

## Stroke Associated with Left Ventricular Noncompaction in Osteogenesis Imperfecta

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**ABSTRACT** Osteogenesis Imperfecta (OI) is an autosomal inherited disorder characterized by blue sclera, hyperexcitable ligaments, fragile bones, deafness and teeth malformations. A 36-year-old man with undiagnosed OI was admitted to hospital with acute onset speech disorder, left sided hemiparesis and hemihypoesthesia. Magnetic Resonance Imaging (MRI) showed acute infarction on the right middle cerebral artery (MCA) territory. Transesophageal echocardiography (TEE) revealed left ventricular noncompaction (LVNC). Right MCA occlusion, stenosis of the proximal left internal carotid artery (ICA), vertebrobasilar contour irregularities were observed in MR angiography. Ischemic and hemorrhagic vascular events may be observed in disease course since Type 1 collagen is the key structural composition of the vessel wall. Furthermore, ventricular noncompaction is a special cardiomyopathy which has gained increasing attention and might cause ischemic cerebrovascular diseases. The purpose of presenting this case is the fact that OI with LVNC is a rare clinical entity in the etiology of cerebrovascular disorders in young adults.

**Keywords:** Osteogenesis imperfecta; stroke; noncompaction of the ventricular myocardium

Stroke in people under 45 years of age, is observed less frequently than older patients, and it is classified as young stroke.<sup>1</sup> Although cardioembolic causes were determined more frequently in some studies, the most common underlying aetiologic cause has been remained 'undetermined' in some of.<sup>2,3</sup>

Osteogenesis imperfecta is a heterogeneous connective tissue disorders in which neurovascular diseases are uncommon. It is characterized by blue sclera, hyperexcitableligaments, fragile bones, teeth malformations, and deafness.<sup>4</sup> Osteogenesis imperfecta is associated with type 1 collagen abnormalities and decreasedsynthesis of normal type 1 collagen. Since type 1 collagen is a major structural component of vessel wall, musculoskeletal and cardiovascular system, ischemic stroke may occasionally be observed in connective tissue disorders.<sup>5</sup>

### CASE REPORT

A 36-year-old man was admitted to our emergency clinic with loss of consciousness, slurred speech and weakness on his left side. Physical examination showed blue sclera, dysarthria, left-sided hemiparesis and hemihypoesthesia (Figure 1). There were multiple bone deformities in his legs and arms induced by minor trauma.



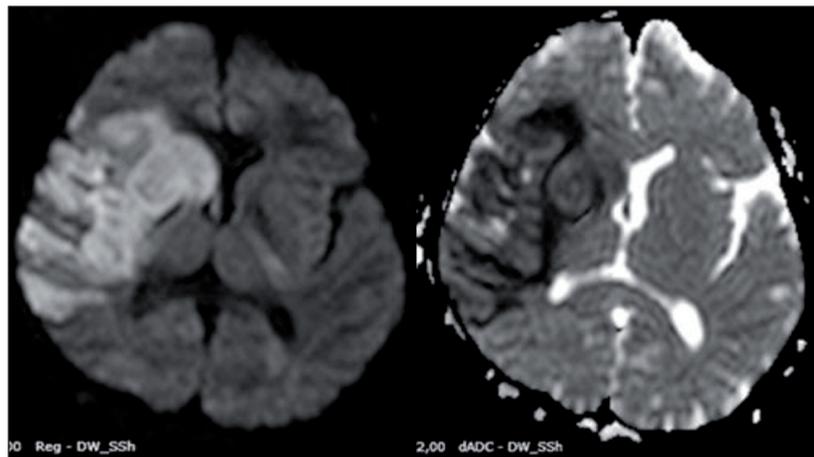
**FIGURE 1:** Blue sclera on his physical examination.

Diffusion-weighted magnetic resonance imaging on admission revealed an acute hemispheric infarction involving right MCA area (Figure 2).

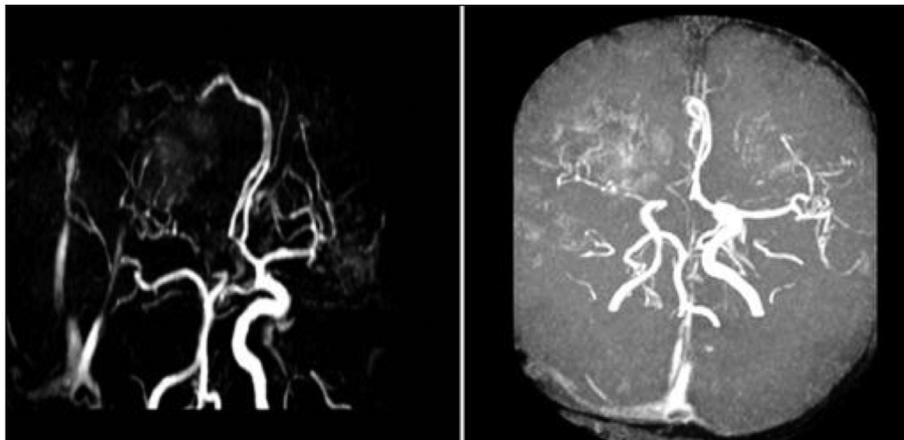
The initial workup included biochemical blood tests, vasculitis panel, electrocardiography, transthoracic echocardiography and color dopp-

ler ultrasound of carotid and vertebral arteries. No pathology could be found in initial examination. Patient underwent transesophageal echocardiography (TEE) and MR angiography of carotid and vertebrobasilar system. Transesophageal echocardiography revealed left ventricular noncompaction (LVNC) and MR angiography showed right MCA stenosis, proximal stenosis of left MCA, vertebrobasilar contour irregularities and bilateral collateral formations around MCA (Figure 3).

