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Life-Threatening Aortic Dissection during Pregnancy: A Case Report of Undiagnosed FBN1-Related Marfan Syndrome at 39 Weeks Gestation

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female, 39-year-old
Final Diagnosis: Marfan syndrome
Symptoms: Chest pain
Clinical Procedure: —
Specialty: Anesthesiology
Objective: Rare disease

Background: Inherited deficiencies in the FBN1 gene, which encodes fibrillin-1, result in Marfan syndrome, an autosomal dominant connective tissue disorder that is associated with aortic root dilatation and predisposes to aortic dissection. This report is of a 37-year-old woman presenting at 39 weeks of pregnancy with acute thoracic aortic dissection due to previously undiagnosed FBN1-related Marfan syndrome. This case report aims to illustrate the challenges in the diagnosis and in the peri-operative management of acute aortic dissection during pregnancy.

Case Report: A healthy 37-year-old woman at 39 weeks of gestation presented to our hospital with dyspnea and chest pain. Initial evaluation for pulmonary embolism with chest computed tomography was unrevealing. The patient was admitted to the intensive care unit for further management. Overnight, her clinical conditions deteriorated, and a transthoracic echocardiography was obtained, demonstrating an acute ascending aortic dissection. She emergently underwent a successful combined cesarean section and ascending aortic dissection repair, with no immediate complications. On postoperative day 4 she developed cardiac tamponade, for which she underwent emergent mediastinal exploration. She was discharged home on postoperative day 10. A month later she completed genetic testing, which revealed a pathogenic mutation in the FBN1 gene, consistent with a molecular diagnosis of Marfan syndrome.

Conclusions: This report has shown that FBN1-related Marfan's syndrome has a variable clinical presentation that can include life-threatening aortic dissection during pregnancy. Successful diagnosis and management of these patients is challenging and requires multidisciplinary expertise, including confirmation of the diagnosis by a clinical geneticist.

Keywords: Anesthesia, Obstetrical • Aneurysm, Dissecting • Marfan Syndrome • Pregnancy Complications, Cardiovascular

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/940628

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Background

Aortic dissection in pregnancy is extremely rare and has been reported in only 0.0004% of all pregnancies [1], accounting for 0.1-0.4% of all aortic dissections, but with a high mortality rate for mother and fetus [2]. Risks factors associated with aortic dissection include hypertension, collagen disorders such as Marfan syndrome, Ehlers-Danlos syndrome, bicuspid aortic valve, and Turner syndrome; inflammatory diseases leading to vasculitis such as giant cell arteritis, Takayasu arteritis, rheumatoid arthritis; and a family history of aortic dissection and preexisting aortic aneurism [3-6]. Pregnancy per se is a risk factor of aortic dissection, likely secondary to the physiologic hemodynamic changes that lead to increased circulatory volume and elevated systemic blood pressure, and to the hormonal alterations that cause structural changes in the aorta [7-9]. Pregnant women with underlying aortopathies such as Marfan syndrome are more susceptible to pregnancy-related aortic dissection [7]. In fact, in the National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC) registry [10], pregnant patients with Marfan syndrome had an 8-fold increased risk of aortic dissection compared with non-pregnant Marfan patients [8]. In high-risk women, multidisciplinary preconception counseling is advisable [11]; however, many women at high risk of aortic dissection are not recognized early [7]. This report is of a 37-year-old woman presenting at 39 weeks of pregnancy with acute ascending aortic dissection due to unrecognized FBN1-related Marfan syndrome.

Case Report

A previously healthy, 37-year-old, G1P0 woman, 39 weeks pregnant, and without apparent complications or remarkable family history, presented to the emergency department of our community hospital with severe exertional chest and back pain associated with shortness of breath. Initial vital signs showed a blood pressure of 111/71 mmHg, pulse 85 beats per minute, oxygen saturation 100% on room air, and body temperature of 36.4ºC. The initial physical examination showed a comfortable gravid woman. No cardiac murmur or skeletal abnormalities were appreciated. Shortly thereafter she developed hypoxemia with an oxygen saturation of 80% on room air. Pulmonary embolism (PE) was suspected, and the patient underwent an emergent chest computed tomographic (CT) scan with intravenous contrast, timed to evaluate the pulmonary arteries (CTPA), which showed no pulmonary embolism but did reveal a possible differential density within the aortic arch and descending aorta (**Figure 1**) of unclear significance.

