Radiology Case Reports 20 (2025) 1967–1971

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Gardner syndrome: When cervical-facial osteomas reveal the tip of the iceberg: A case report and literature review ☆,☆☆

Hajar Andour, MD, Amine Mamouch, MD, Soufiane Hassar, MD, Meriem Fikri, PhD, Najwa Ech-cherif Kettani, PhD, Mohamed Jiddane, PhD, Firdaous Touarsa, PhD*

Neuroradiology Department, Ibn-Sina Hospital, Rabat, Morocco

ARTICLE INFO

Article history:
Received 1 October 2024
Revised 13 December 2024
Accepted 14 December 2024

Keywords:
Gardner
Multiple osteoma
Colonic polyposis
CT-scan

ABSTRACT

Gardner syndrome is a subtype of familial adenomatous polyposis (FAP) characterized by colonic manifestations, multiple skull osteomas, dental abnormalities, benign soft tissue tumors, and a high risk of development of both colorectal cancer and papillary thyroid carcinoma. Many patients are incidentally diagnosed when presenting with craniofacial tumefactions related to osteomas. In such cases, further exploration of family history and other clinical manifestations often reveals positive findings. We report the case of a 34-year-old woman who presented with craniofacial tumefactions and recurrent orbital discomfort. A cranio-facial CT-scan revealed multiple osteomas, including one affecting the orbital region. Investigation of her family history, along with her clinical history, confirmed the presence of Gardner syndrome in her father and siblings, with colonic polyposis- under ongoing surveillance.

Introduction

Gardner syndrome is a subtype of a familial adenomatosis polyposis (FAP) characterized by autosomal dominant inheritance of mutations in the tumor suppressor gene adenomatous polyposis coli (APC), leading to a high prevalence of cancers. The condition is multisystemic, manifesting with bone changes, dental abnormalities, colonic polyps, and benign soft tissues tumors. Although digestive symptoms may be present at the time of presentation, craniofacial deformities caused by multiple osteomas, often asymptomatic, initially, are typically the primary indication and may represent just the tip of the iceberg. However, the various systemic manifestations can lead to delay in diagnosis and management if healthcare professionals focus only on isolated symptoms. Therefore, a multidisciplinary approach and thorough recognition of this complex condition are essential for effective management [1].

☆ Competing Interests: Nothing to declare.

☆☆ Acknowledgments: No funding to cite. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

* Corresponding author.
E-mail address: hajarandour1@gmail.com (H. Andour).

https://doi.org/10.1016/j.radcr.2024.12.043

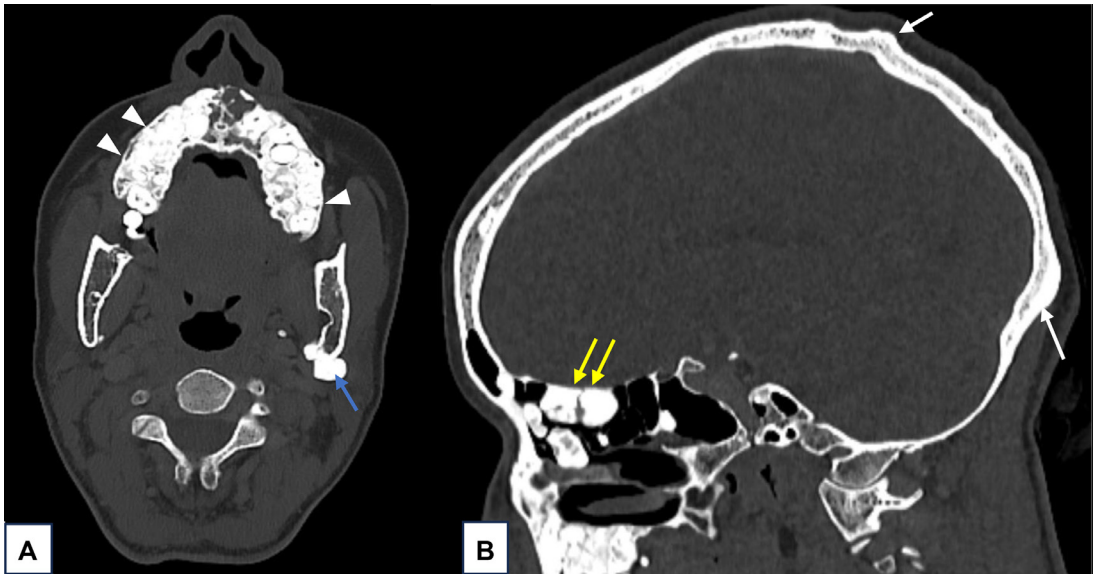

Fig. 1 – Axial (A) and sagittal (B) CT-scans show multiple craniofacial osteomas in the skull and at the posterior angle of the left jaw (blue arrow), with significant accumulation in the ethmoid sinus (yellow arrow). A hypertrophied maxillary bone with abnormal density, compatible with hypercementosis, is also noted (arrowhead).

