Chapter 8

Choroidal Neovascularization other than Age-related Macular Degeneration and Management in Geriatric Population

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INTRODUCTION

The geriatric age group was defined as individuals aged ≥65 years. In parallel with socioeconomic and health developments, the elderly population is increasing in our country as well as all over the world. In this section, choroidal neovascularization (CNV) in geriatric populations other than those with age-related macular degeneration (AMD) will be discussed. Although the geriatric population is the focus of this chapter, it is not possible to limit the disease to a certain age group. Some diseases occur in middle age or childhood, and some even have congenital onset. However, complications and sequelae also affect geriatric populations. Therefore, some of the diseases described here are less common in the geriatric population or are no longer active and do not require treatment. These are considered in the classification and description of the subject, provided that they are based on the literature.[1]

The disc-shaped fibrovascular membrane located under the macula was first described by Pagenstecher and Genth in 1875. CNV, defined as the formation of new blood vessels between the retinal pigment epithelium (RPE) and Bruch's membrane (BM), is usually located at the posterior pole. This structure, originating from the choroid, passes through the pathological opening in the BM and affects the RPE, photoreceptors, and other retinal layers. Although AMD is the first disease that comes to mind when we consider CNV, it is also observed in many eye diseases affecting the BM.[1,2] To the best of our knowledge, many factors affect CNV formation. Let us briefly examine these as follows:

PHYSIO-PATHOLOGICAL BASIS OF CHOROIDAL NEOVASCULARIZATION

Vasculogenesis and Angiogenesis

New vessel formation occurs in two ways: embryonic development and postnatal vascular remodeling. Vasculogenesis refers to the formation of new vessels during early embryogenesis through the aggregation and differentiation of vascular endothelial precursor cells called angioblasts, which refers to the expansion and remodeling of the capillary network originating from pre-existing vessels. Many factors affect angiogenesis; these factors have anti-angiogenic or pro-angiogenic effects and cause physiological or pathological development.[3]

The pathologic proangiogenic mechanism is activated by decreased choriocapillaris (CC) blood flow, relative choroidal ischemia, structural and functional disturbances in the BM, and oxidative stress, which is responsible for the development of CNV. The most important angiogenic stimuli are vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), insulin-like growth factor 1 (IGF-l), angiopoietins, interleukins, and tumor necrosis factor-alpha (TNFα). Pigment epithelial-derived factor (PEDF), transforming growth factor beta (TGFβ), angiostatin, endostatin, and tissue metalloproteinase inhibitors are also major angiogenesis inhibitors. VEGF is a glycoprotein with a key role in vasculogenesis and angiogenesis. It is the most important angiogenic molecule that is involved in CNV development. It has six isoforms: A, B, C, D, E, and placental growth factor (PGF). VEGF A, the most important isoform The major form of VEGF in pathological ocular neovascularization, is VEGFA 165. The most important stimulus for VEGF is hypoxia, which induces VEGF secretion from the vascular endothelium, pericytes, RPE, Müller and glial cells, and the choroidal fibroblasts. VEGF increases endothelial mitosis, survival, vascular permeability, and fenestration. It also has pro-inflammatory and neuroprotective properties. PEDF is the most potent angiogenesis inhibitor and is known to inhibit endothelial cell migration and induce apoptosis. Increased VEGF expression alone does not cause CNV; for CNV to occur, BM integrity must be compromised. BM integrity prevents CNV formation.[4-6]

Age-related Changes

Unlike the general patient population, age-related changes in choroidal tissue also occur in the geriatric population and contribute to the development of diseases. With cell aging, cumulative oxidative damage, mitochondrial DNA deletions, acceleration in protein degradation, slowing of the removal of free radicals, and advanced glycosylation end products occur. Cell and extracellular matrix adhesion is impaired. Lipofuscin (LF), which is formed as a result of photoreceptor metabolism, accumulates in the RPE over time. The thickness of the BM increases throughout life because of increased extracellular matrix production and decreased extracellular matrix degradation. Thinning of the choroid (especially in the macula), including the CC, and the decrease in blood flow reduce the clearance and permeability of waste in the BM. Catalase activity and vitamin E levels were also reduced in RPE. As our current knowledge does not fully explain the occurrence of CNV, treatment is not always successful. In addition, CNV may be an ocular manifestation of a systemic disease. In such cases, the related disease should be treated, as well as ocular pathology.[7,8]