Thinning of bone cortex and low bone density were detected in radiographs (Figure 4). He had low bone mineral density in the proximal femur associated with osteopenia. Sensorineural hearing loss was detected by audiogram. Based on these findings, the patient was diagnosed with OI. His



**FIGURE 2:** Diffusion-weighted MRI showed acute infarction on the right Middle Cerebral Artery territory.



**FIGURE 3:** Right Middle Cerebral Artery occlusion, stenosis of the proximal left internal carotid artery, vertebrobasilar contour irregularities in MR angiography.

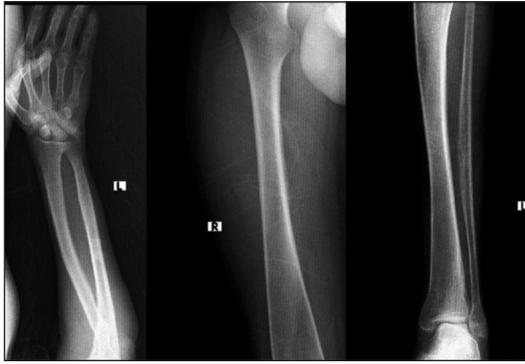


FIGURE 4: Radiographs.

family refused genetic analyses. Oral anticoagulant therapy was included in treatment, however it was discontinued because of the intramuscular bleeding in the right leg of the patient three days later. Consequently his treatment was continued with antiagregant therapy after resorption of hematoma. He received physical rehabilitation following the stroke.

## DISCUSSION

Osteogenesis imperfecta has many clinical forms and type 1 is the most common form. COL1A1, COL1A2, IFITM5, SERPINF1, CRTAP are the mutations associated with clinical severity and production of defective type 1 collagen.<sup>4</sup> Children with OI who are born into family with no history of the disorder have a new dominant mutation or autosomal recessive pattern of inheritance similarly with our patient.<sup>6</sup> Even though we could not perform analysis on our patient, we think that performing genetic analysis may be unnecessary in a patient whose clinical presentation is so well defined.

Neurovascular diseases and cardiovascular involvement are relatively rare in OI among the connective tissue diseases such as Pseudoxanthoma elasticum, Ehlers-Danlos and Marfan syndrome and it doesn't correlate with severity of the disease.<sup>7,8</sup> Carotid-cavernous fistula, vertebral artery dissection, aortic root stiffness, cerebral aneurysms, Moyamoya disease, ulnar artery aneurysm, type 1 aortic dissection are the vascular pathologies reported.<sup>9</sup> Aortic root dilatation is the most frequently reported cardiovascular pathology specific

for OI, as well.<sup>9</sup> MR angiography showed stenosis and occlusion of the cerebral arteries in our patient. However TTE was normal, TEE revealed LVNC on apical, mid-inferior segments of ventricular wall. Left ventricular noncompaction is a cardiomyopathy characterized anatomically by deep trabeculations in the ventricular wall. It can occur in isolation or in association with other cardiac disorders.<sup>10</sup> It's shown in Figure 5.<sup>11</sup> However, left ventricular trabeculations may also be found in healthy hearts and hypertrophic hearts secondary to dilated valvular or hypertensive cardiomyopathy. Trabeculation localization is common on mid-lateral, apical, mid-inferior segments in left ventricular noncompaction as in our patient. Normal hearts frequently have trabeculations from the free wall to the ventricular septum.<sup>12</sup>

We thought that LVNC could be probably linked to a collagen pathology, which is at the origin of OI. Type 1 collagen is a major structural component of myocardium.<sup>13</sup> Oral anticoagulant therapy has been recommended to patients due to these additional reasons. We also used warfarin as anticoagulant therapy, but as a result of increased capillary fragility and platelet dysfunction in OI, bleeding occurred. Platelet dysfunction also plays a role in subdural, subarachnoidal and intraparenchymal hemorrhagic events. Tendency to bleeding and bruising is well-documented in these patients.<sup>14</sup> Increased capillary fragility, decreased platelet retention, and decreased factor VIII production have been reported.<sup>15</sup>



FIGURE 5: Left ventricular non-compaction of apical and lateral wall.

In conclusion, we have described the case of 36-year-old man with undiagnosed OI and left ventricular noncompaction, which presented with cerebral embolism. Ventricular noncompaction is thought to be responsible for cerebral infarction in this patient. Occlusion and stenosis of cerebral arteries as a result of impairment of arterial wall also facilitate ischemic events. To our knowledge, there is no report presenting OI with left ventricular noncompaction. Our case has been presented due to the presence of stroke as a result of LVNC and abnormalities of cerebral arteries in OI. Since neurological complications can be the first manifestation of the connective tissue disorders, as a neurologist, we should know how to manage these diseases.

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### Informed Consent

Informed consent was obtained from the patient.

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### Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

### Authorship Contributions

**Idea/Concept:** Hülya Tireli, Derya Bayram; **Design:** Derya Bayram, Tamer Bayram; **Control/Supervision:** Hülya Tireli, Derya Bayram; **Data Collection and/or Processing:** Derya Bayram, Tamer Bayram; **Analysis and/or Interpretation:** Hülya Tireli, Derya Bayram; **Literature Review:** Derya Bayram, Tamer Bayram; **Writing the Article:** Derya Bayram, Tamer Bayram; **Critical Review:** Hülya Tireli, Tamer Bayram; **References and Fundings:** Hülya Tireli; **Materials:** Derya Bayram.

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