Case report

A 34-year-old woman initially presented with craniofacial swellings and left orbital discomfort that had persisted for 2 years. An ophthalmologic examination revealed normal results, with no field of view or decrease in visual acuity. Laboratory tests, including hemoglobin (Normal values: 12-14 g/dL) and inflammatory screening (reactive protein C; normal value<5 mg/L). A CT-scan revealed multiple osteomas (more than 7) located in various regions of the craniofacial area. A left orbital osteoma presented a particular risk of optic nerve compression. Additionally, areas of abnormal bone density were noted, particularly along the dental alveolar bone, and evidence of left frontal soft tissue ablation was also noted (Figs. 1 and 2).

These findings, coupled with the increased number of osteomas, raised the suspicion of Gardner syndrome. At this point, the family history was not considered, and detailed medical and family history was gathered. Information revealed that the patient's brother had been diagnosed with multiple colonic polyps.

The patient's brother was the first in the family to be diagnosed with Gardner syndrome, presenting with vague abdominal pain, and a small tumefactive mandibular osteoma. Histological analysis of a colonic biopsy showed no malignancy, but after consultation, recommended that the patient undergo regular controls and family screening. While the mother's screening was normal, the father and sister's laboratory tests and colonoscopies identified colonic polyposis with cellular atypia in one of the father's polyps, as well as microcytic hypochromic anemia in the father (Hb=11 g/dL, normal values: 13-16 g/dL in men). A prophylactic colectomy was performed.

The patient's frontal mass was a desmoid tumor. She was already undergoing regular colonoscopies with a gastroenterologist to monitor her condition. A multidisciplinary discussion involving an ophthalmologist and maxillofacial surgeon, was scheduled to determine the best therapeutic management for the left orbital osteoma. This team decided to attempt surgical ablation during the next medical work-up, scheduled within 6 months. The initial approach would be a trans-nasal endoscopic technique, as the osteoma is closely located near the medial orbital wall. However, a combined approach, including a coronal incision through the hairline, may be required to achieve a complete resection. A possible reconstruction was also planned in case of associated cosmetic concerns following surgery. The patient requested time to consider and provide informed consent for the procedure.

Discussion

Gardner syndrome is an autosomal dominant phenotypic variant of Familial Adenomatous Polyposis (FAP), characterized by a high potential for malignancy and notable extracolonic manifestations. The reported prevalence of the syndrome varies across studies, ranging from 1 in 7000 to 1 in 30.000 births [2]. It affects both genders equally and occurs worldwide, with up to 30 % of cases presenting without a family history [3]. Symptoms usually manifest in the second decade of life, with the onset ranging from as early as 2 months to as late as the seventh decade.

The primary cause of the syndrome is a mutation in the APC tumor suppressor gene, leading to the subsequent hyperactivation of the beta-catenin protein [4,5]. The APC regulates cell growth by ensuring the adequate timing in cell cycle. Other genetic abnormalities have been identified in Gardner syndrome including loss of DNA methylation, mutation in the RAS gene on chromosome 12, deletion of colon cancer gene

