส่าย ได้รักษาที่โรงพยาบาลต่างจังหวัด การตรวจคอมพิวเตอร์สแกนพบสมองบวมมาก เจาะน้ำไขสันหลังมีอักเสบและโปรตีนสูง ผู้ป่วยชักและหมดสติ ก่อนย้ายมาพบมีอัมพาตขา 2 ข้าง ประสาทหน้าซีกขวาอ่อนแรง คอแข็งและถึงแก่กรรมในวันที่สองหลังรับ การตรวจเลือดและน้ำไขสันหลังไม่พบเชื้อใด ๆ แต่โปรตีนสูงมาก เลือดมีแอนติบอดีย์ต่อเชื้อเอ็ชไอวี นับไวรัสได้สูงและเซลล์ซีดี$_4$ 108 ตัวต่อ ล.มม. นับเป็นผู้ป่วยไทยรายแรกที่เกิดอาการแทรกซ้อนทางสมองหลังฉีดวัคซีนไข้เหลือง ซึ่งเป็นวัคซีนที่ทำจากไวรัสไข้เหลืองที่ยังมีชีวิตแต่ทำให้อ่อนฤทธิ์แล้ว ซึ่งถึงแม้รายนี้จะไม่ได้แยกเชื้อไวรัสไข้เหลืองจากเนื้อสมองหรืออวัยวะอื่น แต่จากรายงานในวารสารต่างประเทศแยกได้เชื้อไวรัสไข้เหลืองที่ทำวัคซีนจากผู้ป่วย ผู้ป่วยมีลักษณะอาการคล้ายกัน มีรายงานว่าพบได้ในเด็กอ่อนหรือคนชรา และห้ามใช้วัคซีนนี้ในผู้มีภูมิป้องกันบกพร่อง

รายงานนี้เป็นรายงานแรกในโลกที่พบในผู้ป่วยที่เป็นเอ็ชไอวีด้วย ผู้รายงานเตือนให้ประเทศที่มีโรคเอ็ชไอวีระบาดอยู่ เช่น ประเทศไทย ควรให้ผู้จะฉีดวัคซีนได้ทราบถึงภัยที่อาจเกิดขึ้นและควรได้เจาะเลือดตรวจหาเอ็ชไอวีก่อนฉีดวัคซีนไข้เหลือง เพราะในประเทศเหล่านี้ยังมีผู้ติดเชื้อที่ไม่รู้ตัวเองและไม่มีอาการใด ๆ ทั้ง ๆ ที่มีภูมิต้านทานต่ำแล้ว ถ้าได้วัคซีนไข้เหลืองไปอาจเกิดภาวะแทรกซ้อนรุนแรงถึงชีวิตได้ โดยไม่มีทางรักษาเช่นผู้ป่วยที่รายงานนี้

คำสำคัญ : วัคซีนไข้เหลือง, ไขสันหลังและสมองอักเสบ, การติดเชื้อเอ็ชไอวี

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