She was then admitted to the intensive care unit for further monitoring. Her symptoms worsened overnight, and a transthoracic echocardiogram (TTE) was obtained, demonstrating acute

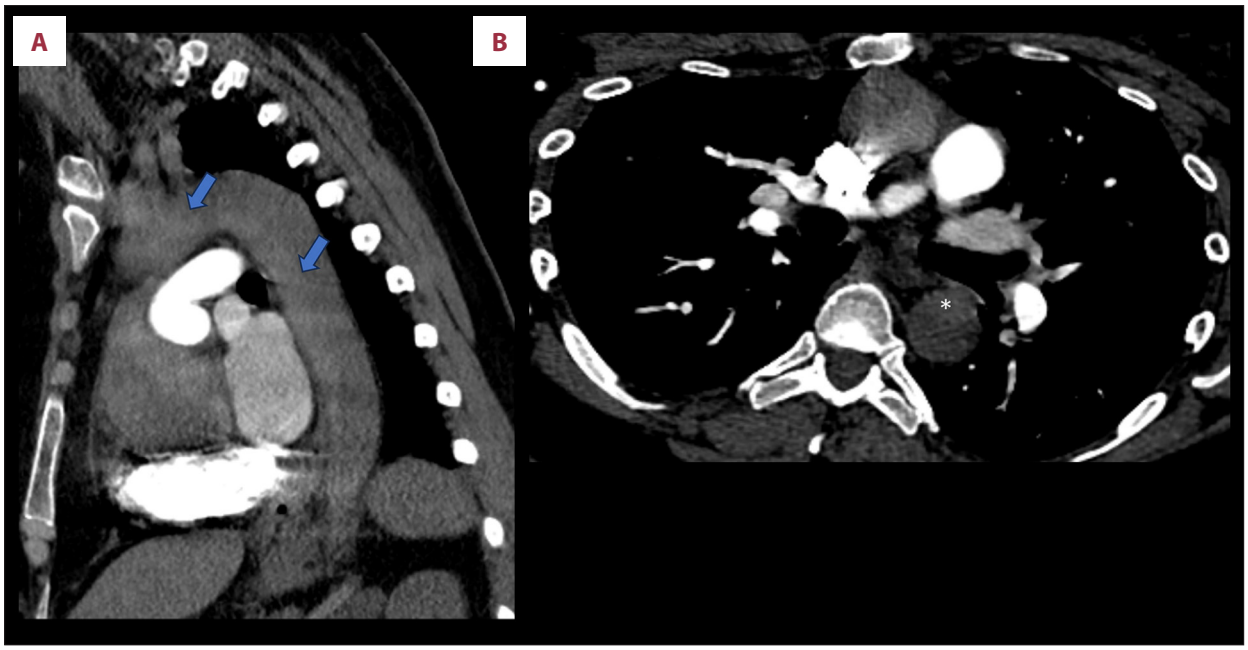

Figure 1. Chest computed tomography scan with contrast. (**A**) Sagittal chest computed tomography scan with contrast administration timed to evaluate the pulmonary arteries. No pulmonary embolic disease was detected. Higher density of blood along the aortic arch and descending aorta (arrows) was appreciated. The fetus was intentionally not imaged to minimize radiation exposure. (**B**) Axial chest computed tomography scan with contrast administration timed to evaluate the pulmonary arteries showing the true lumen of the descending aorta dissection (star).

