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LUPUS CEREBRITIS: A FATAL DISEASE

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Abstract:
The reported prevalence of systemic lupus erythematosus (SLE) in the general population is 20-150 cases per 100,000 population. The female to male ratio ranges from 7-15:1. An estrogen effect has been suggested by a number of observations for this difference. Presenting a case of subarachnoid haemorrhage that was labelled as lupus cerebritis but the delay in presenting to the hospital caused the patient to suffer leading to death. A vigilent eye of the physician is required to maintain a strong index of suspicion, as it is generally missed and patients land up at late stages, which is invariably fatal.

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INTRODUCTION:

Systemic Lupus Erythematosus (SLE, lupus) is the most commonly recognized and well-studied neurological manifestations among the Collagen Vascular Diseases [1]. SLE affects multiple organ systems in women nine times more frequently than men. The prevalence is approximately 130/100,000 in the United States, with African Americans, Hispanics and Asians more frequently affected than Non-Hispanic Whites [2]. Neuropsychiatric lupus (NPSLE) manifestations can occur in the absence of either serologic activity or other systemic disease manifestations [3]. Approximately 28%–40% of NPSLE manifestations develop before or around the time of the diagnosis of SLE [4]. Estimates of the prevalence of NPSLE have ranged from 14% to over 80% in adults [5] and 22%–95% in children [6].

We present a case of subarachnoid haemorrhage that was labelled as lupus cerebritis and nephritis according to American Rheumatism Association (ARA) criteria, which needs a minimum of four of 11 points to be fulfilled for the diagnosis, but due to the delay in diagnosis & treatment the patient couldn't survive.

CASE PRESENTATION:

An 18 year old young, unmarried, non-smoker, non-addict female,with no known pre morbids was being referred from a peripheral hospital to holy family hospital rawalpindi. She was received in medical ER of holy family hospital at 3 am with GCS 8/15, on ambulatory bag. At that time BP 110/90, temperature 105 and BSR :132 were recorded. Patient was retained in ER and was managed on lines of SAH, malaria, cerebral infection

Patient had history of fever and headache from 2 days along with vomiting, Shortness of breath and general tonic clonic fits from 1 day.

Patient was in her usual state of health 2 days back when She started having frontal headache which was sudden in onset, moderate in intensity and relieved on its on within 2-3 minutes. Next day patient developed general tonic clonic fits which were sudden in onset, associated with up-rolling of eyeballs and frothing from mouth. however, there was no history of fecal or urinary incontinence. Seizures remained for 20-30 minutes. Past medical and surgical history of patient was unremarkable.

Patient was immediately brought to nearby district hospital. In hospital she experienced 6-5 episodes of GTC fits with 4-5 episodes of vomiting after which she aspirated and became tachypnic. she was intubated and referred to holy family hospital on ambulatory bagging after being given emergency medication. Ct scan done at district hospital was blurred due to repeated fits hence any diagnosis could not be made.

CT scan was repeated in holy family hospital that suspected subarachnoid haemorrhage and brain edema. During night patient experienced 3-4 episodes of GTC fits. Patient was shifted to medical ICU on ambulatory bag with GCS of 6/15, bilateral pinpoint pupils reactive to light, temp :105 BP:108/60PR:108 CVP:12cm respiratory effort present SPO2 :98% with 10L oxygen. She was put on ventilator with PEEP of 05

On examination patient was tachypnic with raised temperature (102F). On CNS examination patient had GCS of E1V7M2 (sedated and relaxed). Pupils were bilateral pinpoint, neck stiffness was negative, planters were mute B/L

Respiratory examination revealed right sided decreased air entry at base and
Left sided course crackles over base. Genitourinary was cola coloured urine.

CNS and GIT examination was unremarkable. CT scan was repeated after 4 days and it was unremarkable. EEG was also normal. Echo shows ejection fraction of 60%. However, ultrasound indicated bilateral parenchymal disease along with mild pleural effusion. All labs were normal except raised CRP and ANA profile that showed homogenous pattern being associated with SLE and rheumatoid arthritis

On the basis of history, examination and investigations, diagnosis of lupus cerebritis and nephritis was made and patient was treated accordingly.

