Leaders

How to tackle a possible Creutzfeldt-Jakob disease necropsy

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Introduction
The clinical diagnosis of Creutzfeldt-Jakob disease is based on a history of rapidly progressive dementia, presence of myoclonic movements, and a characteristic electroencephalogram. However, clinical features are not always clearcut, and diagnostic overlap with other forms of dementia, including Alzheimer’s disease, remains a problem in many cases. Some patients have atypical dementing illnesses which defy clinical categorisation; post-mortem examination is necessary to achieve correct diagnosis in all cases of atypical dementia and suspected Creutzfeldt-Jakob disease. Most patients with classic Creutzfeldt-Jakob disease display at least some spongiform change in brain tissue. This well recognised neuropathological feature is strongly supportive of a diagnosis of Creutzfeldt-Jakob disease, but is not pathognomonic because it is also found occasionally in cases of diffuse Lewy body disease and even in Alzheimer’s disease. However, other histological features, such as neurofibrillary tangles, senile plaques, and Lewy bodies assist in clarifying the final diagnosis. Creutzfeldt-Jakob disease can be transmitted to animals or man following inoculation or transplantation of infected tissue. Research has shown that Creutzfeldt-Jakob disease and the related Gerstmann-Straussler syndrome are characterised by the presence of prion protein (PrP) which constitutes a significant part, if not the whole, of the infective agent. Recent progress in molecular biology has identified abnormalities in the PrP gene in some cases of familial Creutzfeldt-Jakob disease and in other cases of familial dementia with no characteristic pathology. These findings represent a challenge to the current classification of dementia and require urgent investigation. This places a very high priority on performing necropsy in cases suspected of having Creutzfeldt-Jakob disease. Creutzfeldt-Jakob disease resembles spongiform encephalopathy in animals and the epidemic of bovine spongiform encephalopathy (BSE) has led to anxiety that the incidence of Creutzfeldt-Jakob disease will rise. Because of this concern, the Department of Health has funded the setting up of a nationwide surveillance project to monitor the incidence of Creutzfeldt-Jakob disease, and this study is based in Edinburgh. The clinical surveillance is supervised by Dr R Will to whom all patients with a likely diagnosis of Creutzfeldt-Jakob disease should be notified. A very important part of the study is to obtain the brain for histological examination in as high a proportion of Creutzfeldt-Jakob disease cases as possible. Although guidelines for Creutzfeldt-Jakob disease necropsies have been published before, the safety protocols contained therein need to be updated in the light of current knowledge. The Creutzfeldt-Jakob disease agent is a category 2 pathogen which presents special hazards in that it survives formalin fixation.

Some Creutzfeldt-Jakob disease cases are cared for in neurology units, and a neuropathologist with access to a specialised "high risk" mortuary may be asked to do the necropsy. In these circumstances, provided with dedicated instruments, autoclavable power saw, and full protective clothing, an extended necropsy, including removal of the spinal cord, can be undertaken. However, some cases occur in hospitals with no ready access to such facilities, and in these cases a more limited necropsy has to be performed.

This article has been prepared in response to numerous requests for practical guidance by general histopathologists who have been asked to perform a necropsy in a case of possible or probable Creutzfeldt-Jakob disease. It is possible to remove the brain in a way which avoids contamination of staff and environment in all mortuaries with standard facilities. The method is outlined below and illustrated in figs 1–8.

Method
THE NECROPSY
Attendance at the necropsy is limited to the pathologist and a maximum of two mortuary staff. All staff should wear disposable suits, masks, visors and two pairs of rubber gloves. Details of additional protective equipment are given in the Addendum.

The body is placed supine on the table with the neck supported on a block so that
the head does not project beyond the end of the table. The table beneath the head is covered with impermeable material such as a sheet of polythene which is then covered by an absorbent pad (fig 1). The necessary tools which are to be used in the necropsy are gathered on the absorbent pad. These include scalpel, T-chisel, electric saw, mallet, dura stripper, forceps and scissors (fig 1).

