INTRODUCTION

We report the case of a 27-year-old woman with McCune-Albright Syndrome (MAS) and a mild scoliosis, with thorax deformity that altered aortic anatomy. Scoliosis in MAS is reportedly associated with fibrous dysplasia of lumbar spine. Our patient had instead dorsal scoliosis, without documented fibrous dysplastic lesions of spine.

McCune-Albright syndrome (MAS) is a rare disease, caused by noninherited pathogenic variants of the gene GNAS, encoding for a subunit of the cAMP pathway G-protein (Gα). Mutations give rise to a mosaic activation of Gα with the classical association of hyperfunctioning endocrinopathies (gonadotropin-independent precocious puberty, non-autoimmune hyperthyroidism, growth hormone excess, neonatal hypercortisolism, and fibroblast growth factor 23-mediated phosphate wasting), irregular café au lait skin alterations, and fibrous dysplasia (FD) of bone. Allegedly, FD is the most common component of MAS and typically involves the peripheral and basicranium bones, therefore with a lesser involvement of the spine. Lesions are more frequently monostotic (of single bones) and unilateral, rather than polyostotic (of multiple bones). Incomplete forms of MAS are described in patients showing only one or two clinical features in the presence of a documented GNAS mutation. Even though the bone replacement with fibrous tissue, as occurs within FD lesions, may contribute to cause vertebral and spinal deformity, other factors may also play a role and contribute to the genesis of scoliosis. Here, we report the case of a patient with MAS showing a mild scoliosis with peculiar radiological features.
2 | CASE PRESENTATION

M.A., female, was referred to our pediatric endocrinology unit at the age of 5 years and 9 months for a clinical suspicion of MAS. Patient presented with prepubertal vaginal bleeding and clinical examination revealed a premature thelarche and three café au lait spots. Precocious pseudo-puberty was evidenced by suppressed levels of gonadotropins at gonadotropin-releasing hormone stimulation test and by the finding of an ovarian cyst on pelvic ultrasound. As patient complained from lower limbs pain, bilateral X-ray of tibia and fibula was made, revealing areas of FD on proximal tibias. Bone scintigraphy did not document further lesions. Upon the presence of the classical triad (bone FD, café au lait skin macules, and precocious puberty), the patient had MAS diagnosis at the age of 6 years.

Blood chemistry showed normal serum calcium of 9.7 (normal range, NR: 8.6-10.3) mg/dl, phosphate of 4.0 (NR: 2.7-4.5) mg/dl, parathormone of 35.4 (NR: 12.0-72.0) pg/mL, and alkaline phosphatase of 121 (NR: < 127) UI/L. Her thyroid function was normal, with thyroid-stimulating hormone (TSH) of 2.7 (NR: 0.4 - 4.0) mIU/L and free T4 of 9.3 (NR: 8.0 - 19.0) pg/mL. Insulin growth factor was within normal limits of 128.0 (NR: 117.0 - 329.0) ng/mL. Likewise, prolactin was of 5.7 (NR: 1.9 - 25.0) ng/mL. Her morning serum cortisol was 11.4 (NR: 4.3 - 22.4) μg/dL, and adrenocorticotropic hormone (ACTH) was 17.7 (NR: 6.0 - 57.0) μg/mL. By contrast, basal serum luteinizing hormone (LH) and follicle-stimulating hormone (FSH) values were suppressed, respectively, of 0.1 IU/L and 0.2 IU/L. After stimulation test with gonadotropin-releasing hormone, peak levels of LH and FSH were, respectively, of 1.8 IU/L and 2.1 IU/L. These latter values were indicative of a peripheral precocious puberty.

Since the patient showed a further episode of prepubertal bleeding, the adnexal mass found on pelvic ultrasound was surgically removed two months later and revealed an estradiol secreting ovarian cyst, causing the suppressed values of gonadotropins. A genetic testing was made on cystic fluid and peripheral blood, evidencing a GNAS gene mutation (R201C) and confirming therefore clinical diagnosis.

Ever since the time of MAS diagnosis, patient attended a yearly follow-up with periodical tests and instrumental investigations. The regular assessment of baseline TSH and thyroid hormones, prolactin, ACTH, and cortisol levels always resulted within the normal limits. Given that the cyst was removed, hormonal or medical treatment was not required and menarche occurred at 11.5 years.

To monitor the burden of skeletal involvement, bone scintigraphy was repeated once (when patient was 12 years old) during follow-up, but the examination did not evidence a progression of FD, or novel FD lesions. At the age of 21 years old, following a history of persistent back pain, the patient underwent spine radiographs that revealed spondylolisthesis at the L5-S1 level and dorsal scoliosis with left-sided ...