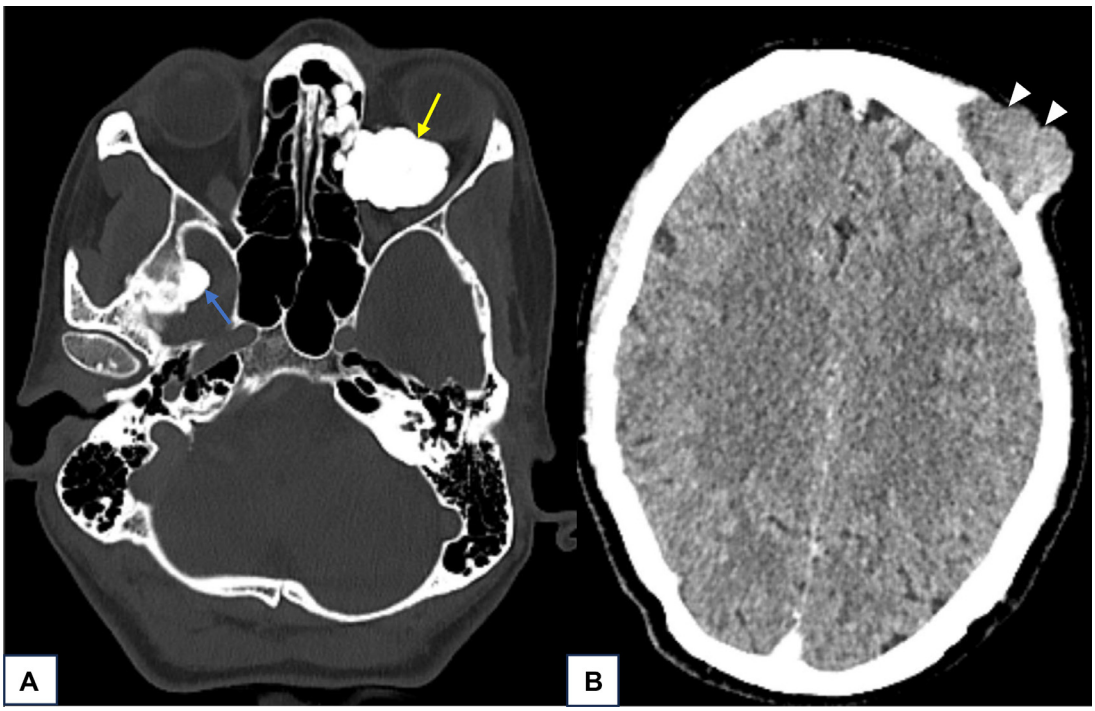

Fig. 2 – Axial CT-scan in bone and parenchymal windows shows a middle fossa osteoma (blue arrow) and a left orbital osteoma (yellow arrow). A lobulated soft tissue mass is noted in the left frontal region within the skull, consistent with recurrence of a desmoid tumor (arrowhead).

(DCC) as well as mutation of TP 53 [6]. With a near-complete penetrance, the manifestation of Gardner syndrome in the inheritance is always observed.

The range of manifestations in Gardner syndrome includes intestinal polyposis, bone and dental abnormalities, and soft tissues tumors. Intestinal symptoms are usually present at time of polyposis diagnosis. Patients often report diarrhea, cramping, rectal pain with bleeding, and fatigue secondary to their anemia. Although phenotypically heterogeneous, polyps are frequently present in large numbers, ranging from hundreds to thousands. In symptomatic FAP, the prevalence of malignancy is reported from 47 % to 67 %, with a 100 % risk of malignant transformation if left untreated [7,8]. Polyps typically appear around adolescence, with malignant transformation occuring around the fourth decade of life [9].

Osteomas are the primary presentation of extra-intestinal lesions in Gardner syndrome, often manifesting during puberty. They most commonly involve the frontal bones of the skull's outer cortex, followed by the maxilla and the mandible, in decreasing order of frequency [10,11]. Understanding the behavior of osteomas is crucial for predicting disease progression and determining the optimal timing for treatment. Condylar osteomas may restrict mouth opening, while those near the mandibular foramen can lead to obstruction and paresthesia. Continued growth of these osteomas can result in facial disfigurement.

In our patient, all the aforementioned bones were involved. Additionally, the inner surface of the ethmoid was affected, leading to both aesthetic concerns and a serious functional problem that could result in additional complications. While the patient did not experience reduced vision or restricted ocular motility, she did begin to report orbital discomfort, prompting the need for therapeutic ablation. Lobulated osteomas are frequently found at the mandibular angle, arising from the surface of the bone [7], and an increase in both their number and size has been reported even into adulthood [12].

Dental abnormalities account for up to 70% of the skeletal manifestations in Gardner syndrome, including tooth ankylosis, impacted or supernumerary teeth, anodontia, cementosis, and odontomas. These dental anomalies have been linked to a specific mutation in the APC gene [13]. In our patient, only diffuse mandibular sclerosis was observed. A significant number of Gardner syndrome cases may be diagnosed early by dentists based on dental abnormalities seen in panoramic radiographs. However, the limited scope of this 2-dimensional technique, along with the superimposed bony structures, makes CT-scan the preferred modality for characterizing these lesions.

CT scans provide superior bone delineation, enabling visualization of cross-sectional images and offer detailed information on the extension and localization of osteomas. This is particularly valuable for assessing their relationship with adjacent structures, such as the optic nerve in cases of orbital osteomas or the mandibular foramen. Additionally, CT-scans help study bone pattern modifications, aiding in both therapeutic planning and follow-up care [14].