The scalp is incised and reflected in the usual way and the skull is prepared for the application of the saw (fig 2). A large, clear, polythene bag is placed over the head of the cadaver and secured with string around the neck so that quite a quantity of air separates the inside of the bag from the surface of the skull (fig 3). The electric saw is then introduced through a hole in the top of the bag which is sealed around the neck of the saw as far back as possible, but not enclosing the air vents further back on the shaft. This arrangement should allow enough movement of the saw blade within the bag so that it can be applied easily at any point around the circumference of the skull. Keeping the bag clear of the blade when it is switched on, the skull cap is drilled in the usual way. All the bone dust collects at the base of the bag. When this stage has been completed, the necropsy saw is removed through the hole at the top of the bag and this hole is resealed. The necropsy saw is laid down on the absorbent pad (as are all other instruments before and after use).

With the polythene bag still in place over the head, the skull cap is removed using T-chisel, mallet, and dura stripper introduced through small incisions on the superior surface of the bag (figs 4 and 5). The skull cap falls to the bottom of the bag.

The polythene bag may now be removed, handling with care because it contains bone dust and blood (fig 5). The skull cap is retained on the absorbent pad (fig 6).

The dura is incised and reflected from the surface of the brain. At this stage, a specimen of cerebrospinal fluid may be aspirated from
the third ventricle and tissue for freezing removed from the frontal lobes and from the cerebellum. These should be placed directly in universal containers labelled with warning of hazard and with patient identification. The brain is subsequently removed in the usual way (fig 6) and placed directly into a pre-weighed container of 10% formalin which is similarly labelled (fig 7). The container is handled by a clean assistant who brings it to the necropsy table. The container is sealed and weighed again to determine brain weight. Finally, the pituitary gland is removed and fixed in formalin. Phenol should not be added to the formalin as it has been shown to be ineffective in decontamination.15

The body is reconstituted in the usual way by packing the skull cap with cotton wool and replacing it before the scalp is sutured.

If desired, the body cavities may be opened and the organs examined as usual, with tissue sampling for histology. Care should be taken, as before, to avoid contamination of the mortuary environment. The organs should be examined on the necropsy table, or possibly in situ in the body cavities. Large absorbent pads with impermeable backing should be in place under the cadaver.

Great care should be taken to avoid cuts and needle stick injuries, particularly from contact with sharp bony edges, and during sewing up.

POST-NECROPSY PROCEDURE

All instruments apart from the necropsy saw are gathered from the absorbent pad into a large stainless steel dish, wrapped, and steam autoclaved at 136°C for 1 hour, after which they may be cleaned by routine methods. The necropsy saw is cleaned by wiping repeatedly with 2N sodium hydroxide solution. The absorbent pad and impermeable table cover, together with all disposable clothing, are double bagged for incineration. After removal of the body, the table and necropsy suite are cleaned in the usual way. No special precautions are needed because the surfaces have not been contaminated. However, if contamination is suspected, a solution of 2N sodium hydroxide should be used for cleaning surfaces by repeated wetting over 1 hour. The recommended dilution of chlorine solution for decontamination (20 000 ppm of free chlorine) is highly unpleasant to use and corrosive to steel.

The fixed brain can be stored safely in 10% formalin, in a box and an outer polythene bag, pending histological study. Samples for freezing should be double bagged and stored at −70°C. Notification of the necropsy to the Edinburgh Creutzfeldt-Jakob disease Surveillance Unit (see below) will be followed by collection of the specimens and, in due course, return of a full pathology report.

Any tissue blocks from non-central nervous system tissues may be decontaminated for routine microtomy by immersion for 1 hour in 96% formic acid, after formalin fixation and before processing.17

