Case Report

Bilateral Breast Ochronosis: a Case Report

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ABSTRACT

Ochronosis is a syndrome characterized by bluish black discoloration due to the deposition of polymerized products of homogentisic acid (HGA) in the connective tissues. The endogenous variety (alkaptonuria), is a rare autosomal recessive metabolic disorder. The disorder is manifested by deficiency of the enzyme homogentisate 1,2-dioxygenase. The characteristic of the condition is a triad of pigmentation of skin, cartilage, and sclera; ochronotic arthropathies and homogentisic aciduria (resulting in darkening of urine). More rarely, it may affect the breast. This rare and interesting case of a woman with ochronosis of both breasts and chest wall, prompted us to write this case report.

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INTRODUCTION

Ochronosis is a rare syndrome inherited as autosomal recessive trait with an incidence of 1/200,000.1-2 The two main types of ochronosis are endogenous and exogenous.
Exogenous ochronosis is an acquired condition that presents similar to alkaptonuria clinically and histologically. It has no systemic manifestations. The disorder presents as asymptomatic bilaterally symmetrical gray-brown macules, typically affecting the malar areas, lower cheeks, temples, and neck, that can be caused by the application of topical compounds such as phenols or hydroquinone.\(^3\)

The endogenous type is known as alkaptonuria that is caused by a lack of homogentisate oxidase enzyme. This leads to homogentisic acid (HGA) accumulation, of which is oxidized, polymerized, and deposited in connective tissues, causing characteristic yellowish discoloration (ochre-like) that has given the disease its name. The deposits can also contribute to the rigidity of the connective tissues.\(^1\),\(^4\)

Ochronosis affects different tissues in the body, predominantly skeletal system, although other systems, including cardiovascular, urinary, and auditory systems, may also be affected.\(^5\)-\(^6\) The involvement of breast in ochronosis is rare, and there are only few reports in the literature focusing on the histopathological features of the disease.\(^7\) We present the clinical, radiological, and histological features of a case that had severe ochronosis involving her breasts.

**THE CASE**

A 66-year-old lady, known to have alkaptonuria, presented for the evaluation of progressive bilateral hard painful breast lumps. These were associated with bilateral breast pain and heaviness that had worsened over the last 2 years. She was diagnosed with alkaptonuria as a child and did not have any treatment other than symptomatic pain relief over the years. She was initially seen in the breast clinic 9 years ago, when the first lump appeared in her left breast. A series of investigations, including mammograms were performed. The recommendation was a close follow up with clinical examination every 6 months and yearly mammograms. Her initial mammograms (2011) showed coarse calcifications with no radiological evidence of malignancy (Figure 1). According to the patient, she developed lumps in both the breasts, which progressively became bigger and harder in consistency adding to the feeling of heaviness with worsening of pain. Furthermore, she had started developing neck and upper back pain, which she attributed to the weight of her breasts. She had an older sister with the same condition but without the involvement of breasts.

Physical examination revealed characteristic features of ochronosis with the pigmentation of the sclera and the ear. Breast signs included asymmetry and grade II ptosis. (Figure 3) There were associated multiple, stony hard, tender masses of variable sizes in both breasts. There were no associated skin changes, nipple retraction, or palpable lymph nodes in the axillae. A new set of mammograms and ultrasound were performed in 2017 (Figure 2) and compared with the previous studies from 2011.
Fig 2. Right and left breast repeated mammogram findings (2017) showing very dense calcifications more on the right side. The appearance of the calcifications is benign.

Fig 3. Preoperative picture of the patient.

Very dense calcifications in both breasts more on the right side were noted. The appearance of the calcifications was reported to be benign, and there was no interval development of suspicious findings. The sensitivity of mammograms and ultrasound was significantly limited by the breast density in the presence of very dense calcifications.

The patient had to be followed up regularly to detect any suspicious clinical and radiological changes. As time passed, she unfortunately suffered from progressive lumps in her breasts, which were tender and heavy. These changes prevented her to perform her daily activities and had a psy-
The case was discussed at our multidisciplinary breast meeting, and a decision was made to proceed with bilateral mastectomy and immediate reconstruction, keeping in mind the patient’s symptoms and difficulties in clinical and radiological screening. The decision of breast-conserving mastectomy and the difference and risks of different immediate reconstructive options were discussed with the patient. She had a BMI of 18 and did not possess adequate lower abdominal skin redundancy to allow her to have a free DIEP flap reconstruction. However, other autologous options such as transverse upper gracilis (TUG) flap were discussed with her and she preferred having an implant-based reconstruction to be able to have a speedy recovery with no donor site morbidity.

