Heterotopic bone formation in the eyeball is a rare finding. Some etiologic factors, such as trauma, chronic inflammation, and long-standing retinal detachment have been associated with the onset of intraocular ossification. We report here on a case of a 21-year-old woman with a history of blunt trauma fifteen years ago, who complained of right eye blindness. When the right eyeball eviceration was done, a hard, grayish mass was found. On histopathologic examination, the mass showed lamellar bone with fatty marrow and hyalinized tissue with dystrophic calcification. We diagnosed her case as intraocular ossification.

Key Words: Eye-Ossification, Heterotopic

Intraocular Ossification
- A Case Report -

Ho Sung Park · Tae Shik Kong
Kyu Yun Jang · Myoung Ja Chung
Woo Sung Moon · Dong Geun Lee
Myoung Jae Kang

Department of Pathology, Chonbuk National University Medical School, Jeonju, Korea

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Corresponding Author
Myoung Jae Kang, M.D.
Department of Pathology, Chonbuk National University Medical School, San 2-20 Keumam-dong, Dukjin-gu, Jeonju 561-180, Korea
Tel: 063-270-3075
Fax: 063-270-3135
E-mail: mjkiang@moak.chonbuk.ac.kr

Heterotopic bone formation may occur almost in any tissue but it is rarely found in the eyeball. A few cases of the intraocular ossification have been reported since it was first investigated. According to the study of Finkelstein and Boniuk who examined 2,486 enucleated eyes, intraocular ossification was found in only 119 cases (4.8%). Intraocular ossification is known to occur in association with trauma, chronic inflammation, long-standing retinal detachment, microphthalmos, buphthalmos, and some intraocular tumors. Although the pathogenesis of intraocular ossification is still under consideration, we are going to review the suggested theories of its pathogenesis. We are also going to review the clinicopathologic features of intraocular ossification.

CASE REPORT

A 21-year-old woman, was admitted to our Department of Ophthalmology due to loss of visual acuity of the right eye. She had a history of blunt trauma to the right eyeball fifteen years ago. Since then, her visual acuity of the right eye gradually decreased, but she had never been treated. On ocular examinations, the visual acuity of her right eye was at a state of non-light perception, the right iris showed atrophy and posterior synechia, the right pupil was fixed to 0.2 cm in diameter, and there was a mature cataract on the right lens. The fundus of the right eye couldn’t be examined due to media opacity. Her left eye was normal. The eviceration with hydroxyapatite implantation of the right eye was done. When the right eyeball contents were removed, a hard, grayish, 1 × 0.9 × 0.8 cm-sized mass was found. On microscopic examination, the ocular tissue adjacent to the mass was too disorganized to distinguish the origin of the mass, but we could suggest the origin as choroid because the ocular tissue adjacent to the mass showed abundant pigmented melanocytes and prominent vascular systems. The mass was made up of bone tissue that showed lamellar arrangement of mature osteocytes and hyalinized tissue with dystrophic calcification. The bone marrow was entirely replaced by adipose tissue and there was no hematopoietic tissue found (Fig. 1). There was transition from hyalinized tissue with dystrophic calcification to bone tissue noted in the
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The mass is made up of lamellar bone, fatty marrow, and hyalinized tissue with dystrophic calcification (Fig. 1). In the periphery of the mass (Fig. 2), foci of dystrophic calcification and hyalinization were found (Fig. 3). In the stroma of the choroid separated from the mass, foci of dystrophic calcification (arrows) and hyalinization are found.

DISCUSSION

Heterotopic bone can be formed at the focus of calcification, and calcification can occur in degenerative tissues accessible to body fluids. If calcification persists for a long time, it may be changed to ossification. So, calcification is said to be a necessary precursor to ossification.

