Case report

Forensic Diagnosis of Sudden Death due to Pyogenic Meningitis

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Abstract

Acute bacterial meningitis remains a major cause of mortality and long term neurological sequelae worldwide. Despite of availability of potent antibiotic the mortality rate due to acute bacterial meningitis remains significantly high in India and other developing countries. There is a need for periodic review of bacterial meningitis worldwide, since the pathogens responsible for infection vary with time, geography and patient’s age.

We are reporting a case of 40 years old married male who became unconscious suddenly with history of fever since last one day. There was no history of any major illness. He was died in hospital under suspicious condition within 12 hours of hospitalization. Forensic experts finally gave the opinion that the death was natural and it was due to pyogenic meningitis after considering autopsy findings, histo-pathological findings and microbiological and biochemistry reports. Klebsiella pneumoniae was responsible for acute pyogenic meningitis.

Key Words: Sudden Death, Meningitis, Bacteremia, Pyogenic

Introduction:

Sudden or unexpected deaths occur from unnatural causes, such as violence or poison, as well as from natural causes. Unnatural deaths have always to be investigated by the police, but very often natural deaths form the basis of investigation form the basis of medico-legal investigations, if they have occurred suddenly in apparently healthy persons and under suspicious circumstances. Definition of sudden death is variable. It is based on the interval between the onset of symptoms and death. In sudden death, time interval varies any where from 1-24 hours. [1]

Meningitis is an inflammation of the covering of the brain, spinal cord. This results in unconsciousness, seizures, raised intracranial pressure, and stroke. Involvement of pia and arachnoids matter is called “leptomeningitis” and for dura “Pachy meningitis” is used. In pyogenic meningitis the pathogens enter in cerebrospinal fluids. Pyogenic meningitis continues to be a formidable illness with high morbidity and mortality in India. Gram positive cocci and gram negative bacilli have been incriminated as bacterial etiological agents of pyogenic meningitis in various studies. [2]

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The most recent meningococcal meningitis epidemic began in 1996 and has resulted in more than 300,000 cases and 30,000 deaths had been reported to the World Health Organization. [3] Apart from epidemics, at least 1-2 million cases of bacterial meningitis are estimated to occur each year and of which 135,000 were fatal. [4] These numbers have made bacterial meningitis a top-ten infectious cause of death worldwide.

Total 43 bacteria were isolated from 7759 clinically suspected cases of meningitis. Pseudomonas aeruginosa was the most common isolate followed by Klebsiella pneumoniae, Acinobacter spp, Streptococcus pneumoniae, Neisseria meningitidis, Streptococcus pyogenes, Enterococcus spp, and other Streptococcus spp which were found to be responsible for pyogenic meningitis. [5]

The etiological agents of community acquired meningitis may differ from hospital acquired meningitis. Delay in diagnosis and initiation of treatment can result in poor outcome of the disease. [6] Since clinical signs and symptoms can not be always relied upon, laboratory support is imperative to achieve early diagnosis. As a result of emergence of antimicrobial resistance being reported, recommendations for therapy are changing. Laboratory surveillance of isolates is crucial to identify targets for formation of rational empirical treatment for fatal bacterial meningitis.

Case History:
A 40 year old adult male, resident of Surat, Gujarat became unconscious in his house on 6th May 2009, 12:50 pm with history of mild to moderate fever since last one day. He had been well prior to this and had not suffered from any medical illness.
Immediately he was shifted to the New Civil Hospital, Surat by his neighbor in ambulance. General treatment was started by Casualty Medical Officer in Emergency ward and admitted in the hospital. On the same day at 11:30 pm, suddenly he collapse and died inspite of using life saving drugs. In this case, treating doctor could not give the cause of death. He informed the concerned police station stating that patient had died in suspicious circumstances within 24 hours of admission.

On 7th May 2009, police made an inquest and requested to conduct postmortem examination in the Department of Forensic Medicine & Toxicology at Surat Municipal Institute of Medical Education and Research (SMIMER), Surat to find out exact cause of death as it became a medico-legal case due to sudden death under suspicious condition.

During post mortem examination, following findings were observed:

**External Findings:**
- Body was moderately nourished
- Rigor mortis present all over the body in strong form.
- Post mortem lividity present on back of the body except pressure areas.
- No abnormal discharge came out from mouth, nose and ear.
- No evidence of any injury was found over the body.
- Injection mark of size 0.1cm x 0.1cm present over the dorsum of the right hand.

**Internal Findings:**
- Brain was edematous and congested. Meninges congested, yellow color exudates found in the subarachnoid space.
- Frank pus collection was found in the subarachnoid space of the cerebellum
- Pleura was adherent to the chest wall at places.
- Both lungs were congested, edematous and adherent to the chest wall at places.
- Coronaries were patent and heart valves were normal.
- All organs were congested.

