AN AUTOPSY REPORT OF LASSA FEVER IN
ONITSHA/NGERIA/1974

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Abstract: The present report is one of the autopsy report of Lassa fever in Nigeria, 1974. Hospital epidemic of Lassa fever occurred in Onitsha of Nigeria. A 29 year old German physician, E.S. working at the St. Charles' Borromeo Hospital in Onitsha complained abdominal pain on February 10, 1974. At that time intermittent high fever up to 40°C, headache, malaise and vomiting were also noticed. On Feb. 15, sore throat and high fever lasted. On February 17, sore throat got worse and temporary fall of temperature. On February 19, severer sore throat involving tonsillitis, ulceration in the soft palate and cervical lymphadenopathy were found. Tracheotomy was performed because of dyspnea and resulted in profuse bleeding, clotting time 17 minutes. Some petechiae developed on the face. On February 20, 1974 there came convulsion and coma, then death. Blood culture was negative. Isolation of Lassa virus was successfully performed from the pleural and ascites fluid of the cadaver. Histopathologic examination of the organ specimens was performed in Tokyo and disclosed following findings. (1) Viral hepatitis. (2) Acute splenitis. (3) Focal glomerulonephritis. (4) Localized fibrosis of myocard. (5) Marked congestion and edema of both lungs. (6) Lymphadenitis. (7) Meningoencephalitis. According to these findings, we obtained following comments: Necrosis of nerve cells in the brain and liver cells, and focal necrosis of glomeruli may be attributed to primary damage by the virus. However, pathognomonic change in the spleen, acellular eosinophilic necrosis around follicle and in Billroth cord (Edington 1972) seems to be deposition of hyaline like substance resulting from increased permeability of capillary in the marginal zone of follicle and Billroth cord.

INTRODUCTION

Lassa fever is an acute febrile viral disease first observed at Lassa in Northern Nigeria in 1969 (Frame et al. 1970). The new virus was first isolated by Buckley et al. in the same year of 1970. Up to 1973, four autopsies have been performed out of a total of 19 deaths recorded in 4 outbreaks. The first and second cases were performed at Lassa in 1969 (Frame et al. 1970). The third and the fourth cases were performed at Jos in 1970 (Troup et al. 1970). No histological findings of the first case were published (Frame et al. 1970). Troup et al. (1970) had reported the third and the fourth autopsy findings in 1970 and Edington et al. (1972) had described detailed pathological findings of the same autopsies in 1972, but the changes in the brain were not described by any of these authors.

Authors had an autopsy case of Lassa fever in hospital epidemic that occurred in St. Charles' Borromeo Hospital/Onitsha in the East Central State of Nigeria in February 1974. The present report described the autopsy findings of our own.

**Clinical Abstracts**

Dr. E. Saurwald., a 29 year old German Missionary Medical Doctor in St. Charles' Borromeo Hospital became ill on February 10th 1974 with generalized abdominal pain and loose stool for one day. Later he developed intermittent fever (40°C) associated with headache, general malaise and vomiting. Ampicillin 250mg 6 hourly was given from the 5th day, but was ineffective. On the 6th day, he developed sore throat and his fever continued. On the 7th day, his therapy was changed to Chloramphenicol following a diagnosis of typhoid. On the 8th day, his sore throat got worse and he was given to start on 60 mg of Predonisolone. His temperature now fell and remained steady until the 10th day, but in the meantime his throat infection became severer with involvement of tonsils and ulceration of the soft palate. He also had cervical lymphadenopathy and developed respiratory obstruction, for which tracheotomy was performed by a colleague, Dr. Mandrella. Following this, the patient developed profuse bleeding from the operative wound. A clotting time of 17 minutes was recorded and he also developed some petechie on the face. A few hours after the operation he started having convulsions and went into coma. He died 10 hours later on February 20th, 1974.

Laboratory investigations showed normal haemoglobin throughout the illness. W.B.C. varied from 4,100/cmm. to 7,500/cmm. with a differential count showing relative lymphocytosis. The blood culture grew contaminants only. The isolation of the virus was not performed clinically. An autopsy was performed later at the University of Nigeria Hospital.