Intraocular ossification is rare, as was shown in the study of Finkelstein and Boniuk. They examined 2,486 enucleated eyes and found intraocular ossification in 119 cases (4.8%); 67% were from men, 32% were from women. In their study, the most frequent cause of intraocular ossification leading to enucleation was both perforating and nonperforating trauma. There are other causes including inflammatory diseases such as polio-induced keratitis, toxoplasmosis, and endophthalmitis, long-standing retinal detachment, congenital anomalies such as microphthalmos, buphthalmos, and persistent hyperplastic primary vitreous, and some tumors such as choroidal hemangioma, choroidal osteoma, choroidal melanoma, and teratoma.

Monsalie et al. found an interesting correlation between age and the etiological factors for this condition. In the 10-50 year old age group, trauma was the leading etiological factor, while in the 51-90 year old age group inflammation was the leading cause. It is clear that trauma is the leading etiological factor in the young age group and inflammation is the leading cause in the older one.

Intraocular ossification has been found in lens, retina, all part of the posterior segments and the cyclitic membrane, and the most frequent site is in the region of the retinal pigment epithelium and the inner surface of the choroids. Bone usually forms...
in the eye at least ten years after the initial injury or disease, but several cases have been reported in which bone formed in less than two years.\textsuperscript{1} Although the stimulus for osteogenesis is still not understood, we do know that bone formation in general requires precursor cells such as osteoblasts, and they are derived from two types of mesenchymal precursor cells. The first type is the osteogenic precursor cell found only in the marrow stroma; the second is the inducible precursor cell found in the connective tissue framework of many tissues and in the circulating blood.\textsuperscript{7} It has been assumed that the predisposition to ossification of the choroid plexus was due to its inherent high vascularity resulting in the vascular delivery of osteoblasts. However, it is now suggested that intraocular ossification results from osteoblastic transformation of the retinal pigment epithelium.\textsuperscript{5} Retinal pigment epithelium is now known to be a multipotential cell with the capacity to differentiate into a mesenchymal phenotype, including fibroblasts and osteoblasts. Moro\textsuperscript{9} investigated osteogenesis of ocular tissues by injecting 95\% alcohol into the vitreous humor and then he repeated the injection two months later, and he also implanted lens fibers, lens capsule, and choroids beneath the skin of the ear. This only led to the development of compact bone when the uveal tissue was implanted. He concluded that bone formation within the eyeball depends upon the osteogenic power of uveal tissue and the presence of fresh connective tissue that may act as a framework for development of bone tissues. This study supports the likelihood of the second hypothesis. Our case revealed a transition from hyalinized tissue with dystrophic calcification to bone tissue. This finding supports the notion that ossification may be formed at the focus of calcification, but it gives no information about which one of the two hypotheses is more possible.

The inducible osteogenic cells can form bone only in the presence of an inducing agent. In the eye, the inducible cell for osteogenesis appears to be the pleuripotential retinal pigment epithelium, while the inducing agents, although not specifically identified, could possibly be mediated by trauma, inflammation, or anoxia subsequent to chronic retinal detachment.\textsuperscript{1,8}

What kind of bone tissue is formed in intraocular ossification? In the report by Monselise \textit{et al},\textsuperscript{6} they examined 20 cases of intraocular ossification, and compact bone was found in 9 cases and spongy bone was found in 10 cases. One case showed both types. These results show that the bone formation is not related to the bone type for intraocular ossification. However, these findings support an interesting correlation between the type of bone and the etiological factors; compact bone is more frequently encountered in post-traumatic cases, while spongy bone is more frequently encountered in post-inflammatory cases. So, we can presume trauma is a leading cause for compact bone and inflammation is a leading cause in spongy bone.

Our case had a trauma history, and this is most common cause of intraocular ossification in the young age group. It seems that trauma may have acted as an inducing agent of osteoblastic transformation of retinal pigment epithelium to form compact bone in this case.

The hematopoietic elements in the marrow of intraocular bone may be present (5-70\%), or this may be totally absent despite the close association of osteogenesis and hematopoiesis.\textsuperscript{1,6}

More study is needed to clarify the pathogenesis of intraocular ossification. However, case reports are rare due to lack of interest because ossification is regarded simply as a well-known end-point in long-standing degeneration, in spite of its rare occurrence in the eyeball.

REFERENCES