**Photograph No. 1**
Yellow color exudates seen under the subarachnoid layer

**Photograph No.2**
Frank pus collection in subarachnoid space

Viscera for histo-pathological examination and CSF for routine and microscopical examination were sent the Pathology Department of SMIMER, Surat. Blood for culture and sensitivity and CSF for bacteriological examination were sent to the Microbiology Department. Sample of CSF was also sent to the Biochemistry Department for sugar and protein level.

Cause of death was kept pending for histo-pathological, microbiological and biochemistry reports.

**Histo-Pathological Report:**
Brain showed inflammation of leptomeninges and contain neutrophils and fibrins. Subarachnoid space had congested blood vessels and infiltration of polymorphonuclear leucocytes. Brain parenchyma showed mild congestion. CSF was yellowish in color, turbid and reaction was acidic. On cytological examination of CSF, total cells 40-50/ c.mm, polymorphs 80% and lymphocytes 16%.

**Photograph No.3**
Acute Inflammatory Infiltrate (Polymorphs) In Subarachnoid Space of Brain

**Photograph No.4**
High Power View of Pyogenic Meningitis
Congestion (Dilated Blood Vessels with RBCs) With Severe Acute Inflammation

Microbiology Report:

Blood culture showed growth of Klebsiella species which were sensitive to ceftriaxone, chloromphenicol, ciprofloxacin, cotrimoxazole and gentamycin. Bacteriological examination of CSF showed Klebsiella organism.

Biochemistry Report:

Chemical examination of CSF showed protein 150 mg/dl, glucose 5mg/dl, chloride 160 mEq/L and Pandy’s test was positive. After considering autopsy findings, histo-pathological findings, microbiological and biochemical reports, finally cause of death was given as pyogenic meningitis.

Discussion:

The term “sudden” has no agreed universal definition. In the material for the various studies, the duration of the death process has ranged from 1-24 hours, but it is difficult to determine exactly how long fatal symptoms have been present, as death often occurs before the victim reaches hospital. In such circumstances no data on the symptoms are available for want of eye witnesses. Sudden unexpected death in children and young adults due to undiagnosed natural process is extremely uncommon and can prove a diagnostic challenge to the practicing forensic pathologist.

Forensic pathologists routinely certify death certificates in case of sudden, unexpected deaths. Because of the broad scope of this casework, medical examiners inevitably investigate rare diseases that culminate in death. There are many causes of sudden deaths like coronary artery disease, myocarditis, valvular heart disease, pulmonary Koch’s, pneumonia, COPD, pyothorax, atelectasis, intracerebral and subarachnoid hemorrhage, meningitis, encephalitis, brain abscess and infarct, cirrhosis of liver, hepatitis, fatty liver, preeclampsia, liver abscesses, puerperal abscess etc. [7]

Bacterial meningitis is the most common form of suppurative intracranial infection, with an annual incidence >2.5 cases/100,000 population. The epidemiology of bacterial meningitis has changed in recent years. Currently, the organisms most commonly responsible for community acquired bacterial meningitis are Streptococcus pneumonia (~50%), Neisseria meningitidis (~25%), group B streptococci (~10%), and Listeria monocytogenes (~10%). Haemophilus influenzae was once the most common cause of bacterial meningitis in United States. [8]

The CNS is protected against blood-borne pathogen invasion by an effective blood-brain / CSF barrier and by an external covering of meninges and skull. Thus, the effective CNS pathogen needs either a defect in the external barrier (e.g. purulent mastoiditis, post-traumatic or post-neurosurgical dura leak) or must run a biological gauntlet of host defenses to gain access to the CNS. Effective invasion of the CNS involves multiple interactions between the pathogen and the host that sequentially result in mucosal colonization, invasion into, and survival within the intravascular space, and traversal of the blood-brain/CSF barrier.

Sustained (high-grade) bacteraemia is thought to be necessary, although not sufficient, for microbial entry into the subarachnoid space [9]. To invade the meninges, the blood-borne pathogen must cross the physiological barriers between the bloodstream and the CNS. Two different structures separate the bloodstream from the CNS: the blood-brain barrier and the blood-CSF barrier.

Meningitis can present as either an acute fulminant illness that progress rapidly in a few hours. The classic clinical triad of meningitis is fever, headache, and nuchal rigidity (“stiff neck”). Each of these signs and symptoms occurs in >90% of cases. Alteration in mental status occurs in 75% of patients and can vary from lethargy to coma.

Nausea, vomiting, and photophobia are also common complaints. Focal Seizures are usually due to focal arterial ischemia or infarction. Rashes and raised intracranial pressure are also seen in bacterial meningitis. Nuchal rigidity is the pathognomonic sign of meningeal irritation and is present when the neck resists passive flexion. Kernig’s and Brudzinski’s signs are also classic signs of meningeal irritation.[8]

Clinical and neuropathological studies have clearly shown that a fatal outcome of the disease is often caused by neurological complications secondary to bacterial meningitis (e.g. cerebral ischemia, brain oedema formation, hydrocephalus, or increased intracranial pressure).

