Delirium: Clinical Features, Diagnosis and Differential Diagnosis

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Delirium is an acute brain dysfunction which develops over a short period of time and may result from several different aetiologies. It is characterized by disturbance in various cognitive functions primarily of attention and awareness. It can develop easily in the elderly who are already vulnerable with several predisposing and precipitating factors. Delirium is a common, serious and often fatal disorder that affects as many as 50% of people older than 65 years who are admitted to the hospital (Inouye et al. 2014). The significance of delirium is not limited to its high prevalence; at the same time, it has marked negative effects on various parameters such as medical morbidity, duration of hospital stay and outcome after discharge (Cole and Primeau 1993; Fong et al. 2009). Delirium is an alarming sign that underlying medical condition is serious to an extent of increasing mortality and morbidity rates. It may not be recognized in the elderly patient and might be misinterpreted as dementia, depression or a natural course of ageing.

3.1 Clinical Features

Delirium is defined as a reversible and temporary impairment of brain function. It is a syndrome, not a disease, and it has many causes, all of which result in a similar pattern of signs and symptoms. The type and severity of signs vary depending on the patient and the aetiology. However, common signs and symptoms which make the core syndrome are similar. The essential feature of delirium is a disturbance of attention or awareness that is accompanied by a change in baseline cognition that cannot be better explained by a preexisting or evolving neurocognitive disorder (American Psychiatric Association 2013).

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3.1.1 Onset of Symptoms

One of the most characteristic features of delirium is rapid development of its symptoms. The symptoms usually emerge within hours or days. The onset sometimes may be abrupt. The relatives or carers might state that the patient was well until a short while ago and that it all changed suddenly. Relatives and care staff may describe features such as an acute change or decline in function, disturbed sleep/wake cycle or sleeplessness, rapid memory decline, 'confusion' or a rapid change in personality or behaviour. This type of onset helps differentiate delirium from other neurocognitive disorders mainly dementia.

3.1.2 Prodromal Phase

In some patients there could be prodromal changes for 1–3 days before the onset of florid symptoms. Patients might appear irritable, perplexed and restless. In cases where the onset is more gradual, there could be mild and temporary symptoms such as anxiety, decreased concentration, fatigue and sleep problems (Krahne et al. 2006). In some patients certain cognitive impairments like mild confusion or difficulty in remembering and hypersensitivity to light and sound and changes in perception can be noticeable. The most commonly seen sign is sleep disturbance like daytime sleepiness. Prodromal signs can recede after a short while or can develop into a marked delirium. The presence of prodromal signs should be taken into consideration when elderly patients are treated both in the inpatient and outpatient settings and during their first presentation for assessment. The interventions for diagnosis and treatment towards general medical conditions could prevent development of a likely delirium syndrome.

3.1.3 Fluctuating Course

Fluctuations and changes in severity and type of symptoms are one of the most typical features of delirium. Fluctuation in clinical manifestation with worsening in attention, awareness and other realms of cognitive function interspersed with periods of lucid intervals during the course of the day is a diagnostic feature of delirium. A somnolent patient can become fully alert and later on within minutes can get worse with agitation. This feature undoubtedly is one of the most important reasons why diagnosis can be overlooked in patients who are not assessed frequently. These fluctuations in symptoms and intermittent worsening are unpredictable and irregular; however, there is often some improvement during the daytime and worsening at night.

3.1.4 Signs and Symptoms

There are various signs and symptoms of delirium. Although most of these can be seen during the course of normal ageing or dementia, some are typically seen in

delirium. When Gottlieb et al. (1991) compared two groups of hospitalized elderly patients with and without delirium by using DSM-III criteria, clouding of consciousness, disorientation, memory impairment, fluctuation and acute onset were present in 100% of patients with delirium, while the same symptoms were present in 5%, 34%, 64%, 9% and 12%, respectively, of patients without delirium. Similarly, perceptual disturbances, incoherent speech, sleep disorder and psychomotor changes occurred in 75%, 76%, 96% and 93%, respectively, of delirious patients and 3%, 6%, 65% and 40%, respectively, of non-delirious patients. The review studies of delirium cases done in the 1990s showed the most common signs of delirium as follows: clouding of consciousness (65–100%), disorganized thinking (95%) and short-term memory and recall difficulties (62–90%) (Meagher and Trzepacz 1998; Trzepacz 1999).

In delirium, depending on the personal vulnerability, cognitive capacity and the type and severity of underlying pathology, all or some of the symptoms described below can be seen. For a diagnosis of delirium, those symptoms or signs may not be evident all the time as they will fluctuate, but they must be of recent onset.

- Disturbances in consciousness: Consciousness is described as being aware of internal and external stimuli. For consciousness, a normal level of arousal is required but not sufficient. It also requires to be able to give appropriate responses to stimuli. Disturbance in consciousness is a cardinal feature of delirium, but it is difficult to describe and examine it. In reality, consciousness shows a continuum from hyperalertness/hyperarousal to coma. For a diagnosis of delirium, the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V), requires that impairment in attention and other cognitive functions do not occur in the context of a severely reduced level of arousal, such as coma (American Psychiatric Association 2013). However, low-level arousal states with minimal responses should be considered in the context of delirium. In some patients disturbances in consciousness can manifest itself as hyperalertness/hyperarousal or with lethargy and reduced arousal in others. In delirium patients may not be woken up fully and can fall asleep easily, or there could be increased attention with excessive alertness and startle reaction. Some patients might fluctuate between the two extremes during the course of the day.
- Reduced ability to direct, focus, sustain and shift attention: Attention is a process of direction and focus of perception towards selected stimuli. The maintenance of this process for certain activities and attending to various stimuli simultaneously is described as the content of attention. Impairment in attention is the most characteristic feature of delirium. This can be assessed by observing the ability of patient following the instruction during the medical examination/interview. Patients have difficulty focusing on the stimulus, and the question/stimulus needs to be repeated in order to get a response. The ability of attention can be objectively assessed by some bedside tests.
- Disorientation: Impairment in orientation is the most common sign of delirium. Besides being a common sign, it plays a main role for recognizing delirium. People can be easily assessed by asking about the place and time they are in

which is quite useful for a diagnosis of delirium. It is particularly important to do regular assessments on the elderly vulnerable patients for early recognition and treatment. Disorientation may occur in time (not knowing what time of day, day of week, month, season or year), place (not knowing where one is) or person (not knowing who one is). The earliest and most common impairment is seen in temporal orientation. Disorientation to person is very rare and indicates the seriousness of the condition.

- Disorganized thinking and speech: In most delirious elderly patients, the clarity, consistency and the speed of speech get impaired. There could be inconsistent flow of thoughts with loosening of associations between the words, sentences and topics. This is known as disorganized thinking which is observed as a difficulty to understand and inconsistent speech. Other speech and language disturbances such as dysarthria, dysnomia, dysgraphia and even aphasia may occur in delirium.
- Memory disturbances: Short-term memory problems and difficulties with remembering are common problems in delirium. However, these impairments are temporary and unlike in dementia are not a result of a neurodegenerative process and are due to fluctuations in consciousness and disturbance in attention. There is impairment in registration, recall and recognition. It impacts short-term memory more than long-term memory (American Psychiatric Association 2013). There could be no problem with easy short-term memory tasks such as repeating a word or answering simple questions. However, there are usually problems with relatively difficult tasks throughout the delirium such as repeating a telephone number. Registration of newly learned knowledge in the long-term memory requires high-level concentration which is often impaired in delirium. Recalling old memories does not require concentration which is generally not effected in delirium. However, in cases where the underlying pathology causes severe brain damage, long-term memory can also get disturbed as a result, not because of delirium itself.
- Sleep-wake disturbances: Sleep-wake cycle disturbances are very common in delirium and have been proposed as a core criterion for the diagnosis. Due to impairment of circadian sleep cycle, there are sleep-wake rhythm disturbances in most patients with excessive sleepiness during the daytime and increased alertness at night. Decreased or broken sleep at night could be the first sign of delirium in many patients. Patients wake up with vivid dreams and nightmares. They can confuse dreams with real life due to sleepless nights and excessive sleepiness during the day.
- Perceptual disturbances: Hallucinations, misperceptions, illusions and delusions are reported to occur in at least 40% of cases of delirium (Cole et al. 2002). Perceptual disturbances are usually visual but may occur in other modalities. They are mostly illusions. Patients might, for example, misperceive the blood pressure device that a nurse is using as a weapon or a water pipe in the room as snake or folds in bed as various animals. Hallucinations are perceptions without external stimuli. Hallucinations are usually visual, ranging from dreamlike experiences to terrifying visions. They are particularly common in patients with

delirium due to multiple aetiologies and receiving more active medical treatment (Webster and Holroyd 2000). They are experienced mostly at night, when it is dark and when the patient is alone. When there's no one around, they might see a group of people around the bed, dangerous animals or strange figures. There could be interesting hallucinations like macropsia (a disorder of visual perception in which objects appear larger than their actual size) or micropsia (seeing tiny human or animal figures). Less frequently auditory hallucinations or those involving taste and smell may occur. There could be very disturbing tactile hallucinations particularly in deliriums secondary to alcohol/substance withdrawal.

- Emotional disturbances: Emotional changes can last long which can be reported as personality change by others or can be intermittent changes with lability. There is no mood or affect changes specific to delirium. However, there are often disturbances in the form of anxiety, anger, apathy, depression, euphoria or irritability.
- Thought content: There are often persecutory delusions in thought content (they will kill me; they will slaughter me). Misperceptions (a nurse preparing a medicine can be perceived as if he/she is trying to poison the patient) can lead to these thoughts. Delusions are short-lived and temporary and are not considered as fixed delusions.
- Altered psychomotor activity: This is one of the most important signs of delirium making the monitoring of the patients difficult. It varies according to the type of delirium which will be discussed below. Patients with hyperactive delirium show increased alertness and hypervigilance. They can be agitated, disruptive and aggressive. On the other hand, hypoactive ones are sleepy with marked motionlessness and retardation.
- Other features: Higher integrative functions are affected; the result is a reduced ability to plan and solve problems or disrupted sequencing or praxis of actions (e.g. rising from a bed or walking which can lead to injury or falls). Disturbances can also occur in visuospatial abilities and in writing. It is important to note that the sensory features tend to be less common in elderly than in younger patients. Somatic features such as urinary incontinence, gait impairment, tremor and language disorders (including receptive and expressive dysphasia) tend to be more common in older people with delirium (Lipowski 1980).

3.2 Clinical Subtypes

Based on the levels of arousal and psychomotor functions, three types of delirium are described (Lipowski 1983; Meagher et al. 1996). It has been suggested that each delirium subtype can result from different pathophysiological mechanisms and that each might carry a different prognosis (Fong et al. 2009).

Hyperactive delirium which is marked by increased psychomotor activity occurs in 15–46% of delirium patients (Meagher et al. 1996; Liptzin and Levkoff 1992; Marcantonio et al. 2002; Camus et al. 2000; Margiotta et al. 2006). There is hyperarousal with increased sensitivity to immediate surroundings to the point

where patients can be verbally and physically aggressive. Patients present with repetitive behaviours such as plucking at sheets, picking or pulling the bed linens, rubbing his/her genitals, attempting to get out of bed and wandering or perceptual disturbances such as illusions or hallucinations. Patients with hyperactive delirium have shorter hospital stay comparing to other subtypes, and they are accepted to have better prognosis. This variant of delirium is most commonly recognized and tends to be readily apparent even to the casual observer. It is often associated with the adverse effects of anticholinergic drugs, drug intoxication and withdrawal states. Characteristically, patients may exhibit agitation, psychosis and mood lability, may refuse to cooperate with medical care, may demonstrate disruptive behaviours (such as shouting or resisting) and may sustain injuries from falling, combativeness or pulling out catheters and intravascular lines (Rummans et al. 1995; Rudberg et al. 1997).

Hypoactive delirium which occurs in 19–71% of patients is typically unrecognized or misattributed to dementia or depression (Spronk et al. 2009; Meagher et al. 1996; O'Keeffe and Lavan 1999; Liptzin and Levkoff 1992; Marcantonio et al. 2002). Some researchers are of the opinion that due to the restriction of diagnostic criteria in DSM, actual higher rates are not detected (Treloar and Macdonald 1997). Hypoactive type is also described as somnolent type which is marked by psychomotor slowing and withdrawal and may be misidentified as depression (Ross et al. 1991). Patients appear quiet, withdrawn and lethargic and present with clouding of consciousness with reduced mobility/movement. They often have daytime sleepiness. Spontaneous movements and speech are slowed down a lot. Therefore communication can be provided with difficulty. They may need to be reminded several times to respond to the questions. These patients are confused and look tired. This is the most common type of delirium seen in the elderly patients. However, they can be easily overlooked because of being calm and sleepy, not displaying any aggression towards themselves or others and having no bizarre behaviours. It is known that hypoactive delirium is caused by severe, acute underlying pathologies such as infections, hypoxia, hypothermia, hyperglycaemia, hepatic and renal failures and thyroid diseases (O'Keeffe and Lavan 1999; Trzepacz 1994; Justic 2000). Delirium in the elderly is usually caused by these conditions; therefore, hypoactive type is thought be more often in this patient group.

Mixed forms: Mixed forms may occur in 43–56% of patients (O'Keeffe and Lavan 1999; Liptzin and Levkoff 1992). Patients with mixed delirium demonstrate both hyperactive and hypoactive features. This presentation is marked by obvious fluctuations in activity level, cognitive disturbance, level of consciousness and organization of thinking. There is usually sedation, sleepiness and no movement during the daytime while agitation, increased activity and disruptive behaviour at night.

Certain types of delirium may frequently occur in patients with particular disease states; however, they are neither exclusive nor diagnostic of specific underlying medical conditions. Similarly, the manifestation of delirium cannot be fully predicted by the presence of a particular aetiological toxin or illness. Because of the multiple aetiological factors, the fluctuating course and the individual medical comorbidities, many patients who experience delirium have a mixture of both

hypoactive and hyperactive variants. Some studies suggest that such patients present the greatest risk of substantial morbidity and mortality (Stagno et al. 2004).

In an observational study done on 225 prospective admissions to the geriatric unit of a training hospital, it was founded out that from 94 admissions with delirium, 20 (21%) had a hyperactive delirium, 27 (29%) had a hypoactive delirium, 40 (43%) had a mixed hypoactive-hyperactive psychomotor pattern and 7 (7%) had no psychomotor disturbances. Patients with hypoactive delirium were sicker on admission, had the longest hospital stay and were most likely to develop pressure sores. Patients with hyperactive delirium were most likely to have a fall in the hospital. There were no differences in aetiological factors between the groups (O'Keeffe and Lavan 1999).

3.3 Diagnosis

The diagnosis of delirium is primarily clinical and is based on careful bedside observation of key features. There is no specific test. One should always suspect delirium when elderly patients particularly those with dementia present with acute or subacute disturbances in behaviour, cognition or functioning. There is a need for full physical examination with detailed history including mental state examination in these cases. The history should confirm that an acute change in baseline cognitive function has occurred. It is important to ascertain the time course of the mental status changes, as well as any history of intercurrent illnesses, medication usage (including any changes in medication and use of over-the-counter and herbal products), alcohol withdrawal and changes in the environment. Because patients with delirium are often confused and cannot give a proper history, the information obtained from family, carers and nurses is important. It is important to check nursing notes particularly for night-time disorientation, abnormal behaviour and perceptual disturbances.

3.3.1 Diagnostic Difficulties

Delirium is often unrecognized by the patients' physicians and nurses, in part because of its fluctuating nature, its overlap with dementia, lack of formal cognitive assessment and underappreciation of its clinical consequences (Saxena and Lawley 2009). The bedside mental status examinations and interviews show dramatic fluctuations. Therefore, cognitive assessments which will be performed at regular intervals in an elderly patient are too helpful to determine the developing delirium. It might not be likely to do standard cognitive tests particularly on patients at the surgical and intensive care units as they are intubated and cannot respond verbally to questions.

Hypoactive patients which comprise the majority of the delirium cases can be overlooked due to "quite" symptoms. It also makes measuring the changes from baseline difficult when there is not sufficient information on premorbid personality

and functioning of the elderly patients. Cognitive/mental problems in the elderly patients with medical conditions are usually considered as reasonable or expected by relatives and hospital staff which can prevent to focus enough on delirium symptoms. Problems with the system or clinics such as ward transfers due to multiple medical problems and shift changes can also make the diagnosis difficult. Studies suggest that between a third and two thirds of delirium goes unrecognized (Siddiqi et al. 2006). In a study, it was shown that only 31% of the patients could be diagnosed with delirium. In the same study, it was determined that delirium diagnosis could not be made especially in the patients over 80 years with hypoactive delirium, visual problems and dementia diagnosis (Inouye et al. 2001). Another study measured nursing identification of delirium using standardized case vignettes, only 21% of nurses were able to correctly identify the hypoactive form of delirium superimposed on dementia (DSD) and 41% correctly identified hypoactive delirium alone in the case vignettes (Fick et al. 2007).

3.3.2 Diagnostic Criteria

The essential feature of delirium is a disturbance of consciousness and attention that is accompanied by a change in baseline cognition that cannot be better explained by another neurocognitive disorder. The appearance of symptoms within a short period of time like hours or days and the fluctuation of symptoms during the course of the day are the diagnostic features related to the course of delirium. In addition to these criteria, there is evidence from the history, physical examination or laboratory findings that the disturbance is a physiological consequence of a general medical condition.

A formal diagnosis can be made by using the DSM-V or International Classification of Diseases 10 (ICD-10) criteria (American Psychiatric Association 2013; World Health Organization 1992). Diagnosis of delirium according to the DSM-V requires disturbance of attention and awareness; change in cognition (including memory deficit, disorientation or language disturbance); development over a short period of time, usually hours to a few days; fluctuations during the course of the day; and evidences from the history, physical examination or laboratory findings that the disturbance is a physiological consequence of an underlying medical condition, substance intoxication or withdrawal, use of a medication or a toxin exposure or a combination of these factors (Table 3.1).

DSM-V recognizes seven diagnostic categories:

1. Substance intoxication delirium
2. Substance withdrawal delirium
3. Medication-induced delirium
4. Delirium due to another medical condition
5. Delirium due to multiple aetiologies
6. Other specified delirium
7. Unspecified delirium

Table 3.1 DSM-V diagnostic criteria for delirium

A.	A disturbance in attention (i.e. reduced ability to direct, focus, sustain and shift attention) and awareness (reduced orientation to the environment)
B.	The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness and tends to fluctuate in severity during the course of a day
C.	An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability or perception)
D.	The disturbances in Criteria A and C are not better explained by another preexisting, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma
E.	There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication) or exposure to a toxin or is due to multiple aetiologies
Specify if:	
Acute: Lasting a few hours or days	
Persistent: Lasting weeks or months	
Specify if:	
Hyperactive: The individual has a hyperactive level of psychomotor activity that may be accompanied by mood lability, agitation and/or refusal to cooperate with medical care	
Hypoactive: The individual has a hypoactive level of psychomotor activity that may be accompanied by sluggishness and lethargy that approaches stupor	
Mixed level of activity: The individual has a normal level of psychomotor activity even though attention and awareness are disturbed. Also includes individuals whose activity level rapidly fluctuates	

Diagnostic criteria for delirium according to ICD-10 are shown in Table 3.2. The ICD-10 definition appears to be much narrower than DSM-IV. It has separate requirements for cognitive disturbance (which must be evidenced by impairment in immediate recall and recent memory with intact long-term memory and disorientation to time, place or person), one of four types of psychomotor disturbance and one of three specified manifestations of disturbance of the sleep-wake cycle.

3.3.3 Examination

Delirium remains a clinical diagnosis made on the basis of a detailed history, behavioural observation and cognitive assessment. A careful and complete physical examination including a mental status examination is necessary for the diagnosis. Establishing previous functional and cognitive status and recent events such as falls or medication changes is essential. For a proper diagnosis, it is necessary to do periodic assessment of diagnostic criteria and have information about baseline mental status of the patient. During the assessment, elderly patients should be provided with sensory aids such as spectacles or hearing aids.

It is a clear necessity to take history from a family member or carer in elderly patients who has medical problems. The history should confirm that an acute change in

Table 3.2 ICD-10 diagnostic criteria for delirium

For a definite diagnosis, symptoms, mild or severe, should be present *in each one* of the following areas:	
(a)	Impairment of consciousness and attention (on a continuum from clouding to coma, reduced ability to direct, focus, sustain and shift attention)
(b)	Global disturbance of cognition (perceptual distortions, illusions and hallucinations—most often visual; impairment of abstract thinking and comprehension, with or without transient delusions but typically with some degree of incoherence; impairment of immediate recall and of recent memory but with relatively intact remote memory; disorientation for time as well as, in more severe cases, for place and person)
(c)	Psychomotor disturbances (hypo- or hyperactivity and unpredictable shifts from one to the other, increased reaction time, increased or decreased flow of speech, enhanced startle reaction)
(d)	Disturbance of the sleep-wake cycle (insomnia or, in severe cases, total sleep loss or reversal of the sleep-wake cycle, daytime drowsiness, nocturnal worsening of symptoms, disturbing dreams or nightmares, which may continue as hallucinations after awakening)
(e)	Emotional disturbances, e.g. depression, anxiety or fear, irritability, euphoria, apathy or wondering perplexity
The onset is usually rapid, the course diurnally fluctuating and the total duration of the condition less than 6 months. The above clinical picture is so characteristic that a fairly confident diagnosis of delirium can be made even if the underlying cause is not clearly established. In addition to a history of an underlying physical or brain disease, evidence of cerebral dysfunction (e.g. an abnormal electroencephalogram, usually but not invariably showing a slowing of the background activity) may be required if the diagnosis is in doubt	

baseline cognitive function has occurred. It is important to ascertain the time course of the mental status changes, as well as any history of intercurrent illnesses, medication usage (including any changes in medication and use of over-the-counter and herbal products), alcohol withdrawal and changes in the environment (Fong et al. 2009).

The main mental status change in delirious patients is cognitive impairment, and the most important risky group for delirium is hospitalized older people. The guidelines recommend that all clinical encounters with sick older people should routinely include assessment of cognition (Young and Inouye 2007; Michauda et al. 2007).

The key problem is fluctuations in consciousness. In order to assess consciousness level, patients can be given verbal, auditory or motor stimuli, and then they are assessed for their comprehension or responses. The Glasgow Coma Scale may be used to quantify level of consciousness (Teasdale and Jennett 1974; Teasdale 2014).

Attentional process can be evaluated by observing patient's ability to follow instructions and medical interventions. There are short bedside tests to assess attention. Digit Span and Continuous Performance tests are among the most commonly used ones. Digit span task involves asking the patient to say out loud a string of 4–6 digits after the assessor (Blackburn and Benton 1957). In continuous performance test, the patient is asked to put his hand up every time he hears letter X or A among a string of letters read out with 1 s interval during 30 s (Cornblatt et al. 1988). Assessment of orientation is easy and has an important role in diagnosis. It can be assessed by asking questions related to time, place and persons.

Bedside mental state examinations and interviews show dramatic fluctuations. Hence, this assessment should be carried out frequently in patients with delirium or at risk of developing one. Older patients should be aroused during rounds and evaluated daily for the hypoactive form of delirium, which is often overlooked.

3.3.4 Screening Instruments

In addition to a standard clinical interview, several screening tools and scales have been developed to identify patients with delirium. Simple cognitive tests for inpatients such as the Mini-Mental State Examination (MMSE), Standardized MMSE (SMMSE) and Clock Drawing Test (CDT) are not specific to delirium but still useful for screening and monitoring as they demonstrate cognitive dysfunction. It is recommended to perform these tests daily for early diagnosis in patients at risk (O'Keeffe et al. 2005). Mini-Cog, despite its limitations for sensitivity and predictive validity, is another test used to screen for cognitive impairment (Ismail et al. 2010).

There are several tools developed and validated to screen for delirium. It can help not to miss delirium in those who cannot talk such as patients at intensive care unit. The Confusion Assessment Method (CAM) is the most widely studied research tool in delirium and is perhaps the best tool for screening delirium (Inouye et al. 1990; Saxena and Lawley 2009). The CAM has four items based on the DSM-III-R criteria, which are determined by the patient, nurse and family interview. These features are as follows: (1) an acute onset of mental status changes or a fluctuating course, (2) inattention, (3) disorganized thinking and (4) an altered level of consciousness. The patient is diagnosed as delirious (i.e. CAM positive) if he or she has both features 1 and 2 and either feature 3 or 4. The CAM algorithm has a sensitivity of 94–100% and a specificity of 90–95%. It has a high inter-rater reliability when administered by trained interviewers. Most of US and UK guidelines recommend the CAM for routine use (Young and Inouye 2007).

Other frequently used tools are the Confusion Assessment Tool for Intensive Care Unit (CAM-ICU) (Ely et al. 2001), Intensive Care Delirium Screening Checklist (ICDSC) (Bergeron et al. 2001), Nursing Delirium Screening Scale (Nu-DESC) (Gaudreau et al. 2005) and NEECHAM Confusion Scale (Neelon et al. 1996). Informant Assessment of Geriatric Delirium Scale (I-AGeD) was developed to identify older people with delirium (Rhodius-Meester et al. 2013). Delirium Detection Score (DDS) is a useful scale to assess the degree of delirium and guide treatment, and the tool may also serve as a diagnostic scale (Otter et al. 2005). Delirium Rating Scale and Delirium Rating Scale-Revised-98 are the most commonly used tools to measure the severity of symptoms of delirium (Trzepacz et al. 2001).

It is extremely important to do a brief bedside neurological examination for a quick diagnosis in delirium like in all organic mental disorders. If there is suspicion of delirium, pupillary and fundoscopic examination should be carried out as well as checking for neck stiff ness. Patients with delirium can also demonstrate

nonspecific focal findings, such as asterixis or tremor on neurological examination, although the presence of any new neurological deficit, particularly with accompanying focal neurological signs, should raise suspicion of an acute cerebrovascular event or subdural hematoma. In many elderly patients and in individuals with cognitive impairment, delirium could be the initial manifestation of a new serious disease (Fong et al. 2009). In speech, dysphasia (anomia) usually presents as systematic misnaming. Most of the time there is misnaming reflecting people's previous experiences. A carpenter patient, for example, can call the stethoscope pliers.

A full physical examination should be carried on every patient who presents with changes in mental state. Once a diagnosis of delirium has been established, the potential cause—in particular, any life-threatening contributors—must be determined. All preadmission and current medications should be reviewed. A medical history must be meticulously obtained to detect some medical emergencies. An examination of temperature, pulse rate, blood pressure and respiration must definitely be performed. Delirium should be considered to be a medical emergency until proven otherwise; mortality rates for patients admitted to hospital with delirium can range from 10 to 26% (McCusker et al. 2002). Basic medical care, including airway protection, assessment of vital signs and laboratory tests to exclude treatable conditions such as infections, should be administered (Fong et al. 2009).

In cases where it proves difficult to do all the examinations and assessments required due to agitation or restlessness, assessing vital signs is an easy way of obtaining valuable information. Particularly general appearance, vital signs, hydration status and signs of physical trauma should be meticulously assessed. Enlargement of thyroid, hear murmurs and cardiac arrhythmias should be looked for. Chest auscultation, abdominal examınatıon for a possible liver or spleen enlargement and examination of the skin for jaundice or rash would very helpful. General appearance would point to some clues about substance or alcohol use. High fever, pupillary dilation or constriction and changes in respiratory rate, pulse rate and blood pressure can be diagnostic for certain medical conditions.

3.3.5 Laboratory Investigations

Laboratory tests for full blood count (helpful in infection and anaemia), electrolytes (high or low values) and glucose (hypoglycaemia, ketoacidosis); renal and liver function tests (renal and liver failure); thyroid function tests (hypothyroidism); urine sample (urinary tract infections); screening for substances in the urine (toxicological causes), thiamine and vit B12 levels (vitamin deficiencies); tests for bacteriologic and viral aetiologies (for infections) and sedimentation; screening for substance use including alcohol level; and tests for HIV and other infections if needed should be carried out. Neuroimaging is performed in selected patients to exclude a focal structural abnormality, such as an acute stroke, that might mimic delirium in its presentation (Fong et al. 2009).

3.4 Differential Diagnosis

Delirium can be confused with several psychiatric disorders due to various cognitive, behavioural and psychological symptoms. Variability of symptoms and the clinical picture of hypoactive and hyperactive types can make the diagnosis difficult in the majority of cases. Because of its primary presentation with cognitive symptoms in the older people, delirium mainly gets confused with other neurocognitive disorders especially dementia. However, it might still be difficult to distinguish it from other psychiatric disorders. Differential diagnosis is mostly based on the history, cognitive deterioration and the presence of underlying medical condition.

3.4.1 Distinguishing Delirium and Dementia (Major Neurocognitive Disorder)

"Dementia" describes a chronic and usually irreversible decline in cognitive and psychosocial functions. It usually results from an identifiable degenerative brain disease (e.g. Alzheimer's disease). Distinguishing delirium from dementia (which is subsumed under the newly named entity major neurocognitive disorder in DSM-V) is a common clinical dilemma. In order to make diagnosis of delirium or major neurocognitive disorder, DSM-V requires the exclusion of other diagnosis. "The cognitive deficits do not occur exclusively in the context of a delirium" for major neurocognitive disorder and "The disturbances are not better explained by another pre-existing, established, or evolving neurocognitive disorder" for delirium (American Psychiatric Association 2013). However, there is a strong interrelationship between delirium and dementia, both pathophysiological and clinical (Fick et al. 2002). First, delirium and dementia share the same clinical and psychological features to a great degree. Both are the most important causes of cognitive impairment and can mask each other. Second, dementia is the most important risk factor for delirium in the older patients (Margiotta et al. 2006; Pisani et al. 2007). Patients with dementia have already a fragile brain which is a high-risk factor delirium. The underlying vulnerability of the brain in patients with dementia may predispose them to the development of delirium as a result of insults related to acute medical illnesses, medications or environmental perturbations (Inouye 2006). Thus, delirium episodes can superimpose on a preexisting dementia, such as that due to Alzheimer's disease. Delirium superimposed on dementia (DSD) is increasingly problematic as the population ages. The prevalence of DSD ranges from 18 to 89% in hospitalized and community-dwelling older adults (Fick et al. 2002; Fong et al. 2009). Additionally, a co-existing major cognitive disorder can make the case of delirium more complicated. Finally, delirium can signal underlying vulnerability of the brain, with decreased cognitive reserve and increased risk for development of dementia in the future. Although it is not likely that the delirium itself causes the pathologic changes of dementia, severe precipitating factors such as prolonged hypoglycaemia or hypoxaemia can lead to permanent neuronal damage and dementia. Delirium might also mediate the effect of many factors, such as general surgery, anaesthesia,

critical illness, acute respiratory distress syndrome, prolonged intubation or sepsis, on long-term cognitive outcomes. There is no question that delirium contributes to worsening functional status, loss of independence and poorer outcomes among patients with dementia (Inouye 2006).

Because of all the listed factors above, it is a complex task to distinguish delirium and dementia in older people. The clinician must determine whether the individual has delirium; a delirium superimposed on a preexisting NCD, such as that due to Alzheimer's disease; or an NCD without delirium. But the traditional distinction between delirium and dementia according to acuteness of onset and temporal course is particularly difficult in those elderly individuals who had a prior NCD that may not have been recognized or who develop persistent cognitive impairment following an episode of delirium. Clinical features may be useful in distinguishing delirium from Alzheimer or Lewy body dementia. An impaired consciousness with fluctuating levels is one of the most helpful symptoms in the diagnosis of delirium. Although disorientation is substantially typical for delirium, it can be hard to examine the patients with memory impairment or amnesia. Studies showed that delirium is phenomenologically similar in patients with or without dementia (although patients with dementia have more symptoms). Cole et al. (2002) reported that frequency of ten symptoms of delirium investigated by them in the elderly hospitalized patients was largely similar to each other in two delirium patient groups with and without dementia; only the rates of baseline psychomotor agitation and disorganized thinking and disorientation were higher in the group with dementia. Similar findings have been confirmed in some other studies despite some small differences in the distribution of symptoms. The authors concluded that delirium may not be phenomenologically different in patients with and without dementia (Levkoff et al. 1992; Trzepacz et al. 1998; Liptzin 1999; Margiotta et al. 2006).

Despite the above, when there is a sudden change in cognition or behaviour in an older patient, one should first consider delirium. Although it is very difficult to distinguish delirium and dementia, some clinical features can be guiding. Dementia presents insidiously with a gradual course of decline, while delirium presents as a sudden loss of global cognitive function. With delirium, attention and level of consciousness are reduced and fluctuating; with dementia, these cognitive domains typically remain intact until the advanced stages. A careful history is very important to diagnose dementia with or without delirium. Dementia frequently presents with a history of chronic, steady decline in memory and is associated with difficulties in social relationships, work and activities of daily life. It is of paramount importance to compare current mental status or cognition with their baseline according to information taken from relatives or carers. It should always be evaluated in favour of delirium when there are cognitive and behavioural changes which develop over hours or days in the older people. The resolution of symptoms following treatment of an acute illness or precipitating factors can sometimes retrospectively confirm the diagnosis of delirium.

In most demented patients, there is increased wandering, confusion and agitation in late afternoon and early evening (15.00–19.00 h). This is known as "sundowning syndrome" which can mimic the symptoms of hyperactive delirium (Drake et al.

1997). In cases where there is worsening in the second half of the day, it is important to get information from carers about previous pattern. In dementia this is usually chronic, and every day it tends to recur almost at the same time of the day. There could be a similar picture in delirium but in delirium symptoms fluctuate day to day both in timing and severity. Whether or not they have dementia, worsening of the symptoms in older patients in the late afternoon, it is best to query other symptoms of delirium and if in doubt investigate it as delirium.

It can be particularly difficult to distinguish delirium from Lewy body dementia (DLB) because some features, such as visual hallucinations and symptom fluctuation, are common to both. But in dementia with DLB, the history is usually longer (months or years) and there could be parkinsonian symptoms. Still, the safest clinical approach is to consider that all older people presenting with confusion have delirium until proved otherwise (Young and Inouye 2007).

3.4.2 Distinguishing Hypoactive Delirium and Depression

Delirium is misdiagnosed as depression in up to 40% of cases (Farrell and Ganzini 1995). Particularly, hypoactive delirium can mimic a retarded depression with slowed thinking, psychomotor slowing, sleep disturbance, irritability, decreased concentration and memory impairment. Cognitive symptoms like poor concentration, memory difficulties and delusions, hallucinations and sleep problems can be seen in elderly patients with psychotic depression. The history of the patient is important in such cases. The presentation in delirium tends to be more acute, whereas in depressive illness mood symptoms predominate and are pervasive and persistent. Depression usually has a history of previous episodes and no fluctuations. The level of consciousness and attention remains unaffected in depression. The predominance of depressive cognitions like ideas of guilt and worthlessness in depression is important in differential diagnosis.

3.4.3 Psychotic Disorders and Bipolar Disorder with Psychotic Features

Vivid hallucinations and delusions as described above are seen quite often in delirium. Language disturbances, abnormal behaviours and agitation can mask the diagnosis particularly in hyperactive delirium. There could be aggressive behaviour to an extent of homicide in agitated patients. This situation could be very uncomfortable for carers and clinical staff. This clinical picture can easily be mistaken as psychosis. On the other hand, in the elderly psychotic patients, there could sometimes be problems with consciousness and orientation which can be mistaken as "confusion". Some acute psychosis, especially with mania, is capable of producing delirium-like states. Hence, delirium must be distinguished from brief psychotic disorder, schizophrenia, schizophreniform disorder and other psychotic disorders, as well as from bipolar with psychotic features. In these cases, the history taken

from relatives and other informants gains more importance. History about when and how symptoms started, episodes of psychosis or mood disorders are all important for diagnosis. In psychosis there is usually no impairment of awareness or attention. Schizophrenia is a longstanding illness which usually starts in young age typically with an insidious onset. Late-onset schizophrenia is very rare, and there is female gender and paranoid type predominance. Studies show that there are nearly 0.5% of people over 65 years with schizophrenia (Howard et al. 2000). Cognitive impairment is seen much less which is helpful in distinguishing from delirium. The sensorium is generally clear in schizophrenia and other psychotic disorders. Disturbance of thought and perception seen in delirium is often fragmentary, fluctuating and less complex than that seen in schizophrenia, in which delusions and hallucinations tend to be much more persistent and consistent. Delusions tend to be highly systematized, bizarre and uninfluenced by the environment. In contrast to psychoses, delusions in delirium are usually poorly systematized, fleeting and related to environmental stimuli. In schizophrenia it is usually auditory hallucinations that patients experience, whereas in delirium they are mostly visual or in other modalities. First-rank symptoms such as thought insertion, voices giving running commentary or talking to each other are not common in delirium.

Manic episodes can simulate hyperactive delirium, with diminished attention, agitation, rapid fluctuations and psychosis. Manic episodes in older adults often present with confusion, disorientation, distractibility and irritability rather than elevated, positive mood. Kraepelin in 1921 categorized mania into three types: acute, delusional and delirious. However, there is no clear consensus on the clinical characteristics associated with delirious mania or guidelines for treatment (Lee et al. 2012). Late-onset mania is more often secondary to or closely associated with other medical disorders, most commonly stroke, dementia or hyperthyroidism; it is also associated with medications including antidepressants, steroids, oestrogens and other agents with known central nervous system properties (Young et al. 1997). In the elderly patients, history and clinical presentation can help differentiate delirium from a manic episode. The history of depressive/manic episodes or elevated mood supports diagnosis of mania. Thought content is important as in depression cases. Increased self-esteem and grandiosity would suggest mania.

3.4.4 Other Disorders

Delirium associated with fear, anxiety and dissociative symptoms such as depersonalization also must be distinguished from acute stress disorder, anxiety and panic attacks. Acute stress disorder develops within the first month after exposure to a severely traumatic event such as rape, abuse, torture or war. One of the more common reasons for acute stress disorder in the elderly is witnessing the death of a friend or a loved one. Some arousal symptoms such as sleep disturbance, irritable behaviour and angry outbursts, hypervigilance, problems with concentration and exaggerated startle response can be seen in acute stress disorder and may be confused with delirium. Symptoms similar to delirium can be seen during an acute

anxiety or panic attack. On the other hand, delirious people with reduced cognitive function and limited speech may exhibit anxiety that can manifest as an anxiety disorder. History from carers and relatives and querying other symptoms of these disorders would be helpful in differential diagnosis.

Conclusion

Delirium is a common and significant healthcare concern in elderly people. It is characterised by recent onset of fluctuating inattention and awareness, linked to several precipitating and aetiological factors. The existing research evidence suggests that delirium could be prevented in a lot of cases. However, it is reported to remain undiagnosed in more than half of clinical cases. History taken from relatives, clinical staff or carers is as valuable as a careful cognitive assessment. A rational approach would be to consider and investigate any new cognitive or behavioural problems in an older patient as delirium.

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