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Encephalitis in Elderly Population

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1. Introduction

The elderly population is increasing worldwide. Population of people above 65 years old was 420 million in the year 2000, and is estimated to be 973 million in 2030 (Centers for disease control and prevention [CDCP], 2003). Mortality rate related to infectious diseases decreased after the discovery of antibiotics, particularly in the second half of the twentieth century, however it is still being a problem in elderly age group.

Several immun alterations arise with aging and these alterations make elderly people more vulnerable to infections. In addition, body composition changes with aging, chronic diseases such as hypertension, diabetes mellitus and cardiac failure are more frequent in elderly age group, so this multi-factorial situation also reduces the immunological resistance to infections. For all these reasons, encephalitis is more frequent in elderly people as compared to younger individuals and it usually causes clinically a more severe course.

Encephalitis in elderly deserves a more sensitive approach. The disease may be difficultly perceived by clinicians for some reasons. Premorbid brain disorders such as dementia and stroke especially, may lead to diagnostic delay. Numerous co-morbid situations in this age group may lessen the efficiency of treatment and may bring about secondary problems. Therefore encephalitis in elderly may result in severe central nervous system damage, high morbidity and mortality.

2. Etiological agents

Defined etiological agents in elderly encephalitis are not fairly different than those in younger patients. However frequency of encephalitis caused by some pathogens and disease severity is dissimilar in elderly age group

Herpes simplex virus is the main cause of encephalitis in adult population including individuals above 60 years old (Lee et al., 2003). However herpes simplex encephalitis is dramatically frequent in aged population (Hjalmarsson et al., 2007). The incidence of the disease is significantly higher in population above 60 years as compared to 3-60 age group (Puchhammer-Stöckl et al., 2001). In addition, clinicians encounter herpes simplex type 1 as the main etiological agent of elderly herpes simplex encephalitis, that is similar to ratios defined in other age groups (Jouanny et al., 1994).

Besides herpes simplex, viral and bacterial, lots of agents have been reported as a cause of elderly encephalitis. Some of these agents are associated with regional/geographical factors,

and a portion with immunological status of patients. West nile virus (WNV) is a considerable etiological agent in aged population as the encephalitis caused by west nile virus is more frequent and more severe in elderly people as compared to younger adults (Berner et al., 2002, 2005, Cook et al., 2010, Roos, 2005). Elderly cases related to St. Louis encephalitis virus (Roos, 2005), Tick borne encephalitis virus (Logar et al., 2000), enteroviruses (EV) (Frantzidou et al., 2008), Ebstein Barr virus (EBV) (Hu & Chan, 2000), Varisella zoster virus (VZV) (Granerod et al., 2010, Gillanders et al., 1994) and Cytomegalovirus (CMV) (Lee et al., 2003) have been reported as far. Encephalitis caused by mycobacterium tuberculosis (Granerod et al., 2010, Lee et al., 2003) and other bacterial agents (Granerod et al., 2010) have also been defined in this age group. Etiological spectrum of elderly encephalitis is shown on Table 1.

HERPES SIMPLEX	West Nile Virus	UNDEFINED ETIOLOGY
	Ebstein Barr virus	
	Cytomegalovirus	
	Herpes Zoster	
	Enterovirus	
	Tick Borne Encephalitis	
	Mycobacterium Tuberculosis	
	Japan Encephalitis	
	St. Louis Encephalitis	
	Other bacterial agents	

Table 1. Etiological spectrum of elderly encephalitis

As the clinical utilization of serological methods and PCR technique become widespread, number of etiological agents in elderly population is increasing. However, it should be borne in mind that, cases with undefined etiology is more frequent in elderly age group as compared to younger adults (Lee et al., 2003).

3. Immune alterations

It is claimed that immune system progresively deteriorates with aging and elderly people are more vulnerable to infectious diseases (Sansonì et al., 2008). Several changes occur in immunity system of elders. The major proportion of these changes are involved in the quantity and the configuration of circulating lymphocytes. Numerical changes appear both in T cell and B cell compartments, thus effectiveness of cellular and humoral responses alter. The most prominent immune alteration is occured in T cell comparment. Response of T cells to mitogens weakens and T cell quantity in circulation decreases (Fahey et al., 2000). It is indicated that both circulating CD 4 (+) and CD 8 (+) T cells diminish with aging (Provinciali et al., 2009). Quantity of CD 4 (+) T cells is proportionally higher in normal immunity, however inverted CD 4 (+) / CD 8 (+) ratio (less than 1.00) is significantly more frequent in elderly individuals as compared to younger individuals (Wikby et al., 2008). Inverted ratio is reflecting the dominancy of suppresor activity in elderly age group. Similar numerical changes have also been occured in B cell compartment. Quantity of CD 5 (+) and CD 19 (+) B cells lessens with aging (Sansonì et al., 2008). Besides the changes in cellular level, several alterations appear in cytokin synthesis, which IL-6 levels increase and IL-2 levels decrease in aged individuals (Lesourd & Mazari, 1999). Immune alterations of elderly is shown on Table 2

As a consequence of age related immune alterations, antibody production diminishes and immunological memory shortens (Fahey et al., 2000). Immunologic response to antigens weakens, infections tend to be frequent and heavier with increased age.

T Cells CD 4 (+) Reduction CD 8 (+) Reduction Inverted ratio of CD 4 (+)/CD 8 (+) Suppressor activity
B Cells CD 5 (+) Reduction CD 19 (+) Reduction
Cytokines IL-6 increase IL-2 decrease

Table 2. Immune alterations in elderly age group

Several clinical and laboratory observations concordant with the above mentioned immune alterations in increased age are present in the literature. These observations are related especially with the infections caused by viral etiology and closely linked with the pathogenesis of encephalitis. For instance, skin infection of herpes zoster is more frequent in aged population (Schmader & Dworkin, 2008) and with situations which impair cellular immunity (Schmader, 1999). Latent Herpes simplex virus existence in trigeminal ganglion is significantly more frequent in elderly individuals as compared to younger adults, which is concordant with the fact that herpes simplex encephalitis frequency is higher in aged population (Liedtke et al., 1993). This data is reflecting the poor immunological response to herpes simplex virus with increased age. (Figure 1)

It is considered that insufficient pleocytosis and low IgG activity in a case with herpes simplex type 2 encephalitis, is associated with age related immune dysregulation (Reuter et al., 2007). Another clinical observation is the high frequency of re-infection or endogen virus activation in elderly herpetic meningoencephalitis as compared to primary infection (Jouanny et al., 1994), which may also reflects the age related immune alterations.

Furthermore, chronic diseases are seen more frequently in elderly population and some of these diseases lessen the immunological resistance to antigens. Immune alterations related to both aging and underlying chronic disorders make elderly people more vulnerable to infectious disorders and complications of infections (Yoshikawa, 2002). For instance essential hypertension and diabetes mellitus presence are found to be associated with the severity of west nile virus encephalitis, moreover they were reported as risk factors for persistancy of symptoms in elderly patients (Cook et al., 2010)

As concordant with the data about immunity alterations in elderly individuals, herpes simplex encephalitis is seen more frequently in elderly age group, makes a more severe clinical course, and mortality is significantly higher in individuals above 70 years old (Hjalmarsson et al., 2007). Increased age is found to be associated with the outcome of herpes encephalitis (Whitley et al., 1986, Kamei et. al., 2005). Also west nile virus leads to a more severe clinical course in elderly patients as compared to younger adults (Cook et al., 2010, Berner et al., 2002). Increased age is an independent risk factor for fatality of west nile

virus encephalitis (Berner et al., 2002). Such that mortality in patients above 70 years old increases 40-50 fold, as compared to younger patients (O’Leary et al., 2002). Also Tick borne encephalitis makes a more severe clinical course in elderly age group (Logar et al., 2000).

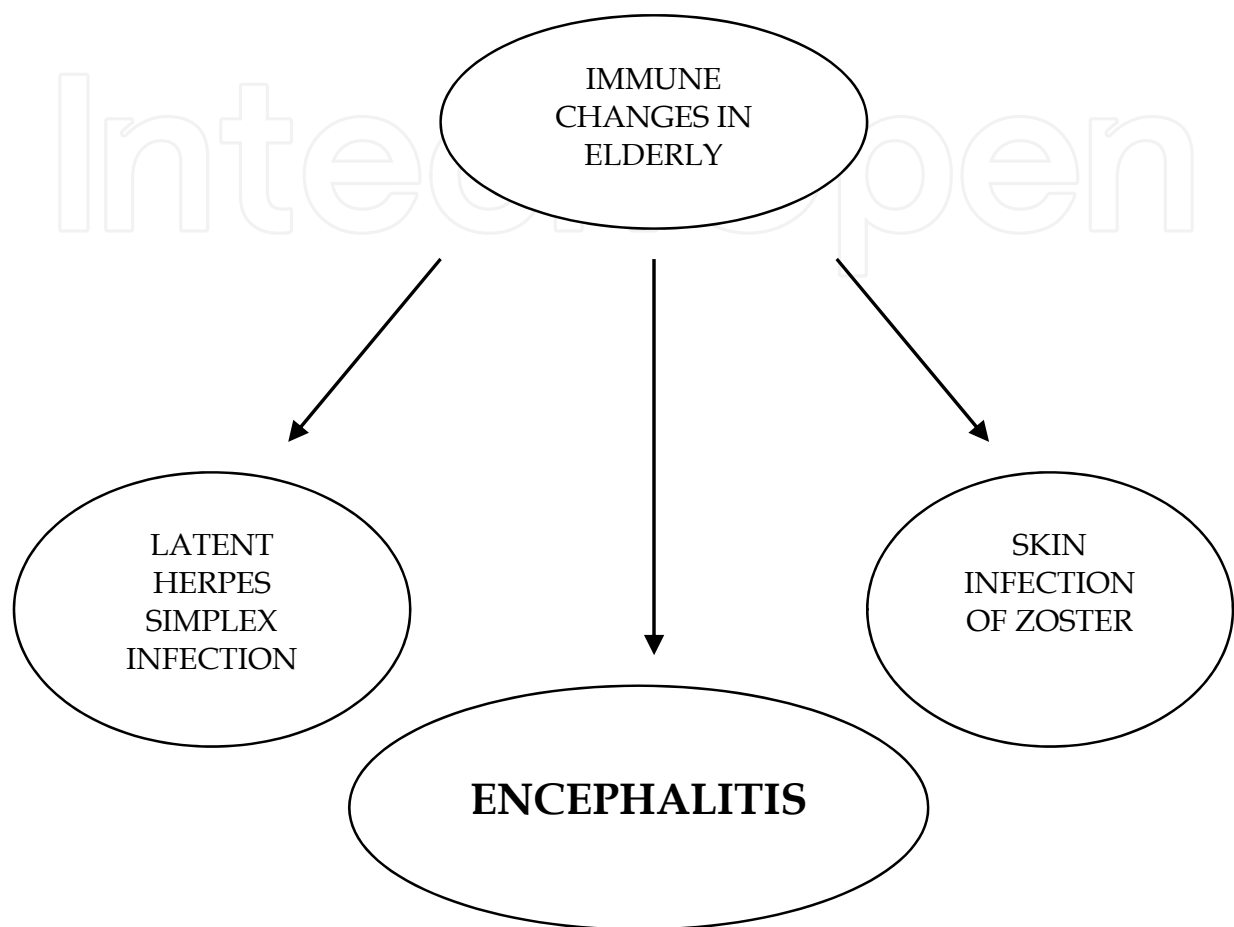


Fig. 1. Clinical entities related to immune alterations of elderly

4. Clinical course

Clinical symptoms of herpes simplex encephalitis are fever, headache, meningeal signs, alteration of conscioussness, focal and generalised seizures and long tract signs. Mortality and morbidity of untreated herpes simplex encephalitis is high. Yet, morbidity and mortality are seen less frequently with today’s spesific antiviral therapy. Currently, clinicians easily perceive and diagnose herpes encephalitis unless co-morbid conditions which may lead to a diagnostic confusion accompany, and if typical signs and spesific laboratory and imaging findings are present; thus spesific antiviral and symptomatic therapy is performed in the early phase of the disease.

However, herpes simplex encephalitis in elderly mostly presents with atypical clinical symptoms, and may difficultly be perceived by clinicians. Encephalitis in elderly, may present with more subtle symptoms such as progresive amnestic cognitive disorder or behaviroual changes, which are fairly different from typical symptoms in younger adults (Wong & Yau, 2007). These clinical signs, may frequently be confused with

neurodegenerative processes, metabolic delirium or stroke. Fever accompanied with progresive receptive aphasia may be a symptom of herpes encephalitis (Lester et al., 1988). As an atypical clinical presentation, progresive dysarthria and hypersalivation with no cognitive impairment in a 65 years old patient has also been defined (Almekhlafi et al., 2010). Short-term memory deficit has been defined as a clinical sign of herpes encephalitis (Reuter et al., 2007).

Encephalitis should be considered in all elderly individuals with progresive mental confusion (Lester et al., 1988, Reuter et al., 2007, Fernandes et al., 2010). Furthermore, progresive mental confusion seems to be the most considerable sign of early phase of elderly encephalitis, and should not be neglected in emergency services (Jouanny et al., 1994). Atypical clinical presentations of elderly encephalitis is shown on Table 3

Herpes simplex encephalitis	Progresive amnestic cognitive disorder Behaviroual changes Progresive receptive aphasia Progresive mental confusion Frontal lobe syndrome Progresive dysarthria + hypersalivation
Herpes zoster encephalitis	Confusion Deteriorating confusion (premorbid illness)
EBV encephalitis	Intermittant confusion
Enterovirus encephalitis	Cognitive + behaviroual impairment
WNV encephalitis	Focal neurological deficits mimicking stroke Febril attacks

Table 3. Atypical clinical presentation of encephalitis in elderly

Herpes simplex encephalitis usually affects the temporo-frontal grey matter and typical clinical symptoms of the disease is closely associated with this localisation. However, atypical localisations of herpes simplex encephalitis have also been reported both in elderly and non-elderly patients and currently, with the widespread clinical utilization of MRI, it is considered that atypical herpes simplex encephalitis localisations are more common than it's supposed to be (Fernandes et al., 2010). Clinicians may encounter cases with exclusively frontal lobe involvement with relatively sparing of the temporal lobes (Taylor et al., 2007). Frontal lobe syndrome in an elderly patient characterised by Bruns ataxia, incontinence and confusion may associated with herpes encephalitis (Ege et al., 2010). (Figure 2) Cerebellum, brain stem, parietal cortex, occipital cortex, thalamus and even white matter lesions due to herpes simplex encephalitis have been reported thus far. This condition however, has been seen more frequently in pediatric population and immun-compromised adults (Taylor et al., 2007). Similarly, aging is associated with several immun alterations, therefore may predispose to atypical localisations which may be confused with neoplasia and stroke. Herpes encephalitis should not be excluded when atypical clinical symptoms and extratemporal localisations appear, and be investigated with advanced diagnostic techniques. Atypical localisations is shown on Table 4.

Atypical anatomical localisations of herpes simplex encephalitis reported thus far	Frontal cortex
	Occipital cortex
	Parietal corex
	Brain stem
	Thalamus
	White matter
	Cerebellum

Table 4. Atypical anatomcal localisations of herpes simplex encephalitis

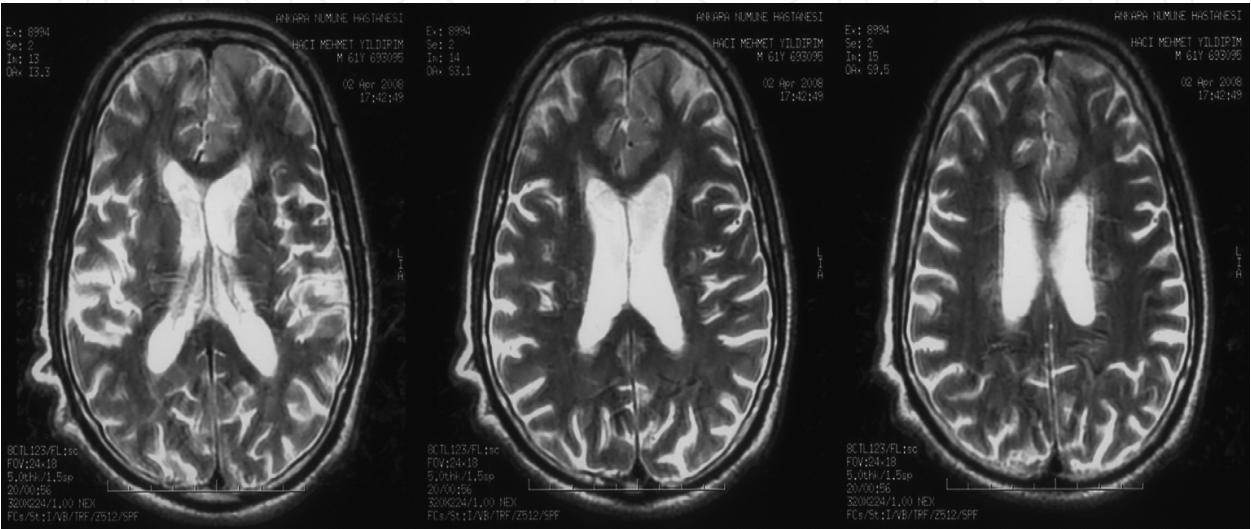


Fig. 2. Frontal lobe cortex involvement in herpes encephalitis

Atypical clinical presentations have also been defined in herpes zoster encephalitis. Confusion which is not accompanied with focal neurological deficits in an elderly patient or gradually deteriorating confusion in a patient with neurodegenerative dementia may be symptoms of zoster encephalitis (Gillanders et al., 1994). Similarly EBV encephalitis in an elderly patient may presents with intermittant confusion and febril attacks (Hu & Chan, 2000). An elderly case with enteroviral meningoencephalitis which is presented with cognitive and behavioural impairment has also been reported in the literature (Valcour et al., 2008)

Regardless of etiology, in patients over 60 years old, meningeal signs are less frequent as compared to non-elderly patients; and motor weakness is seen more frequently. Clinical course of the disease in elderly patients is more severe and outcome is worse than in non-elderly patients (Lee et al., 2003). Despite the fact that encephalitis in the elderly may presents with atypical clinical symptoms in the early phase, typical symptoms frequently arise as the disease progresses.

5. Prognosis

Encephalitis causes a severe central nervous sytem damage, and may result in morbidity and mortality. Although the outcome can be changed by utilizing infection markers and modern treatment strategies in the early phase, the prognosis of the disease is also associated with several defined clinical factors. Old age and severity of clinical course are

the most important prognostic factors. Old age, as well as the deterioration of consciousness are found to be the major risk factors for mortality in herpes encephalitis (Whitley et al., 1986, Kamei et al., 2005). Once again mortality in west nile virus encephalitis is clustered in elderly individuals as compared to younger adults (Berner et al., 2002). Regardless of etiology, encephalitis causes a poorer outcome in elderly population (Lee et al., 2003).

Another considerable problem in elderly patients is the persistency of neurological symptoms. Persistent symptoms not only deteriorate the life quality of patients but also cause secondary medical problems. The frequency of persistent neurological symptoms following west nile virus encephalitis has been found to be associated with diabetes mellitus and hypertension, and not with old age (Cook et al., 2010). However, it is known that chronic diseases are seen more frequently in elderly individuals. Rehabilitation programmes are currently taken into account for patients who have persistent neurological symptoms (Berner et al., 2005). Mortality and persistent neurological symptoms are frequent also in patients over 75 years old in Japan encephalitis (Berner et al., 2005 as cited in Tsai, 2000). Morbidity in herpes encephalitis is still being a problem despite the modern antiviral treatment in elderly patients (Whitley et al., 1986). Cerebellar encephalitis is reported both in elderly and non-elderly patients. However, dissimilar from outcome of younger patients, the disease may lead to a persistent and more severe cerebellar ataxia (Klockgether et al., 1993).

6. Differential diagnosis

Elderly encephalitis may mimic several clinical situations, as the disease presentation in elderly age group is atypical and accompanying vascular and neurodegenerative disorders may disguise markers of encephalitis. In addition, atypical localisations in herpes encephalitis demonstrated by magnetic resonance imaging may increase the confusion. Such that atypical localisations may be confused with ischemic lesions and neoplasias. Encephalitis may mimic stroke, by causing unilateral motor weakness and other focal neurological deficits; furthermore it is reported that the disease may be presented as deterioration of motor weakness in patients having motor sequela of stroke (Berner et al., 2002).

In addition, many disorders in elderly may be presented with clinical symptoms mimicking encephalitis. If so, encephalitis should be differentiated from clinical situations causing mental confusion and delirium in aged individuals.

1. Metabolic encephalopathies (hepatic and renal failure, electrolyte disturbance, hypoglycemia, hyperglycemia)
2. Hypertensive encephalopathy
3. Cerebrovascular disorders
4. Head trauma
5. Bronchopneumonia, urinary tract infections, sepsis
6. Drug adverse effects
7. Paraneoplastic syndromes
8. Space occupying lesions
9. Neurodegenerative disorders, dementia
10. Hydrocephalus
11. Epilepsy

Metabolic encephalopathies in elderly individuals are imitating encephalitis by giving rise to confusion and disorientation; electrolyte disturbances, diabetic coma and uremia should be differentiated. Fever of any cause is a considerable situation in elderly patients and may lead to exacerbation of symptoms of demented patients. Urinary tract, lung, upper respiratory tract and skin infections may cause fever and delirium, so be easily confused with encephalitis. Hypertensive encephalopathy presents with headache, seizures and consciousness impairment and may mimic central nervous system infections. Fluctuations and exacerbations of neurodegenerative disorders, Lewy body dementia in particular, may give rise to diagnostic confusion. Space occupying lesions in frontal and temporal lobes should be differentiated from infectious disorders, as they are presented with cognitive impairment, focal neurological deficits and seizures. Non-convulsive seizures in elderly population are seen both in epileptic patients and symptomatically, and with their clinical symptoms and EEG changes, may bring central nervous infections to mind. Briefly, encephalitis may mimic several conditions such as stroke and dementia, also numerous systemic and neurological disorders may present with symptoms resembling encephalitis in old age. For this reason, multi-disciplinary approach is required at times, in emergency services, for the elderly patients who have fever and mental deterioration.

7. Diagnostic tools

Diagnosis of encephalitis in elderly is based on high index of suspicion in the early course of the disease, as the presentation is atypical. For this reason, MRI and cerebro-spinal fluid examination should be performed in all patients with probable encephalitis. Although MRI is an effective tool for demonstrating the encephalitis lesions, it may reveal negative results in the early course of the disease. Anatomically atypical encephalitis lesions is another problem and clinicians should not exclude the disease in the presence of such lesions.

CSF protein levels increase mild to moderately in the course of viral encephalitis with accompanying mononuclear pleocytosis. Polymorphonuclear pleocytosis may be seen however in WNV encephalitis. CSF is normal in 10% of the cases of viral encephalitis. CSF glucose level is normal in viral encephalitis, nevertheless may found to be decreased in bacterial, fungal and parasitic encephalitis (Tunkel et al., 2008).