Discussion

This method of containment for removal of infective necropsy brain tissue within a polythene bag has been recommended in the past for AIDS cases where specialist pathology suites were not available. It is equally suitable for cases of suspected Creutzfeldt-Jakob disease and is quite straightforward to undertake. It is hoped that use of this method would help to alleviate anxiety among pathology staff when confronted with cases of Creutzfeldt-Jakob disease and would allow the necropsy examination to proceed. Although spread of this disease is not thought to occur through contact with blood or bone, and the main risk remains inoculation, it is clearly wise to limit contamination of staff and mortuary, which is why we recommend use of a polythene bag during skull removal. The relative risk of potential infectivity is lower in non central nervous system tissues apart perhaps from spleen and lymphoid tissue, and examination of the whole body
may be thought desirable at necropsy, to
establish the cause of death.
Creutzfeldt-Jakob disease is a rare disorder; previous epidemiological studies have sugges-
ted an incidence of around 0.5–1/million
population worldwide. Although a few cases
of Creutzfeldt-Jakob disease have been re-
ported in laboratory technical staff, and
very recently in a pathologist, epidemi-
ological studies have repeatedly failed to
demonstrate an excess incidence of
Creutzfeldt-Jakob disease in health care
workers and post mortem room staff. In the
United Kingdom, the theoretical risk of trans-
mission of the BSE agent to humans via the
food chain might result in an illness similar to
Creutzfeldt-Jakob disease, hence the need for
a long-term national prospective survey of
human spongiform encephalopathies. The
need for necropsy examination of (at least)
the brain in suspected cases is of paramount
importance for diagnostic verification and
research, particularly in relation to cell
pathology, molecular biology, and transmissi-
bility. We hope that the work of the National
Creutzfeldt-Jakob disease Surveillance Unit
will continue to be supported by histopathol-
ogists, neuropathologists, and their mortuary
and laboratory technical staff throughout the
United Kingdom, on whose cooperation this
project depends. Without this sort of help the
study will not be successful and any possible
hazards of BSE to human health will remain
undetected.

The need for histological studies in sus-
pected cases of Creutzfeldt-Jakob disease may
pose further difficulties in relation to tissue
handling in routine laboratories. The agent is
classified as a category 2 pathogen, for which
appropriate containment facilities are re-
quired. Furthermore, special precautions are
required in relation to tissue sectioning, the
disposal of contaminated laboratory fluids, and
decontamination of equipment and work
surfaces. These restrictions make it impracti-
cable for many laboratories to process and
section Creutzfeldt-Jakob disease tissue, in
which case the National Creutzfeldt-Jakob
disease Surveillance Unit will arrange the col-
lection, examination, and reporting of such
material on request. Small non-central ner-
vous system tissue blocks which do not
require further trimming may be easily
decontaminated by immersion in formic acid
and processed routinely.

For further details of the National
Creutzfeldt-Jakob disease Surveillance Project
and for copies of necropsy protocols and tis-
ue handling, please contact Miss J Mackenzie (the
Unit Coordinator) at Creutzfeldt-Jakob disease Surveillance Unit,
Old Pharmacy Building, Western General
Hospital, Tel: 031 332 2117.

Addendum

NOTE ON PROTECTIVE CLOTHING AND
EQUIPMENT
Disposable clothing is now readily available in
necropsy suites. As an extra precaution
against cutting injury, a pair of chain mail
gloves can be worn between double rubber
gloves (fig 8). These are surprisingly flexible
and convenient to use but do not prevent
needle stick injuries and they are expensive
(Suppliers—Arco, PO Box 21, Waverley St.,
Hull HU1 2SJ. Tel: 0482 27678).

Because the polythene bag restricts the
amount of aerosol and reduces the risk of
splash during necropsy, the need for eye and
respiratory tract protection is minimised.
However, the use of a visor is recommended
during any neuropathological necropsy. If
further safeguard is desired, a ventilated visor
should be considered. These are light and
comfortable to wear, although bulky, and
provide a filtered stream of air over the face,
(Suppliers—Pureflo Safety Ltd., Moat
House, Wheathampstead, St. Albans, Herts.
AL4 8QT. Tel: 0582 834242).

A necropsy saw, with detachable auto-
clavable head, is now available which is
entirely suitable for all necropsy needs and is
particularly suited for use in possible
Creutzfeldt-Jakob disease cases. (Suppliers—
Mercian Surgical Supply Co. Ltd., 10
Wolverhampton Road, Warley, Birmingham
B68 OLH. Tel: 021 429 1133). A different
model, the Medezine Swordfish (Suppliers—
Alfred Cox (Surgical) Ltd, Edward Road,
Coulson, Surrey, CR5 2XA. Tel: 081 668
2131) has an advantage in that it can be
attached to an extra filtration unit, thus
reducing the amount of aerosol. However, the
Swordfish is not autoclavable and, being of
bulky construction, is less convenient when
removing spinal cords.

Figure 8 Additional hand protection is afforded by the
use of chain mail gloves worn between two pairs of rubber
gloves. These protect against cuts and grazes but not
needlestick injuries.

We are grateful to colleagues from all over the United
Kingdom who have gone to a great deal of trouble to notify us
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