**Macroscopic findings**

External examination of the body showed several petechie on the forehead and on the scalp. There was tracheotomy wound at the 3rd tracheal ring which appeared clean. The peritoneal cavity contained 1000 ml of straw coloured fluid and the pleural cavities together contained about 500 ml of haemorrhagic fluid. The brain weighed 1600 gm. The surface of the brain and the cut surface showed evidence of oedema. The tongue was normal and both tonsils were enlarged and congested. No evidence of any ulceration of the stomach or of the rest of the gut was noticed. Liver (1,500 gm) was normal in colour and surface showed a few distended bile ducts. The gall bladder was distended with bile. The tracheal lumen was patent. The lungs which weighed left 750 gm and right 900 gm were markedly congested massive and subcrepitant, especially in the lower lobes. The pleurae were also congested. The spleen (240 gm) appeared normal. There was no lymphadenopathy. The pericardial sac contained a few millilitres of straw coloured fluid. The heart (400 gm) contained post mortem clots in all chambers. Both kidneys (150 gm each) appeared normal with normal corticomedullary differentiation.
**Microscopic findings**

Section from the brain showed meningoencephalitis. There were oedema, congestion, scattered necrosis and neuronophagia of the nerve cells in the cerebral cortex (Fig. 1, 2). Occasional perivascular infiltration (cuffing) of lymphocytes and histiocytes (Fig. 3, 4). Meninges showed congestion, oedema, slight infiltration of lymphocytes and histiocytes (Fig. 5, 6). The liver showed viral hepatitis. There were scattered eosinophilic necrosis of individual or small groups of the hepatic cells without cell infiltration. Periportal round cell infiltration (up to moderate degree) and slight fibrosis (Fig. 7, 8, 9). And neither bile stasis nor fatty changes were seen. The spleen showed slight fibrinous perisplenitis. There were marked congestion and deposition of hyaline-like substance around follicles and Billroth's cords (Fig. 10, 11). Marked deposition of lymphocytes and reticular cells and occasional intrafollicular bleeding were seen. In addition, there were pavemmenting and subendothelial infiltration of lymphocytes, plasma cells and monocytes of trabecular vein (Fig. 12, 13). In the kidney, there were scattered focal necrosis of the glomeruli, interstitial oedema and slight fibrosis (Fig. 14). Scattered granular and
Figure 5  Meningitis, slight infiltration of lymphocyte and histiocyte in congested meninges. Congestion of grey matter. (H.E., ×100).

Figure 6  High magnification of Fig. 5.; Infiltration of lymphocyte, plasma cell and histiocyte. (H.E., ×400)

Figure 7  Slight fibrosis of periportal area of the liver. (Pap’s silver stain., ×40)

Figure 8  Infiltration of lymphocytes, plasma cells and histiocytes in Glisson’s sheath. No bile stasis. (H.E., ×100)

Figure 9  Necrosis of individual and a small group of the hepatic cell. (Pap’s silver stain., ×200).

Figure 10  Pericapillary deposition of PAS positive substance in marginal zone of follicle. Scattered reticular cells, in spleen. (PAS., ×100)
Figure 11 Perifollicular deposition of hyaline-like substance, in spleen. Lymphocyte depletion of follicle. (Masson., ×100)

Figure 12 Pavementing and subendothelial infiltration of lymphocytes of trabecular vein. Lymphocytic infiltration is seen in media. (PAS., ×100)

Figure 13 Subendothelial infiltration of lymphocytes, plasma cells, eosinophile leucocyte and others in spleen. (PAS., ×400)

Figure 14 Focal necrosis and destruction of glomerular tuft of kidney. Interstitial oedema. Advanced post mortem change of tubular epithelia. Slight thickening of Bowmans’ capsule. (PAS., ×200)

Figure 15 Marked congestion and oedema of the lower lobe of the right lung. (H.E., ×400)

Figure 16 Circumscribed fibrosis of myocardium and degeneration of muscular fiber of the heart. Interstitial oedema. (Azan., ×400)
hyaline casts were seen in the tubules. The lungs showed marked congestion and oedema (Fig. 15). Slight bleeding in the lower lobe of the left lungs and scattered heart failure cells in the alveolar lumen (Fig. 15). No interstitial pneumonitis was seen. The hilar lymphonode showed congestion, lymphocyte depletion and slight anthracosis. No remarkable reticulosis of the lymph node was seen. The cervical lymph node showed lymphadenitis. There were congestion, marked depletion of lymphocytes and reticulosis. The heart showed interstitial oedema, circumscribed fibrosis and degeneration of the myocard (Fig. 16). No remarkable change in the valvace was seen. No ulceration in the gastrointestinal tracts were seen. Peritonitis was present. Congestion and atrophy of the thyroid were seen.