PCR technique which detects the nucleic acids of pathogens is fairly beneficial in elderly patients when findings of MRI and CSF examination are non-specific or insufficient for diagnosis. CSF protein and lymphocyte levels may not increase in the early course of herpes encephalitis, therefore PCR should be performed in all patients. PCR should also be executed for agents such as EBV, CMV, VZV, WNV in suspected cases of encephalitis. Specificity and sensitivity of PCR in herpes simplex encephalitis is high, despite false negative results may rarely be obtained. The test should be repeated after few days in suspected cases. Investigation of CSF IgM anti-bodies is useful in some cases. Detection of virus specific IgM anti-bodies can be utilized so as to diagnose flavivirus infection. 4 fold increase in specific serum IgG anti-body level is also an important marker for determining lots of viral and bacterial agents (Tunkel et al., 2008, Roos, 2005).

Electroencephalogram (EEG) is adjunctive and sensitive method in encephalitis, however its specificity is partially decreased in aged population. Frequent disorders in old age such as vascular lesions, metabolic disturbances and neurodegenerative diseases cause EEG changes, slow wave activity in particular. Still, it is found to be beneficial for demonstrating

the periodic activity in herpes encephalitis. (Jouanny et al., 1994) Efficiency of diagnostik tools in elderly encephalitis is shown on Table 5.

Numerous disorders which may be confused with encephalitis have been defined in elderly patients. For instance bronchopneumonia may cause high fever and progresive mental confusion in elderly patients. Even an urinary tract infection may lead to delirium and be easily confused with encephalitis (Eriksson et al., 2011). For that reason, blood samples should be obtained for studying blood glucose, electrolytes, liver functions (SGPT, SGOT), renal funtions (BUN, creatinin), thyroid homones, blood count, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Urinary Ph, protein, nitrite and leucocyte number should also be determined. Blood and urinary cultures and chest roentgen examination are beneficial so as to scan localised and systemic infections.

Still, it should be borne in mind that, localised and systemic infections, co-morbid metabolic disturbances and chronic diseases may accompany encephalitis in elderly patients. Moreover, metabolic and systemic disorders may also be induced by encephalitis in elderly patients. For example confusion due to viral encephalitis may inhibit drug use in a diabetic elderly individual, so may secondarily causes extreme high glucose levels. Similarly a central nervous sytem infection leading to high fever and dehidratation may secondary impair renal functions. Once again, hyponatremia may be caused by inappropriate ADH syndrome secondary to encephalitis.

Alterations on mental level may mistakenly be related to metabolic disturbances in above mentioned examples, therefore indirect influence of encephalitis should also be remembered. As a consequence, encephalitis should be considered in elderly patients who have confusion and disorientation, yet investigations should be carried out for determining metabolic disturbances and systemic infections.

CLINICAL SYMPTOMS	Atypical presentations are frequent
CT SCAN	Non-spesific, sensitivity is low
MR IMAGING	Sensitive, may reveal atypical lesions
PCR	Sensitivity and specifity is high, beneficial
CSF EXAMINATION	Sensitive, specifity is low, negative in 10%
SEROLOGY	Beneficial for some agents, specificity is high
EEG	Specifity is low, sensitive

Table 5. Diagnostic tools for elderly encephalitis

8. Management of elderly patients

Ampirical antibiotic treatment should be performed in suspected elderly cases before the confirmation of diagnosis. Today, parenteral acyclovir (10mg/kg iv q8h x 14-21 days, if renal functions are normal) is recommended for herpes simplex virus encephalitis. However, other ampirical antibiotic options should be initiated considering the epidemiological data. For instance, doxycycline can be given if there is clinical suspecion of ricetsial or erlichial encephalitis in risky regions (Tunkel et al., 2008).

Parenteral acyclovir is well tolerated in elderly patients, nevertheless nephrotoxic and neurotoxic adverse effects are reported rarely. BUN and creatinin levels should be studied more frequently in elderly patients than in younger individuals, to determine the nephrotoxicity. Neurotoxic side effects are seen more frequently in elderly population and

patients having impaired renal functions and malignency. Neurotoxicity of acyclovir is a neuropsychiatric disorder which conscioussness is altered. Confusion, delirium, lethargia and tremor may appear in patients, so differentiation of this situation from mental changes due to encephalitis is crucial for maintaining the treatment and considering alternative options. Fever and headache do not accompany acyclovir associated neurotoxicity, and finding of lateralisation is not seen in EEG (Rashiq et al., 1993) (Figures 3 & 4)