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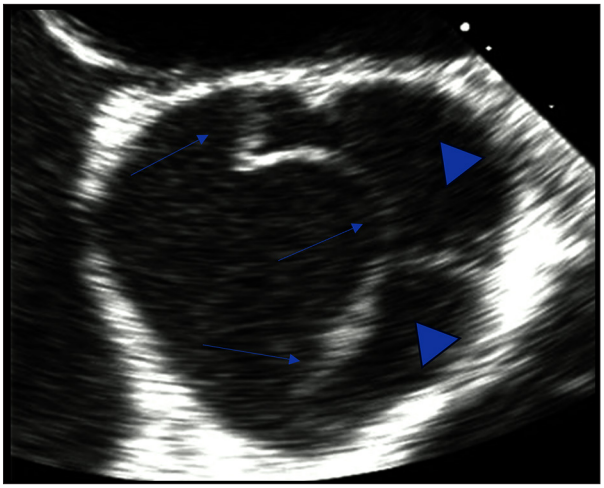

Figure 2. Transthoracic echocardiogram of the aortic valve, short axis view. Short axis view of the aortic valve demonstrating a dissection flap (arrows) in close proximity to, and prolapsing across, the aortic valve (triangles), with significant aortic valve regurgitation.

ascending aortic dissection involving the aortic root and proximal ascending aorta (diameter of 58 mm at the sinus of Valsalva) (**Figure 2**). At that time, fetal heart tone monitoring showed fetal heart rate deceleration for 60 seconds. Consultation from cardiology, cardiothoracic surgery, anesthesiology, critical care, and obstetrics was obtained and the decision was made to take the patient emergently to the operating room without further imaging, for combined cesarean section and ascending aortic dissection repair. A cryopreserved blood sample was also obtained, as blood transfusion was anticipated.

In the operating room, a left-sided radial arterial line was placed under local anesthesia and rapid sequence-general anesthesia was induced with 40 mcg of remifentanil, 150 mg of propofol, and 100 mg of succinylcholine. The patient was intubated successfully, and a pulmonary artery catheter was placed. General anesthesia was then maintained with remifentanil infusion at 1 mcg/kg/min, 2% sevoflurane, and rocuronium. Intraoperative transesophageal echocardiogram (TEE) confirmed a type A aortic dissection associated with severe aortic regurgitation, mild mitral regurgitation, and an ejection fraction of 55% (**Figure 3**). Cesarean section was performed via low transverse incision, with delivery of a single male infant. Initial Apgar scores were 8 and 9 at 1 and 5 min, respectively. After adequate uterine hemostasis was achieved, the patient was fully heparinized and cardiopulmonary bypass was instituted through aortic arterial cannulation and 2-stage venous cannulation in the right atrium and superior vena cava. Circulatory arrest was initiated with a temperature of 18ºC and a flat electroencephalogram (EEG). Retrograde cerebral perfusion was performed via superior vena cava cannula and monitored with cerebral oximetry. On direct inspection of the heart, aortic dissection appeared to extend to the right coronary artery with associated periarterial hematoma. The patient underwent repair of the ascending aortic dissection with partial arch replacement, reimplantation of the innominate artery, resuspension of the aortic valve with root augmentation, and single-vessel coronary artery bypass grafting with a saphenous vein graft to the right coronary artery (**Figure 4**). Her total cardiac bypass time was 6 h 33 min. Her circulatory arrest time was 54 min. She was progressively rewarmed and weaned from cardiopulmonary bypass using a low dose of epinephrine (0.02 mcg/kg/min).

The patient was extubated on postoperative day 1. On postoperative day 4, she developed cardiac tamponade from myocardial bleeding after removal of temporary pacing wires, for which she underwent emergent mediastinal exploration and control of the bleeding with 7-0 Prolene suture. Her remaining postoperative course was uneventful, and she was started on labetalol for blood pressure reduction. Both patient and infant were discharged from the hospital on postoperative day 10. One month after being discharged, the patient was seen by a genetic counselor. She underwent genetic testing with a 35-gene comprehensive aortopathy panel, which showed a heterozygous mutation