Isolation of Lassa virus

During our autopsy, the pleural and peritoneal fluid were obtained and had been kept in isolated refrigerator at outside of our hospital. Later, authors had brought this specimen, which was kept in absolute ice box, to Prof. Fabiyi who was in virus labotatory of Ibadan University/Nigeria. On 29th June 1974, authors received the result of specimen, which was surely described "positive of Lassa virus" (Fig. 17).

Ismail: Dr. I. C. O. Ugochukwu
Head, Department of Pathology.

to: Dr. S. S. Fabiyi
Registrar in Pathology
University Teaching Hospital
Ibadan, Nigeria.

Dear Dr. Fabiyi,

Re: Dr. Ogunsegun's Specimen

The result of Dr. Ogunsegun's specimen is negative.

Thank you for your letter of June 14, 1974 re the above specimen (Pleural and peritoneal fluids). I can confirm that these have been shown to be positive for the presence of Lassa virus (by isolation).

There are no serological reports as you did not send us any serum from this patient.

Several strains of the Lassa virus have been isolated from rodents, *Musara major*, only. Most of these strains were from rodents caught in the households occupied by Lassa fever patients (Smith, S. T., O.L.O. Hospital and Lassa Disease, West Africa, Vol. 22, No. 1, 1977). However, these isolations, important as they are, do not necessarily indicate that *Musara major* is the reservoir for Lassa virus. Work on this subject is in progress.

If you can be of further service please do not hesitate to get in touch.

Yours sincerely,

(Adj. I.) Ogunsegun Babajide
Professor & Director.

cc: Dr. I. C. O. Ugochukwu.

29th June, 1974.
Hospital epidemic in St. Charles' Borromeo Hospital

There was no detailed report of hospital epidemic in St. Charles' Borromeo Hospital/Onitsha of Nigeria in February 1974. However, authors had been given some document about the hospital epidemic by Dr. Mandrella of St. Charles' Borromeo Hospital, before autopsy. According to his document, a boy of 19 year old had got common cold with high fever and was admitted to this hospital, suspecting malaria. However, high fever of this patient did not decreased and continued. In this time, nursing doctor for this patient was Dr. Egon Sauerwald, whose clinical document had already described. In the late stage, Dr. Sauerwald was received tracheotomy by Dr. Mandrella. Dr. Mandrella had been also infected with Lassa fever, after ten days our autopsy. Fortunately, Dr. Mandrella was transferred to his mother country, West Germany and recovered after the antiserum therapy by Dr. Casals.

DISCUSSION

According to the literature, there have been four outbreaks of Lassa fever, two in Nigeria, one in Liberia and one in Sierra Leone before our autopsy. Of these, the first outbreak was seen at Lassa, a town in the North Eastern State of Nigeria in January, 1969 (Frame et al). The second outbreak of Lassa fever was at Jos in January, 1970 (Troup et al. 1970). The third outbreak was in Zorzor area in Liberia in March, 1972 (Mertens et al. 1973, Monath et al. 1973). And the fourth outbreak was in Sierra Leone in September/October, 1972 (Monath et al. 1974).

Four autopsies were performed out of the 19 deaths that occurred in these outbreaks. However, in the first necropsy, only macroscopic findings were described. The second autopsy was performed by Prof. Stoerk, who described the histological findings as marked congestion of the heart, lungs, liver, spleen and kidneys (Frame et al. 1970). Another significant lesion found was in the submu cosa of the intestine which showed severe oedema. The third and the fourth autopsies were performed by Dr. Troup, who, unfortunately, got the infection herself through an accidental cut while performing the autopsy and died in February, 1970. Later, the organs of the third and fourth autopsy cases were handled by Prof. Edington who reported that the findings were somewhat similar to the pathology of Thai and Bolivian haemorrhagic fever and he considered Lassa fever to be a new haemorrhagic fever (Edington and White, 1972). No autopsy was performed on any of the deaths that occurred in the outbreaks in Liberia and Sierra Leone.