FIGURE 1 A, Chest X-ray performed in 2018 shows bulging of the aortic arch increased within one year, mimicking aortic aneurysm. B, Chest X-ray performed in 2017 (in the same center of Figure 1A)

FIGURE 2 A, Computed tomography angiogram, in sagittal maximum intensity projection reconstruction, demonstrating thoracic aorta tortuosity. B, Computed tomography angiogram, in coronal maximum intensity projection reconstruction, shows the aortic arch bulging (arrow), initially referred to an aortic aneurysm on chest X-ray
convexity (Figure S1 and S2). Five years later (at the age of 26), she developed dyspnea associated with hemoptysis and underwent a chest X-ray that documented an abnormal enlargement of the aortic shadow (Figure 1A). Comparison with a chest X-ray made one year before (Figure 1B) revealed how the bulging of the aortic shadow had increased over one year. The clinical picture and radiological findings have thus led to emergency computed tomography (CT) angiogram, which showed a tortuosity of the aortic arch and descending aorta course (Figure 2A, B; Figure S3a, b) and excluded life-threatening focal aortic aneurysm and aortic ectasia, based on vascular diameters (Figure 3A, B). The Haller Index was calculated (Figure 4A and B) to evaluate the severity of the mediastinal narrowing and was 4.03 (NR: <3.25). There was no hemodynamic alteration on Doppler echocardiography, and hemoptysis workup was also negative. Finally, bone scintigraphy did not reveal FD lesions of the spine.

A multidisciplinary team discussed the case in a conference with orthopedic surgeons and radiologists. The possibility of a corrective surgical intervention for scoliosis was excluded due to a high perioperative risk. A conservative approach with a scoliosis brace was hence adopted, and to date, after a one-year follow-up, patient still wears the device that is well tolerated. She does not report limitations in her everyday life, nor in her job as a worker in a manufacturing plant.

3 DISCUSSION

The prevalence of scoliosis in patients with FD has been underestimated over the past years. Through the few case reports and studies in literature that focused on this topic, we found that scoliosis was significantly associated with the evidence of FD lesions of the spine and the majority of patients presented an involvement of the lumbar segment. Conversely, our patient showed a dorsal scoliosis and all the investigations excluded FD lesions of the spine. Besides FD, other factors may contribute to the development of scoliosis in MAS patients. For instance, familiarity should be always considered, and the association between scoliosis and spondylolisthesis has been extensively reported. Fibrous dysplasia may play an indirect role in the genesis of scoliosis causing deformity in other skeletal segments, like lower limbs or pelvis. Accordingly, an accurate staging of skeletal disease burden may help to estimate the risk of developing scoliosis even in patients without a documented spinal involvement. Moreover, once pathological curves have been identified

![Figure 3](image3.png)

**FIGURE 3** A. Axial plane computed tomography scan of ascendent thoracic aortic tract: the diameter is 25.02 mm (normal range <4 cm, Litmanovich et al, 2009). B. Axial plane computed tomography scan of descending thoracic aortic tract: the diameter is 18.29 mm (normal range <3 cm, Litmanovich et al, 2009)

![Figure 4](image4.png)

**FIGURE 4** A. Axial plane computed tomography scan showing the narrowing of the mediastinal anteroposterior diameter (in red), with a minimum width of 5.63 cm (normal values for adult woman 12.5-14.5 cm). Transverse diameter (in green) was 22.9 cm. Haller index resulted 4.03. B. Bone window sagittal reconstruction shows reduction and nearly inversion of thoracic kyphosis leading to mediastinal narrowing.
during childhood or adolescence, an accurate monitoring must be planned through adulthood, to check for a progression. Patients with MAS showing a renal phosphate wasting are thought to be at higher risk due to the greater plasticity of the osteomalacic bone.7 Particular consideration should be put in the assessment of the calcium-phosphate metabolism, which is part of the regular follow-up that MAS patients undergo to exclude Gsα hyperactivation-related complications8 and that in our patient was unremarkable.

Finally, we believe that the narrowing of the physiological mediastinal anteroposterior width due to scoliosis and inversion of the thoracic kyphosis is the actual cause of the vascular deformity that we documented. The diagnostic workup performed, particularly the measurement of the vascular diameter, and allowed us to exclude other conditions (eg, aortic anomalies) in differential diagnosis with the clinical and radiological features herein described.9 In our case, Haller Index was a convenient tool to estimate the entity of mediastinal narrowing, although it is normally used to assess the severity of pectus excavatum. In the preliminary description made by Haller in 1987, patients requiring surgical correction presented an index >3.25, while in normal controls, it was <3.25.10 Severe cases are defined when the index is 3.5 or superior.11 Although in children the index can vary in relation to gender and age, to our best knowledge, standardized values are not yet described for adults.11

The present clinical report suggests that future studies are needed to clarify the role of FD in the genesis of scoliosis in patients without associated lesions of the spine. In addition, the course of our patient highlights the importance of a regular screening and follow-up program for scoliosis in MAS patients.

ACKNOWLEDGMENTS
Published with written consent of the patient.

CONFLICT OF INTEREST
The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS
IB: contributed to definition of intellectual content, design, and concepts. AM: contributed to literature search, manuscript editing, and manuscript preparation. LL: contributed to design, definition of content, and manuscript editing. MPG: contributed to design, definition of content, and manuscript review. GDV and AA: contributed to design, definition of content, and manuscript review. GLM: contributed to design, definition of intellectual content, and manuscript review.

ETHICAL APPROVAL
The manuscript has been read and approved by all named authors.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION
Additional supporting information may be found in the Supporting Information section.

How to cite this article: Michev A, Lungarotti L, Prevedoni Gorone MS, et al. Scoliosis with peculiar radiological features in a patient with McCune-Albright syndrome. Clin Case Rep. 2021;9:e04242. https://doi.org/10.1002/ccr3.4242