During the past 15 years, significant changes were seen in the epidemiology of acute bacterial meningitis. The most important change is the marked decline in the incidence of meningitis due to Haemophilus influenzae in countries that have introduced programs for the immunization of infants with conjugate Hib vaccines, especially in North America and western Europe. [10] In these countries,
Streptococcus pneumoniae and Neisseria meningitidis are the most common causes of acute bacterial meningitis, and bacterial meningitis is now a disease predominantly of adults rather than of infants and children. Additional risk factors include coexisting acute or chronic otitis media, alcoholism, diabetes, splenectomy, hypogammaglobulinemia, complement deficiency, and head trauma with basilar skull fracture and cerebrospinal fluid rhinorrhea. Most developing countries, however, have not added the Hib vaccine to their routine childhood immunization programs. Consequently, an estimated 350,000–700,000 children are worldwide still die from invasive Hib disease each year.

Another epidemiological trend is the emergence of antimicrobial resistance among pathogens causing acute bacterial meningitis. The increasing rate of resistance to penicillin and other beta-lactam antibiotics is of particular importance for the clinical management of meningitis.

The clinical outcome of acute bacterial meningitis varies according to socioeconomic aspects (developed or developing countries), age, and the causative pathogen.[1] In developed countries, S. pneumoniae meningitis has the highest case-fatality rate (about 20%) for community-acquired meningitis.[10] Of the survivors, up to 30% develop long-term sequelae including hearing loss, neurological deficits, and neuropsychological impairment. [12] In the elderly, an unfavorable clinical outcome is markedly more frequent than in children; the case fatality rate among older adults is about 40%. This adverse outcome may be attributable to pre-existing underlying diseases.[13] In developing countries mortality and morbidity rates are dramatically higher than in industrialized countries. About 50% of children with pneumococcal meningitis die while in hospital and up to 60% of survivors have clinical sequelae, whereas the mortality and morbidity rates of this age group in industrialized countries are about 10% and 30%, respectively.[14]

The spectrum of causes of deaths attributed to meningitis is known to be broad, ranging from systemic (e.g., septic shock) to several neurological complications (e.g., brain oedema, hydrocephalus, cerebrovascular involvement, and intractable seizures). Histopathological studies document a wide spectrum of brain injury associated with bacterial meningitis in human beings, including vasculitis, focal necrosis of cortical neurons, apoptotic neuronal cell death in the dentate gyrus, and a loss of myelinated fibres in the subcortical white matter, cerebellum, and brainstem. [15]

One hundred and thirty five cerebrospinal fluid (CSF) samples from children clinically diagnosed pyogenic meningitis (in and around Ahmedabad) were subjected to physical, bacteriological, cytopathological and biochemical examinations. It was found that all CSF specimens, were turbid, the culture positivity varied form 12.12 to 56%. The highest percentage was found in children of less than one year of age. The average percentage of culture positivity was 28.68%. The result of gram stain was more than that of cultural examination. Gram stain of CSF was specific, accurate and highly valuable in the diagnosis of pyogenic meningitis. Among gram positive organisms isolated, Staphylococcus aureus was highest (8.8%) followed by Diplococcus pneumoniae (3.7%), but Klebsiella was predominant (6.6%) among gram negative bacilli. Staph. aureus was 100% sensitive to erythromycin, gentamycin, kanamycin. The results of cytopathological and biochemical tests correlated (67.1%). There was increase in polymorphs and protein, sugar levels decreased. [16]

In case of sudden and unexpected deaths, it is difficult task for the forensic experts or medical officer to find out the cause of death. In case of identified bodies, proper history about illness from relative, duration of emerging signs and symptoms, any documentation from treating hospital are the basic keys for solving the puzzle of sudden death. Only external and internal examination of dead body are not sufficient for giving cause of death in sudden death, appropriate samples from the deceased should be taken for pathological, microbiological and biochemical examination to rule out certain disease.

Laboratory investigations of CSF sample in suspected acute meningitis is extremely important for prompt recognition of the nature of the infecting organism as management and therapy of the patient depend on this information and for labeling the sudden death case according to the disease after post mortem examination. Another test of value is the raised levels of C-reactive protein in CSF of patients with bacterial meningitis as opposed to viral meningitis. [17]

From forensic point of view, if any case of sudden death comes with the history of fever, headache, seizure and altered consciousness should be investigated properly by forensic expert after keeping the possibility of cerebral malaria, bacterial or viral meningitis, brain abscess, Subdural or epidural empyema and subarachnoid hemorrhage in mind. The post mortem findings should be corroborated with laboratory investigations before giving the cause of death.

**Conclusion:**

In case of sudden death, Forensic Pathologist or medical officer cannot presume the exact cause of death by partial or limited post mortem examination such as, “chest only”, “abdomen only” or “excluding the brain.” Complete autopsy in combination with medical history, clinical course of
any pre-existing disease before death, imaging data, laboratory findings, and bacterial culture are valuable to give the exact cause of death.

References: