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MELAS: An neurological disorders

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Abstract
MELAS is condition in which multiple body system impaired. It mainly occurred in children and at any age. MELAS is characterized by headache, weakness in body parts, pains, and loss of appetite, cognitive impairment and seizures. Several mechanisms such as mitochondrial proliferation, nitric oxide synthase, reactive oxygen species, dysfunction of endothelial, RNA and angiopathy are involved in pathophysiolocal basis of MELAS. Several genes mutation are involved in this complex illness. No specific medication available for management of MELAS. It is progressive consequences to severe neurological disorders and even death of patients. This review paper highlights the clinical signs and symptoms, genetic aspect and pathogenesis mechanism of MELAS.

Keywords: MELAS, mitochondria, oxidative stress, seizures

Introduction
Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) impaired the functions of body system mainly of nervous system, muscles and brain. Clinical signs and symptoms of MELAS generally appear in children, which further can initiate at any age (Ayman *et al*., 2015; Pavlakis *et al*., 1984; Ito *et al*., 2011) [2, 24, 25, 12]. MELAS is characterized by headache, weakness in body parts, pains, loss of appetite, cognitive impairment and seizures. It occurred at the age of 40 and in initial phase of MELAS, hemiporesis, impaired consciousness, severe headache, vision defect, and seizures. Repeated stroke type episodes, which leads to impair the functions of brain and caused vision loss, movement disorders and caused the dementia. In some cases of MELAS, lactic acid buildup in body of patients and this is known as lactic acidosis. Fatigue, weakness in muscles, difficulties in breathing caused by rise in acidity in blood. Few patients reported the myoclonus, ataxia, problem of heart and kidney, hormonal imbalance, diabetes and hearing loss (Ayman *et al*., 2015; Koenig *et al*., 2016; Koga *et al*., 2005) [2, 15, 17, 20].
Some of the study indicated that mutations of genes involved in MELAS, which caused the dysfunction of mitochondria (Kerr *et al*., 2010; Ayman *et al*., 2015) [14, 2]. These genes mutation linked to respiratory chain transport (RCT) and dysfunction of RCT caused oxidative stress in brain and muscles. It is progressive consequences to severe neurological disorders and death of patients. Several mechanisms such as mitochondrial proliferation, nitric oxide synthase, reactive oxygen species, dysfunction of endothelial, RNA and angiopathy are involved in pathophysiolocal basis of MELAS (Ayman *et al*., 2015) [2]. No specific medication available for management of MELAS. Some of the preventive measures such as dietary supplements of vitamin, redox compounds, nicotinamide, cytochrome combination with vitamin (C, B1 and B2), idebenone, arginine etc used for the MELAS (Koga *et al*., 2010; Castillo *et al*., 1995; Koga *et al*., 2008; Koenig *et al*., 2016; Hashimoto *et al*., 2015; Koenig *et al*., 2016; Koga *et al*., 2005; Tarnopolsky *et al*., 1997 [15, 3, 17, 19, 20, 9, 29,] Thus, MELAS is condition in which multiple body system impaired. This review paper highlights the signs and symptoms, genes mutations, pathophysiological mechanism involved in this complex rare illness. A better therapeutic therapeutic approach can be available for the management of MELAS by focusing on pathogenesis mechanism in this complex illness.

Clinical sign and symptoms of MELAS
MELAS is characterized by headache, weakness in body parts, pains, loss of appetite, cognitive impairment and seizures. Repeated stroke type episodes, which leads to impaired the functions of brain and caused vision loss, movement disorders and caused the dementia (Ito *et al*., 2008; Ayman *et al*., 2015) [11, 2]. In some cases of MELAS, lactic acid buildup in body of patients and this is known as lactic acidosis. Fatigue, weakness in muscles, difficulties in breathing caused by rise in acidity in blood (Koenig *et al*., 2016; Koga *et al*., 2005; Tarnopolsky *et al*., 1997) [15, 17, 20, 29].

Thus, MELAS is condition in which multiple body system impaired. This review paper highlights the signs and symptoms, genes mutations, pathophysiological mechanism involved in this complex rare illness. A better therapeutic therapeutic approach can be available for the management of MELAS by focusing on pathogenesis mechanism in this complex illness.

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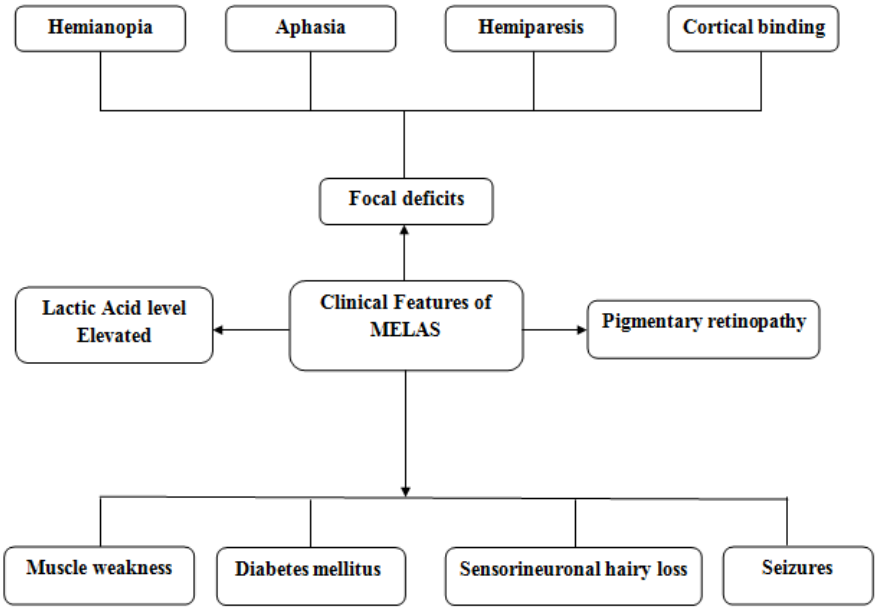

Fig 1: Clinical features of MELAS

Genetic of Melas

Several genes mutation involved in MELAS, which caused the dysfunction of mitochondria. These genes mutation linked to respiratory chain transport (RCT). Dysfunction of the RCT caused oxidative stress in brain and muscles. It is progressive consequences to severe neurological disorders and death of patients (Goto *et al*., 1990; Nesbitt *et al*., 2013; Ayman *et al*., 2015; Wang *et al*., 2015; Kerr *et al*., 2010; Koenig *et al*., 2016; Schon *et al*., 1997) [7, 31, 22, 2, 14, 15, 17]. Several genes mutation linked with MELAS are represented in figure-2.

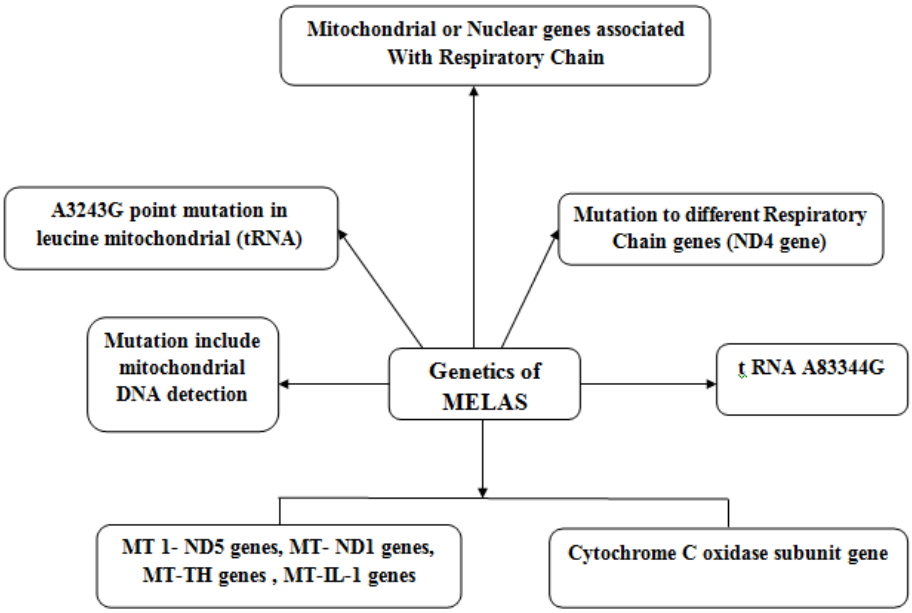

Fig 2: Genes involved in MELAS

Pathogenesis Mechanism Involved In Melas

Several mechanisms such as mitochondrial proliferation, nitric oxide synthase, reactive oxygen species, dysfunction of endothelial, RNA and angiopathy are involved in pathophysiolocal basis of MELAS (Ayman *et al*., 2015; Kerr *et al*., 2010; Koenig *et al*., 2016; Schon *et al*., 1997; Simon and John, 1999) [2, 14, 15, 17].

Gene mutation of m3243A-G leads to decreased mitochondrial protein synthesis. This process ultimately consequences to impaired energy production of mitochondria. Due to dysfunction of mitochondrial functions, it is unable to produce sufficient ATP to full fulfill the requirements of various organ systems. Multiple body's system impaired in MELAS. Decreased nitric oxide synthesis, arginine synthesis and increased the asymmetric dimethylarginine (ADMA) occurred in MELAS. The microvascular perfusion is impaired in this illness (Chomyn *et al*, 2000; Hasegawa *et al*., 1991; Goto *et al*., 1992; Sproule and Kaufmann, 2008) [4, 8, 32, 5]. Deficiency of Nitric oxide linked to MELAS (Wu *et al*., 1998) [6]. Due to multiple defect in metabolic process of glucagon and insulin, deficiency of insulin, resistance of insulin action and through increased glucogenesis developed the diabetes in MELAS (El-Hattab *et al*., 2014) [1]. Key factors in pathogenesis mechanism of MELAS are summarized in figure -3.

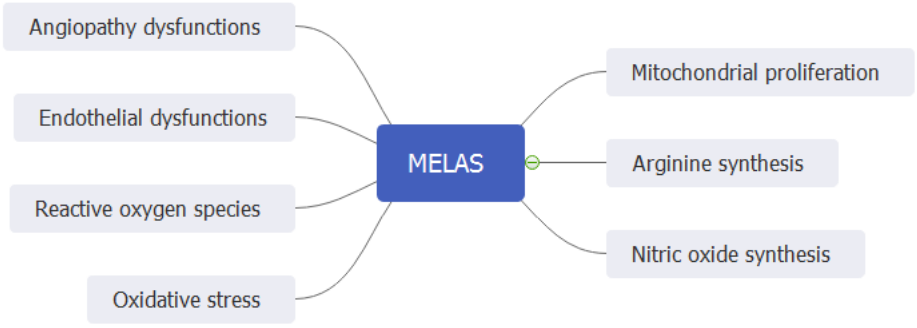

Fig 3: Key Factors in the pathogenesis mechanism of MELAS

Conclusion

MELAS impaired the functions of body system mainly of nervous system, muscles and brain. No specific medication available for management of MELAS. It is generally occurred in children and it is progressive illness, which caused severe neurological diseases and even death of patients. Several genes mutation and disease mechanism involved in the pathogenesis of MELAS. Various key factors such as reactive oxygen species, oxidative stress, nitric oxide synthase, endothelial dysfunction and arginine synthesis and dysfunction of mitochondrial are involved in the pathogenesis of the MELAS.

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