According to the detailed microscopic findings of Prof. Edington, the characteristic lesion of Lassa fever is in the spleen and consists of an eosinophilic necrosis surrounding the depleted white pulp associated with pavementing and subendothelial lymphocytic infiltration of the splenic veins. However, in our case, we did not find the typical eosinophilic coagulative necrosis around the depleted white pulp in the spleen. But we did recognize the deposition of hyaline-like substance around follicles and Billroth's cords (Fig. 11). These findings seemed to be deposition resulting from increased permeability of capillary in the marginal zone.
of follicle and Billroth's cord (Sato and Akiyoshi, 1975). And we also found marked widening of the perivascular space of the brain associated with perivascular cuffing with lymphocytes (Fig. 3), which is suggestive of encephalitis. These histological features of the brain are the first to be described in Lassa fever.

The clinical history of our case was very similar to those previously published (Frame et al. 1970, White 1972, and Mertens et al. 1973). The isolation of the virus from the blood or tissue fluids is the important criterion to the diagnosis of Lassa fever. In our case, Lassa virus was reported to be isolated from both pleural and peritoneal fluids by Prof. Fabiyi (Fig. 17).

ACKNOWLEDGMENT

We would like to thank Dr. B. Mandrella of St. Charles’ Borromeo Hospital, Onitsha, who supplied us with clinical history; Prof. G. M. Edington for his kind advice on the slides, Prof. M. Akiyoshi for his kind advice on histopathologic examinations and Prof. A. Fabiyi of the Virus Research Centre, Ibadan University, for isolating the virus. Finally, we wish to express our thanks to the Japanese International Cooperation Agency for supporting our cooperation.

REFERENCES

1974年ナイジェリア国のオニッチャ市において、ラッサ熱で死亡した医師の剖検報告

佐藤喜一*・Silvanus E. IKERIONWU, Kenneth C. KATCHY

1974年2月、ナイジェリア国のオニッチャ市にあるポロメオ病院内で、ラッサ熱の流行があった。この時期に、この病院で働いていた29歳の西ドイツ人医師（男）が入院中の患者から、ラッサ熱に感染し死亡した。著者らはナイジェリア大学病院（Enugu 市：Onitsha 市より東へ約 70 km）の病理解剖室で本例の病理解剖を行なった。剖検体は、1974年2月10日に 40℃の高熱と腹痛を訴えた。そして嘔吐があった。抗生物質の投与に抗して高熱は5日間持続した。10日目には激しい咽頭痛を訴え、扁桃と軟口盖に潰瘍がみられ、頭部リンパ腺腫脹も現れた。呼吸困難が現われたために気管切開術を行なったが、間もなく意識喪失し死亡した。

病理組織学所見のうち、主たる所見は以下の如くであった。（1）脳（1500 g）：脳膜炎と脳炎の所見を認めた（図1〜6）。すなわち脳膜はうっ血を示し、組織学的には軽度のリンパ球や組織球の浸潤と浮腫がみられた。脳実質にもうっ血と浮腫がみられた。また神経細胞の壊死と Neuronophagia が考えられた（図7〜9）。肝細胞と肝細胞の小塊には好エオジン性壊死像がみられた。（3）脾臓（240 g）：脾周囲炎と脾炎がみられた。脾白色縁の辺縁帯と脾索内に硝子様物質の沈着がみられた（図10〜13）。（4）腎臓：囊状条球体腎炎（図14）。5）胸水と腹水をイバダン大学ウイルス研究所へ送り、ラッサ熱ウイルスの同定試験で陽性であった（図17）。（6）その他として肺のうっ血と浮腫、心筋の局性線維症などがみられた。これらの所見から、ラッサウイルスが直接障害したと考えられる所見として大脳皮質の神経細胞の壊死、肝細胞の散在性壊死、腎条球体の囊状壊死などをみられるような毛細血管内皮細胞の障害などがあげられる。

ナイジェリア大学病院 病理解剖学教室
* ナイジェリア大学客員教授として1973年11月より1年間出向した。現在、金沢医科大学耳鼻咽喉科教室に在籍している。