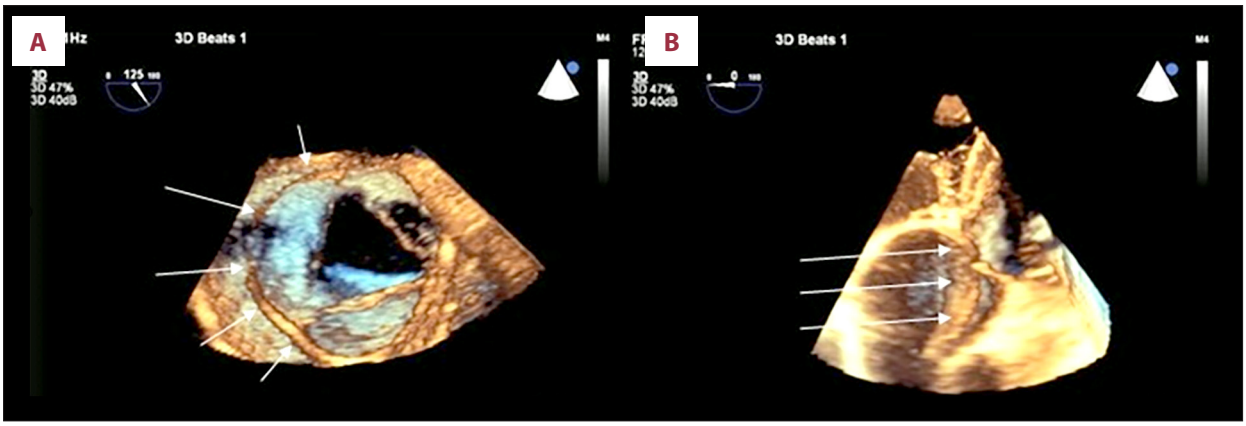

Figure 3. Three-dimensional transesophageal echocardiogram of the aortic valve. Short axis view (**A**) and modified 3-chamber view (**B**) demonstrating a dissection flap in close proximity to, and prolapsing across, the aortic valve (arrows).

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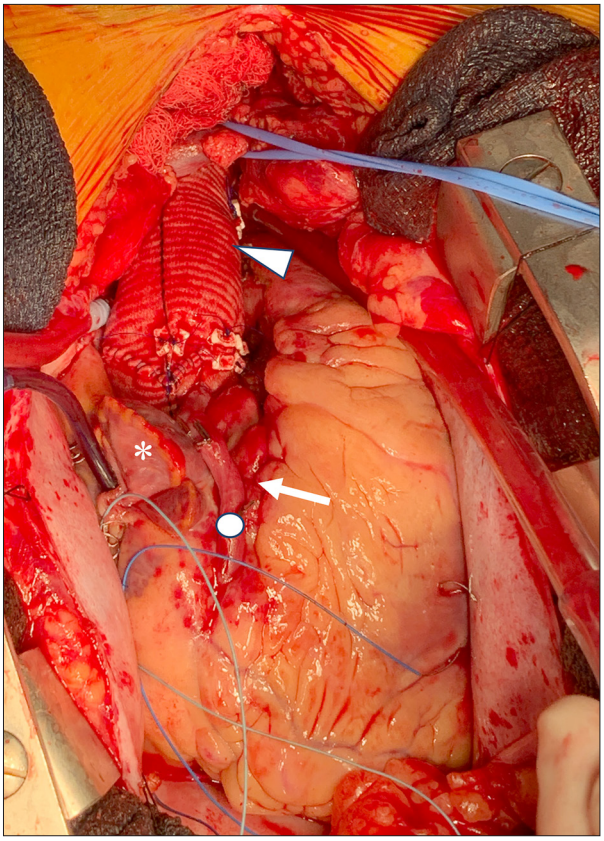

Figure 4. Post-bypass gross photograph of the heart and ascending aorta. The aortic root was reconstructed using a valve-sparing technique. The right atrium (star) was used for central venous cannulation and later secured with a blue tourniquet. The arterial cannula has been removed and hemostasis achieved using a pledgeted purse string suture on the lateral side of the aortic graft (triangle). The right coronary artery demonstrates periarterial hematoma (arrow) from the proximal dissection, which was bypassed with a vein graft (circle). A blue vessel loop is retracting the innominate vein to better expose the innominate artery, which was reimplanted.

in the *FBN1* gene (c.247+1G>A), consistent with a molecular diagnosis of *FBN1*-related Marfan syndrome, which, together with her history, led to a final diagnosis of Marfan syndrome. Genetic testing was also performed on the patient's child, who was found to carry the same *FBN1* mutation. In the 12 months since presentation, the patient has been followed closely in our multispecialty vascular center. She has tolerated labetalol well and has long-term contraception in place. Serial CT imaging has demonstrated a stable dissection of the aorta beginning at the level of the left subclavian artery and extending to the descending thoracic and abdominal aorta and to both common iliac arteries, with a maximum diameter of 4.3 cm at the level of the proximal descending thoracic aorta (**Figure 5**). Her child has also been followed routinely since birth and he appears to be in good health.