ANTI-VEGF SYSTEMIC SIDE EFFECT

Anti-VEGF drugs are used in almost all the following diseases: they have ocular side effects (endophthalmitis, retinal tear, detachment, and hemorrhage). In addition, caution should be exercised regarding systemic side effects, especially in the geriatric population, considering the possible presence of comorbidities. Some studies have suggested a potential increase in the rate of systemic diseases associated with anti-VEGF injections, especially in elderly patients.[9] However, many recent studies have reported that anti-VEGF drugs administered intra-vitreally (IV) rarely enter the systemic circulation and that systemic side effects (especially thromboembolic events, such as subdural hematoma and myocardial infarction) are negligible.[10,11] As a clinician, anti-VEGF treatment should be postponed for a while, or other options should be attempted in patients who have recently had such diseases because of the medical-legal problems that may arise.[10,11]

CHOROIDAL NEOVASCULARIZATION CLASSIFICATION OUTSIDE ICMD

CNVs observed in AMD are called primary CNVs, and those observed in other diseases are called secondary CNVs. Secondary CNVs are usually similar to type 2 CNV (i.e., classical CNV) in the AMD classification, are located on the RPE, and do not cause pigment epithelial detachment (PED). As shown in **Figure 8.1**, optical coherence tomography (OCT), optical coherence tomography angiography (OCTA), and fluorescein angiography (FA) images were also similar to classical CNV (in addition to the features of each disease). The exception is pachychoroid spectrum disease, in which CNVs form PEDs.[10,11]

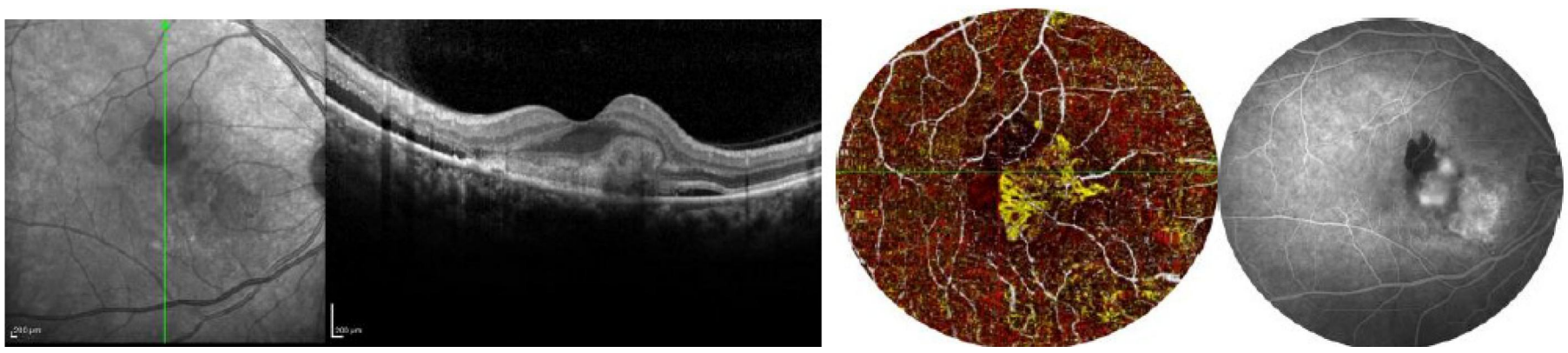

Figure 8.1. Non-AMD CNVs are usually located above the RPE and do not form PED; CNV above the RPE and subretinal fluid on OCT on the left; CNV vascular network on OCTA in the middle; subretinal hemorrhage and classic CNV on FA on the right

Different classifications can be used for non-AMD CNVs. Here, we use the classification according to the etiology previously made by Atmaca et al.[12] by reorganizing it in terms of its frequency and importance in the geriatric age group:

1. Degenerative Diseases (Age-related Macular Degeneration)

Pathologic myopia, angioid streaks, age-related choroidal atrophy, nodular drusen, and diffuse drusen.