She underwent bilateral nipple-sparing mastectomy and immediate reconstruction. Operative findings included blue-black discoloration of the costal cartilages. The breast parenchyma was totally replaced with a collection of blue-black masses. These masses were stony hard in consistency, and it was not possible to cut through them. Mastectomy specimens weighed 485 g in the right and 483 g in the left breast, respectively. Dermal bra technique with the preservation of nipple areola complex (NAC), along with implants (Mentor, Round 295 cc) was used for reconstruction. The pocket for the implant was subpectoral proximally and the dermal flap distally. Unfortunately, she developed postop hematoma in the right breast, which needed evacuation. There was a small area of NAC with doubtful viability, which was debrided and repaired primarily at the time of evacuation of hematoma. Overall, there was a good esthetic outcome of the procedure. (Figure 4) The patient was extremely satisfied with the results and reported that she considered herself normal after a number of years. There was also an improvement in the feeling of heaviness in the breasts.

Histology showed benign breast tissue demonstrating marked fibrosis and calcifications with some pigment noted in histocyte cells. There was no evidence of malignancy.

**DISCUSSION**

The word Ochronosis was described by Virchow in 1866, describing (ochre), which is a brownish yellow pigment that tends to be deposited in the tissues of various organs. It is a rare disorder, which manifests either in exogenous or endogenous forms.\(^8\)
Exogenous ochronosis does not demonstrate systemic involvement. It is caused by the prolonged use of bleaching agents that contain hydroquinone and phenolic compounds, which cause hyperpigmentation of the skin.\textsuperscript{9} The endogenous variant of ochronosis or alkaptonuria, is an autosomal recessive metabolic deposition disorder, caused by the deficiency of the enzyme HGA oxidase. This results in the accumulation of HGA, which is a metabolite of tyrosine. It binds to dermal fibrillar collagen irreversibly, which leads to skin pigmentation and/or arthropathy. It is initially formed within many if not all cells of the body, and eventually reaches the connective tissues and results in its weakness. Moreover, it affects different body locations such as the eyelids, ear cartilage, foreheads, cheeks, sclera, axillae, genitals, nailbeds, buccal mucosa, larynx, tympanic ear drum, and nasal tip. In addition, it can discolor the skin, tendons, ligaments, costochondral junctions, sclera, heart valves, intima of the blood vessels, and intervertebral disc. All the body joints can be affected, particularly the knee.\textsuperscript{10}

Ochronosis of the breast is not common, and its management is challenging. One of the manifestations of breast involvement is the detection of stiff lumps of the breast. This would always raise the suspension of malignancy. The involvement of the breast in ochronosis has not been well reported in the literature. There has been one reported case in literature about ochronosis in the breast. This was a woman aged 46 years, who came to medical attention for the evaluation of breast masses clinically suspicious of neoplasia. The soft tissue of the breast had significant deposition of ochronotic pigment. The paper mainly discussed the ochronotic pigment histochemical features, and the difficulty in differentiating it from melanin.\textsuperscript{7}

In this report, we presented a case of endogenous ochronosis, which resulted in the involvement of bilateral breasts along with other tissues. Our patient was diagnosed in childhood due to noticed discoloration of the urine. She also had the discoloration of the ear and sclera. She suffered breast pain and psychological issues related to the shape of her breasts for a number of years, before the decision of mastectomy and immediate reconstruction was made. She had a good esthetic outcome and described the procedure as a life-changing event for her.

CONCLUSION

Involvement of the breast is a rare manifestation of alkaptonuria. There are not enough reported cases in literature in this regard. Ochronosis that involves the breast can initially mimic neoplasia and create confusion. Furthermore, it would be impossible to diagnose neoplastic lesions of the breast if they happen to coexist with ochronosis of the breast due to difficulties with examination, imaging, and even to obtain biopsies. Our patient had to suffer physically and psychosocially before the decision of mastectomy and immediate reconstruction was made. It is understandable that in the absence of neoplastic lesions, it is hard to recommend a mastectomy. However, this decision could be based to improve the social well-being of the patient. In an era, where immediate breast reconstruction is widely available and has good outcomes, we recommend mastectomy and immediate reconstruction in such patients.

Declarations

We declare that this manuscript is original, has not been published before, and is not currently being considered for publication elsewhere.

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Patient Consent: The patient agreed for possible publication of the photographs.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi: 10.1016/j.jprra.2021.06.005.
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