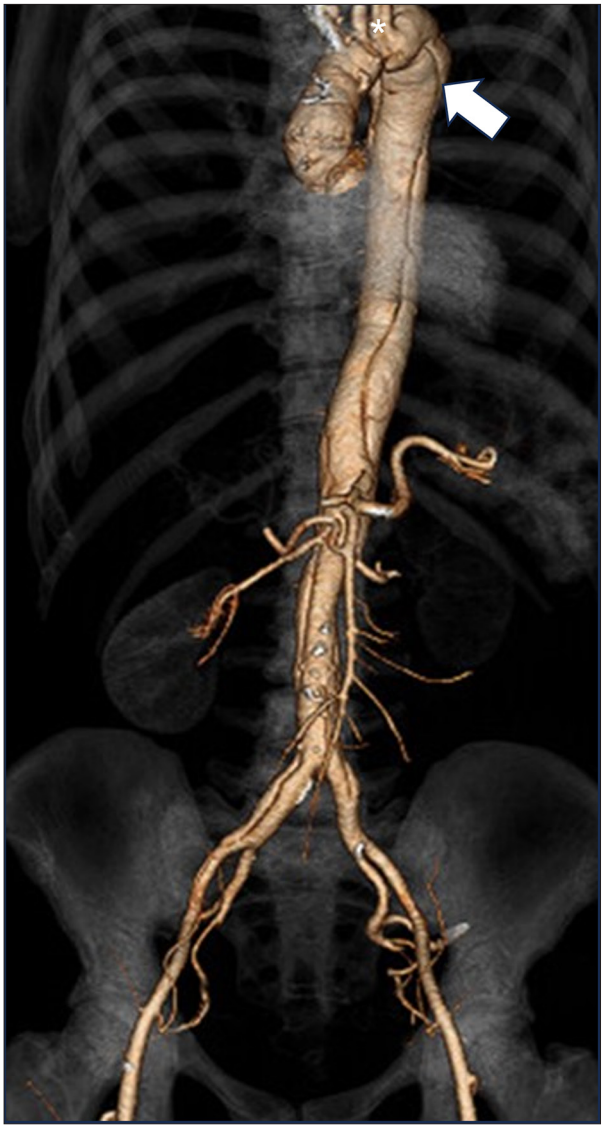

Figure 5. Post-procedure three-dimensional computed tomography scan of chest, abdomen, and pelvis. Postprocedural changes of the aortic root and unchanged aortic dissection extending into the left subclavian artery (star), to the descending thoracic and abdominal aorta, as well as to both common iliac arteries, with a maximum diameter of 4.3 cm at the level of the proximal descending thoracic aorta (arrow).

Discussion

This report demonstrates that FBN1-related Marfan syndrome can present with life-threatening aortic dissection during pregnancy, and a successful outcome requires multidisciplinary expertise. Aortic dissection in pregnancy is a rare but life-threatening event associated with significant maternal-fetal morbidity and mortality [7]. Prior cases of aortic dissection in pregnancy have reported a mean age of 32±5 years, similar to

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our patient, and across all gestational ages [2]. Usually, if the dissection occurs after 30 weeks of gestation, like in our case, a "single-stage delivery and aortic repair" is preferred, as previously described in 30% of cases, with an 83% maternal survival rate and 67% fetal survival rate [2,8,12,13].