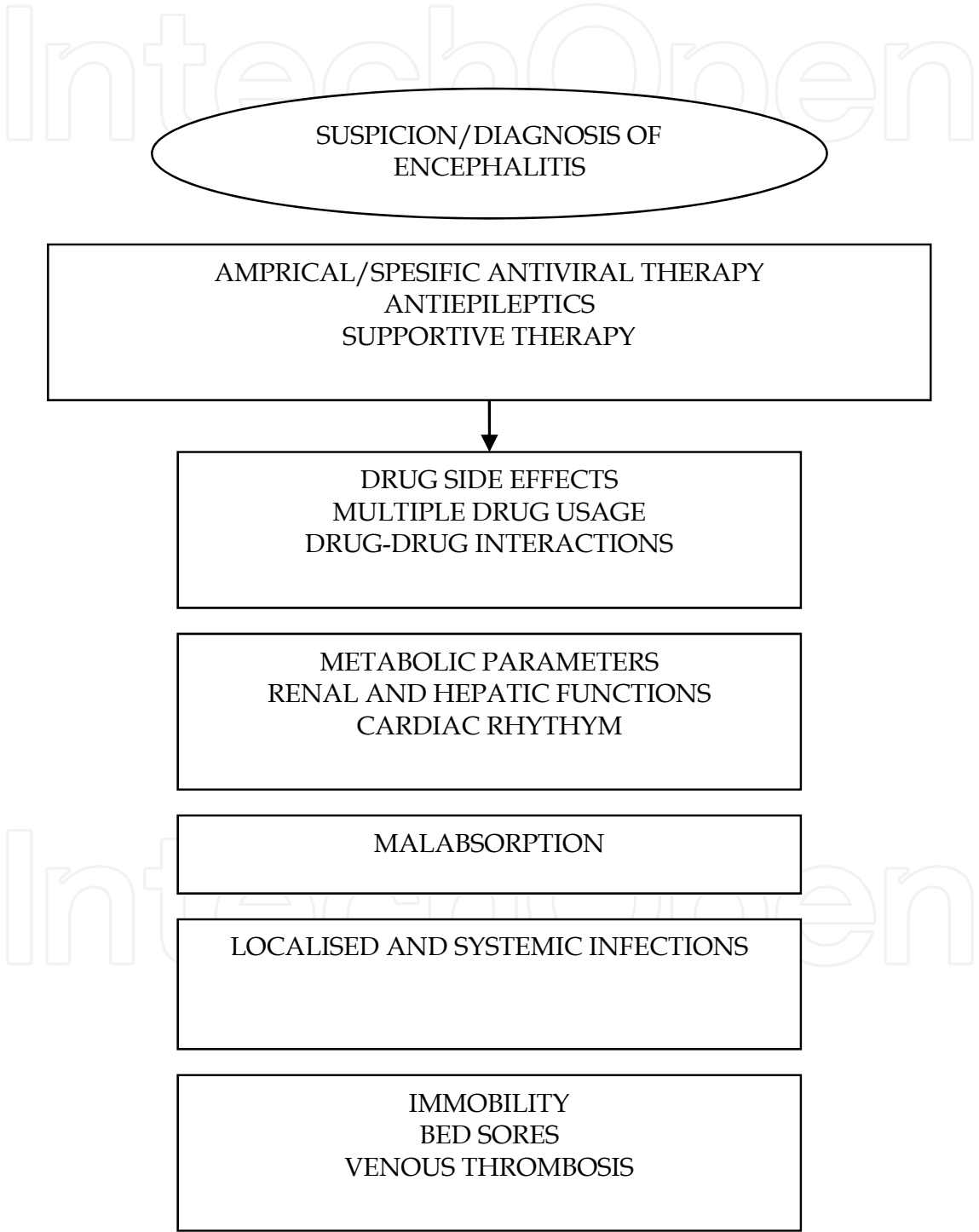


Fig. 3. Problems in management of encephalitis in elderly

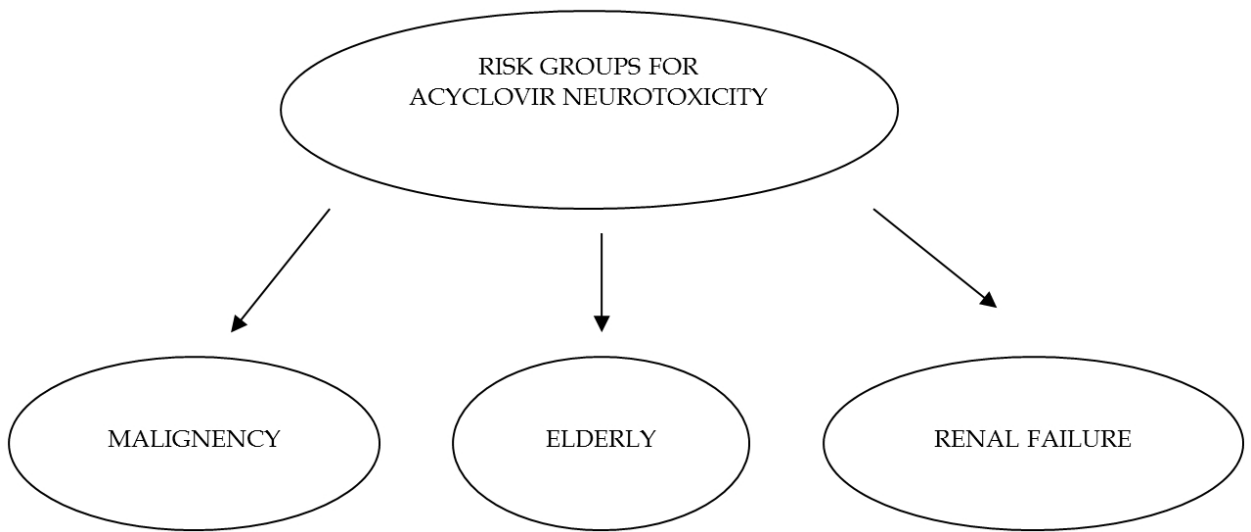


Fig. 4. Risk groups for acyclovir neurotoxicity

Acyclovir or gancyclovir for VZV encephalitis, and gancyclovir (5mg/kg q12h) + foscarnet (60mg/kg q8h) for CMV and HHV type 6 encephalitis can be preferred. Acyclovir can also be attempted in EBV encephalitis. Valacyclovir (1 gr oral 8qh) or acyclovir (10-15mg/kg iv 8qh) can be chosen for B virus encephalitis. However treatment in encephalitis due to other agents is still being a problem; currently supportive therapy strategies preserve their importance as specific antiviral medications do not exist (Tunkel et al., 2008, Roos, 2005).

Renal and hepatic parameters as well as electrolytes should be closely monitored in elderly patients and drug doses should be adjusted to renal and hepatic functions. Metabolic conditions have to be considered in aged group, when initiating anti-epileptic agents, and clinicians should be aware of drug adverse effects in elderly. Hepatic and renal functions, blood count and cardiac rhythm have to be more closely monitored.

Drug-drug interactions is a crucial problem in old age. Elderly patients usually use multiple drugs as they possess chronic disorders. Drug interactions should be considered when choosing antibiotics and antiepileptics and dosing of these medications. Determination of blood levels is beneficial to minimise the drug interactions.

Insufficient alimentation and malabsorption is frequent in demented patients for both sociobiological and pathological reasons. Since malabsorption complicates the treatment of infectious diseases, probability of malabsorption should be evaluated in intensive care units and nutritional support should be supplied in the early course of the disease.

Since old age causes a predisposition to infections, clinicians should be aware of respiratory and urinary tract infections in intensive care units. Development of hospital infections and their complications are easier in elderly patients. Localised and systemic infections should be investigated if deterioration despite antiviral treatment has been perceived or persistency of high fever occurs.