Skin anomalies, such as asymptomatic epidermoid cysts, may complicate due to pruritus, inflammation or rupture. Other extraintestinal manifestations of the syndrome include nasopharyngeal angiofibromas, desmoid fibromatosis, and adrenal adenomas, associated with malignancies of the liver,

gallbladder, biliary tract, thyroid, and central nervous system are another extraintestinal manifestation of the syndrome [15,16]. Hepatoblastomas, the most common hepatic malignancy in the pediatric population, have also been reported to occur at higher risk in patients with APC germline mutations [17].

In presymptomatic patients, APC testing is useful for diagnosis, especially when the patient is at high-risk or has a family history of FAP. Similarly, screening for extra-intestinal manifestations should be conducted carefully in patients with a known mutation or a familial history of FAP. In our patient, gene screening was not indicated, as the father's diagnosis had already been confirmed and the siblings were symptomatic [18].

The evaluation and follow-up of Gardner syndrome are challenging due to the wide variety of symptoms and their variable onset, which can range from as early 2 months to as late as 70 years. When evaluating a patient for Gardner syndrome, all affected systems should be thoroughly examined, and any related abnormalities must be documented.

In the skin, multiple epidermal cysts, fibromas, lipomas, leiomyomas, and pilomatricomas should undergo histopathological examination. Desmoid tumors, in particular, require active surveillance through magnetic resonance imaging and ultrasound, especially if there is a risk of involvement of local structures.

Annual thyroid ultrasounds are recommended to monitor existing abnormalities. Congenital hypertrophy of the retinal pigment epithelium is also reported and requires regular ophthalmologic examinations. Additionally, any changes in neurological status should prompt an evaluation for potential central nervous anomalies [19–22].

Managing Gardner syndrome is another challenge for healthcare professionals, as there is no curative treatment. Addressing dental abnormalities often involves the removal of impacted teeth, jaw and facial cysts, and the resection of osteomas for functional or cosmetic purposes. However, even tooth extraction can be problematic due to increased alveolar bone density and hypercementosis, which can lead to the complete absence of periodontal space [23].

Treatment is primarily based on preventive measures, such as maintaining a healthy diet and avoiding environmental triggers. Nonsteroidal anti-inflammatory drugs (NSAIDs), like sulindac, have shown some effectiveness in inhibiting the growth of colon polyps. Regular endoscopic surveillance of the lower gastrointestinal tract is crucial for detecting malignant transformation. Colectomy is recommended when more than 30 polyps are present to reduce the risk of cancer [24,25].

Conclusion

Gardner syndrome is a precancerous condition with multifaceted manifestations, including extra-intestinal symptoms. Osteomas and dental abnormalities are often the most noticeable and alarming lesions, potentially leading to serious complications. Managing the syndrome is complex and requires a multidisciplinary approach. Radiologists and dentists play a critical role in diagnosis, particularly, by identifying maxillofacial features, raising clinical suspicion, and providing early alerts during the presymptomatic phase, which can lead to a better prognosis.

Authors contribution

The first author, who's the correspondent one: diagnosed the case and wrote the manuscript.

The second and third authors helped at its elaboration.

Other authors revised and approved the case.

The last author diagnosed and validated the case.

Data availability

The published data are available. Supplementary material can be provided if needed.

All authors participated actively to elaboration of this scientific document:

The first author (Hajar Andour), who's the correspondent one: diagnosed the case and wrote the manuscript.

The second author (Amine Mamouch) and third (Soufiane Hassar) authors helped at its elaboration.

Other authors (Merem Fikri, Najwa Ech-Cherif Kettani, Mohamed Jiddane) revised and approved the case.

The last author (Firdaous Touarsa) diagnosed and validated the case.

Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

Patient consent

Patient consent has been obtained for the publication of the manuscript.

REFERENCES

[1] Blackwell MC, Thakkar B, Flores A, Zhang W. Extracolonic manifestations of Gardner syndrome: a case report. Imaging Sci Dent 2023;53(2):169.

[2] Dinarvand P, Davaro EP, Doan JV, Ising ME, Evans NR, Phillips NJ, et al. Familial adenomatous Polyposis Syndrome: aan update and review of extraintestinal manifestations. Arch Pathol Laborat Med 2019;143(11):1382–98.

[3] Waller A, Findeis S, Lee M. Familial adenomatous polyposis. J Pediatr Genet 2016;05(02):078–83.

[4] Tage H, Yamaguchi K, Nakagawa S, Kasuga S, Takane K, Furukawa Y, et al. *Visinin-like* 1, a novel target gene of the wnt/β-catenin signaling pathway, is involved in apoptosis resistance in colorectal cancer. Cancer Medicine 2023;12(12):13426–37.