Marfan syndrome is a well-known risk factor for aortic dissection [6,7]. Marfan syndrome is an autosomal dominant disorder caused by a mutation in FBN1 gene which encodes fibrillin 1, a component of microfibrils located mainly in the media [14]. FBN1 gene mutation predisposes to the development of aortic aneurysms and dissections as well as skeletal and ocular features [14]. FBN1-related Marfan syndrome has a broad spectrum of clinical presentations ranging from mild disease involving 1 or 2 organs to a multisystemic organ syndrome [11]. Most cases of aortic dissections in pregnant patients with Marfan syndrome occur during the third trimester and are commonly due to type A dissection [8,15], although cases of type B dissections have been described [16], as well as cases in the post-partum period [2,17].

Patients with Marfan syndrome should be counseled about the possible maternal and fetal risks associated with pregnancy [11], and if pregnancy is desired, prophylactic aortic repair is suggested for those with aortic root diameter exceeding 40-45 mm according to the most recent American Heart Association/American College of Cardiology and European Society of Cardiology guidelines [8,12,13]. During pregnancy, close follow-up with serial echocardiograms and consultation with cardiovascular specialists are crucial for a successful and safe pregnancy, as has been reported in a recent study by Narula et al [18]. Medical optimization involves strict blood pressure control, and the use of beta blockers can help further reduce the risk of aortic dissection [12,19]. Recognizing high-risk patients with Marfan syndrome is ideal, but is not always feasible. In fact, some patients do not exhibit all characteristic signs or symptoms of the condition, and some Marfan syndrome-causing mutations can be de novo, resulting in a negative family history [12], which further reduces the ability to identify at-risk patients, as in our patient.

Although it is a rare event, clinicians should have high index of suspicion for aortic dissection in pregnant patients presenting with chest or back pain, and potentially life-saving imaging should not be withheld, despite the risks of radiation. Multiple investigations have shown that modern protocols deliver high sensitivity and extremely low fetal radiation doses for PE detection in both ventilation-perfusion (V/Q) scans and CTPA [20]. This has resulted in the gradual shift toward first-line use of CTPA [21]. However, the contrast bolus timed for the pulmonary arterial system, is often inadequate for evaluation of the aorta and systemic arterial vasculature. This timing is even more variable in pregnancy due to the altered blood volume and cardiac output [20,21]. In non-pregnant patients, a triple-rule-out CT scan can be considered to simultaneously evaluate the pulmonary, coronary, and systemic arterial vessels; however, the radiation dose is nearly 10 times greater than a standard CTPA; therefore, this technique is generally avoided in pregnant patients [22]. In hemodynamically unstable patients, TEE can be utilized, with a sensitivity of up to 98% and a specificity of 60-96% [23]. Less favorable is TTE, which can help identifying the possible complications associated with the dissection (such as aortic valve integrity/regurgitation, hemopericardium), but it cannot adequately and fully visualize the entire aorta, particularly the distal ascending, the transverse arch, and the proximal descending aorta [24]. In our case, TTE was able to identify the dissection, which was confirmed with an intraoperative TEE study. Although there was some delay in the diagnosis of acute aortic dissection, our case outcome was favorable due to a prompt multidisciplinary approach involving specialists from obstetrics, cardiology, anesthesiology, neonatology, and cardiovascular surgery. To the best of our knowledge, this is the first successful case of acute aortic dissection in pregnancy reported from a community hospital.

Conclusions

Aortic dissection during pregnancy is a rare but potentially life-threating event. This report has shown that FBN1-related Marfan syndrome has a variable clinical presentation that can include life-threatening aortic dissection during pregnancy. Clinicians must maintain a high level of suspicion in pregnant patients with chest and back pain and continue to pursue appropriate imaging for potentially life-threatening conditions, even when initial testing is unrevealing. Successful emergent care of the pregnant patient with aortic dissection requires close multispecialty collaboration, including confirmation of the diagnosis by a clinical geneticist.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

Abbreviations

PE – pulmonary embolism; **CT** – computed tomographic scan; **CTPA** – computed tomographic scan timed to evaluate the pulmonary arteries; **TTE** – transthoracic echocardiogram; **TEE** – transesophageal echocardiogram; **V/Q** – ventilation-perfusion scans; **GenTAC** – National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions; **FBN1**4– fibrillin 1 gene; **EEG** – electroencephalogram

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