Unfortunately, the patient was at such stage that he couldn't survive despite of modern techniques available and being put on ventilatory support.

DISCUSSION:

Prompt identification of Lupus-Cerebritis is extremely difficult and challenging. There is no definitive laboratory or radiological test to confirm a possible diagnosis. Assessment of the clinical features with presence of antibodies in the serum and CSF are necessary to conclude diagnosis [7]. The basic pathological response in SLE is loss of the normal control mechanism of the immune system, having increased plasma levels of complement

breakdown products (C3a, C3d) and the formation of immune complexes in the tissues is precipitated by an enhanced complement system. The Circulating auto-antibodies formed due to the recruitment of B-lymphocytes may be present in the system even before presentation of the complete clinical picture of SLE [8].

Due to the absence of a functional alternative complement pathway, lupus cerebritis can be alleviated. Such experimental findings have prompted researchers to suggest different neuroprotective approaches to SLE treatment. The alternative pathway might serve as a therapeutic target for Lupus Cerebritis, as it is the key mechanism through which complement activation occurs in the brain [9-10]. The anticardio lipinanti bodies can cause endothelial damage, platelet aggregation, inflammation & fibrosis collectively called as pathological changes, while the lupus antibody prolongs the coagulation process. Various manifestations of stroke-like disorders such as pulmonary emboli, miscarriage, thrombocytopenia, and arterial or venous thrombi, are seen in 30 to 50% of the SLE patients [7].

A CSF study can indicate the possibility of CNS involvement in SLE by the presence of pleocytosis and also shows high protein levels in patients with Lupus-Cerebritis [11-12]. CSF of Lupus-Cerebritis patients may have significantly higher Interleukin-6 and interferon alfa. Researchers have suggested that The presence of nitrates or nitrites in CSF could be used to monitor the progression of Cerebritis, as researchers have suggested that the neuron-reactive autoantibodies or lymphocytotoxic antibodies (LCAs) are seen in the CSF of 80% of the Lupus Cerebritis cases [13-14].

In the study that included 1378 patients with SLE, with a median follow-up of 6.1 years, 118 patients died (8.6%). The overall cumulative probability of survival after disease diagnosis at 5, 10, 15 and 20 years was 95%, 91%, 85% and 78%, respectively. Based on a multivariate model, age at SLE diagnosis >50 years (hazard ratio = 5.9; P <0.001) and male gender (hazard ratio = 2.4; P = 0.004) were associated with poorer survival [15]. In 1999, the SLE patient database at the rheumatology clinic, St. Luke's Hospital, it was seen that serositis was the initial manifestation at presentation [16].

There is still an ongoing search for any specific antibody marker(s) as a gold standard for routine laboratory diagnosis, for neuropsychiatric lupus [14]. Computed tomography scans in Lupus-Cerebritis may show variable features like normal brain or cerebral atrophy, calcification, infarcts, intracranial hemorrhage, or subdural fluid collection [13], as used in our case but MRI is a more sensitive diagnostic tool for Lupus-Cerebritis [11].

A review performed on the progression of the disease found that the disease is more severe in women above 40 years of age, male patients and in those with late-onset lupus [17] but in our case patient was young. Also, there is an increased incidence of thyroid disease in patients with SLE [18].

As the general condition of the patient waxed and waned with the natural course of the disease, we failed to get a response from treatment, and the scenario became complicated with super-added infections and iatrogenic complications. Unfortunately, it was too late when an indication was available and the diagnosis was made.

CONCLUSION:

A vigilent eye of the physician is required for the timely diagnosis. Unless we maintain a strong index of suspicion, the disease is generally missed and patients land up at late stages, which is invariably fatal. Neurological involvement can worsen the prognosis of the disease therefore Lupus-Cerebritis should always be included in the provisional diagnosis, in order to avoid delay in diagnosis and loss of valuable time

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