[5] Groenewald W, Lund AH, Gay DM. The role of WNT pathway mutations in cancer development and an overview of therapeutic options. Cells 2023;12(7):990.
[6] Kiessling P, Dowling E, Huang Y, Ho ML, Balakrishnan K, Weigel BJ, et al. Identification of aggressive Gardner syndrome phenotype associated with a de novo *APC* variant, c.4666dup. Cold Spring Harb Mol Case stud 2019;5(2):a003640.
[7] Cankaya AB, Erdem MA, Isler SC, Cifter M, Olgac V, Kasapoglu C, et al. Oral and maxillofacial considerations in Gardner's syndrome. Int J Med Sci 2012;9(2):137–41.
[8] Akbulut S, Koc C, Dirican A. Unusual complication in patient with Gardner's syndrome: ccoexistence of triple gastrointestinal perforation and lower gastrointestinal bleeding: a case report and review of literature. WJCC 2018;6(10):393–7.
[9] Ma H, Brosens LAA, Offerhaus GJA, Giardiello FM, De Leng WWJ, Montgomery EA. Pathology and genetics of hereditary colorectal cancer. Pathology 2018;50(1):49–59.
[10] Dawlatly EE, Al-Qurain AA, Salih-Mahmud M. Gardner's syndrome presenting with a giant osteoma. Ann Saudi Med 1997;17(5):542–4.
[11] Madani M, Madani F. Gardner's syndrome presenting with dental complaints. Arch Iran Med 2007;10(4):535–9.
[12] Takeuchi T, Takenoshita Y, Kubo K, Iida M. Natural course of jaw lesions in patients with familial adenomatosis coli (Gardner's syndrome). Int J Oral Maxillofacial Surg 1993;22(4):226–30.
[13] Yu F, Cai W, Jiang B, Xu L, Liu S, Zhao S. A novel mutation of adenomatous polyposis coli (APC) gene results in the formation of supernumerary teeth. J Cellular Molecular Medi 2018;22(1):152–62.
[14] Fonseca L, Kodama N, Nunes F, Maciel P, Fonseca F, Roitberg M, et al. Radiographic assessment of Gardner's syndrome. Dentomaxillofacial Radiol 2007;36(2):121–4.
[15] Valanzano R. Genetic evidence that juvenile nasopharyngeal angiofibroma is an integral FAP tumour. Gut 2005;54(7):1046–7.
[16] Attard TM, Giglio P, Koppula S, Snyder C, Lynch HT. Brain tumors in individuals with familial adenomatous polyposis: a cancer registry experience and pooled case report analysis. Cancer 2007;109(4):761–6.
[17] Yang A, Sisson R, Gupta A, Tiao G, Geller JI. Germline *APC* mutations in hepatoblastoma. Pediatric Blood & Cancer 2018;65(4):e26892.
[18] AGA technical review on hereditary colorectal cancer and genetic testing. Gastroenterology 2001;121(1):198–213.
[19] García De La Filia Molina I, Crespo Pérez L, Ríos León R, Barbado Cano A, Moreno García Del Real C, Aburto Bernardo A, et al. Quiste epidermoide cutáneo con células sombra: a la búsqueda de un síndrome polipósico. Gastroenterología y Hepatología 2019;42(6):386–7.
[20] Alman B, Attia S, Baumgarten C, Benson C, Blay JY, Bonvalot S, et al. The management of desmoid tumours: a joint global consensus-based guideline approach for adult and paediatric patients. Eur J Cancer 2020;127:96–107.
[21] Monachese M, Mankaney G, Lopez R, O'Malley M, Laguardia L, Kalady MF, et al. Outcome of thyroid ultrasound screening in FAP patients with a normal baseline exam. Familial Cancer 2019;18(1):75–82.
[22] Chatziralli IP, Papazisis L, Sergentanis TN. Incomplete Gardner's syndrome with blepharoptosis as the first symptom. Int Ophthalmol 2014;34(2):301–3.
[23] Kamel SG, Kau CH, Wong ME, Kennedy JW, English JD. The role of Cone beam CT in the evaluation and management of a family with Gardner's syndrome. J Cranio-Maxillofacial Surg 2009;37(8):461–8.
[24] Greenwald P, Witkin KM. Familial adenomatous Polyposis: a nutritional intervention trial. JNCI 1989;81(17):1272–3.
[25] Belfiore A, Ciniselli CM, Signoroni S, Gariboldi M, Mancini A, Rivoltini L, et al. Preventive anti-inflammatory diet to reduce gastrointestinal inflammation in familial adenomatous polyposis patients: a prospective pilot study. Cancer Prevention Res 2021;14(10):963–72.