Immobility due to dementia, stroke or other reasons is frequent in elderly population, in addition encephalitis may cause or worsen immobility for causing consciousness impairment and long tract injury. It is better to take earlier measures for bed sores: patients position should be changed frequently and protein nutrition should be supplied. Abrasions and erythematous lesions have to be treated as soon as they noticed. Prophylactic anti-coagulant therapy should be given to all immobilised patients unless there is clear contraindication.

Briefly, management of encephalitis in elderly also includes sensitive approach to co-morbid situations, drug-drug interactions, premorbid chronic disorders and their exacerbations. Vital signs and metabolic parameters should be more closely monitored and nutritional support should be given beginning from the early course of the disease.

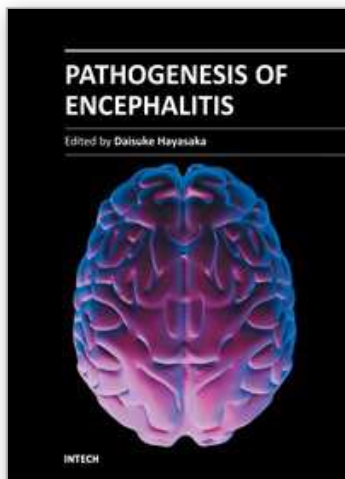
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Pathogenesis of Encephalitis

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Many infectious agents, such as viruses, bacteria, and parasites, can cause inflammation of the central nervous system (CNS). Encephalitis is an inflammation of the brain parenchyma, which may result in a more advanced and serious disease meningoencephalitis. To establish accurate diagnosis and develop effective vaccines and drugs to overcome this disease, it is important to understand and elucidate the mechanism of its pathogenesis. This book, which is divided into four sections, provides comprehensive commentaries on encephalitis. The first section (6 chapters) covers diagnosis and clinical symptoms of encephalitis with some neurological disorders. The second section (5 chapters) reviews some virus infections with the outlines of inflammatory and chemokine responses. The third section (7 chapters) deals with the non-viral causative agents of encephalitis. The last section (4 chapters) discusses the experimental model of encephalitis. The different chapters of this book provide valuable and important information not only to the researchers, but also to the physician and health care workers.

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