ACTAS
Dermo-Sifiliográficas

Full English text available at
www.actasdermo.org

CASE AND RESEARCH LETTERS

Breast Implant–Associated Anaplastic Large Cell Lymphoma☆

Linfoma anaplásico de células grandes asociado a implantes mamarios

To the Editor,

Breast implant–associated anaplastic large cell lymphoma (BIA-ALCL) is a very rare form of T-cell lymphoma and its incidence has grown in recent decades. The most common presentation is breast swelling due to periprosthetic seroma. In this article, we describe a case of BIA-ALCL whose first clinical manifestation was skin lesions in the intermammary area. There have very few reports of this presentation in the literature.[1]

A 70-year-old woman was referred to our department for evaluation of an erythematous, indurated plaque with slight superficial scaling in the intermammary area and increased right breast volume (Fig. 1). She had been diagnosed with right breast carcinoma 5 years earlier and had undergone mastectomy and prosthetic breast reconstruction. She was receiving hormone therapy. No signs of recurrence had been detected in a follow-up mammogram 4 months earlier. The ultrasound examination had shown waves indicating possible periprosthetic fluid collection but no findings suggestive of malignancy. The patient reported asthenia and considerable weight loss in recent months. Skin biopsy showed spongiotic dermatitis with a superficial and deep perivascular lymphohistiocytic infiltrate. No tumor cells were observed and immunohistochemical staining was negative for cytokeratin 19 and CD30.

Magnetic resonance imaging was ordered to assess the possibility of a cutaneous metastasis from breast cancer or a prosthetic complication. The findings showed a retroprosthetic mass invading the chest wall and extending into the mediastinum (Fig. 2). Aspiration of the periprosthetic fluid showed large $CD30^+$, $CD3^+$, and ALK- tumor cells, confirming the diagnosis of BIA-ALCL (Fig. 3). Given the presence of extramammary disease, the patient was treated with systemic chemotherapy (cyclophosphamide, hydroxydaunorubicin, and prednisone) and brentuximab before surgical explantation of the implant and capsulectomy.

BIA-ALCL is a lymphoproliferative disorder caused by tumor cells invading the capsule or periprosthetic fluid.

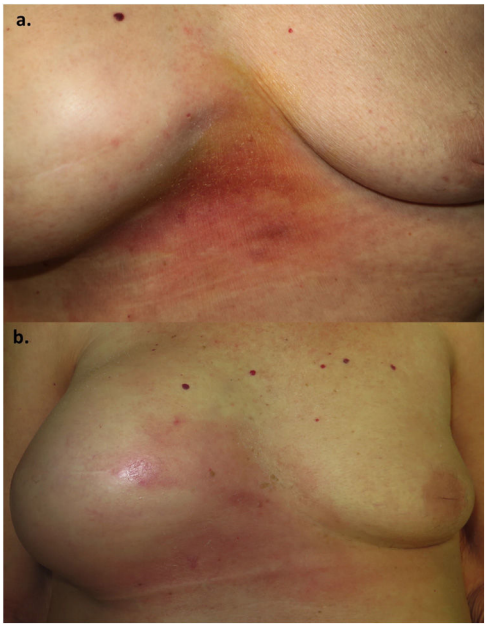

Figure 1 A, Indurated erythematous plaque with slight scaling in the intermammary area. B, Note the growth of the erythematous plaque and the considerable increase in volume of the right breast after 1 month.

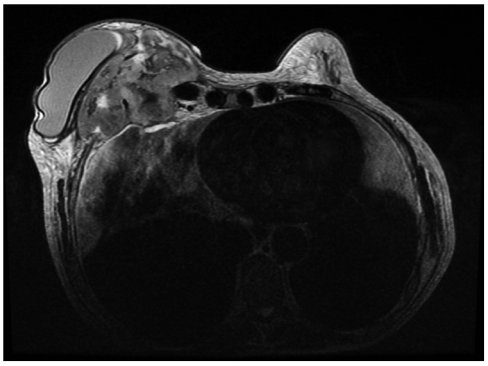

Figure 2 Magnetic resonance image of a retroprosthetic lobulated mass measuring 14 × 10 × 7 cm with irregular margins in addition to peripheral enhancement and central necrosis and invasion of the chest wall through to the mediastinum.

☆ Please cite this article as: Gracia-Darder I, Izquierdo N, Boix-Vilanova J, Ramos D. Linfoma anaplásico de células grandes asociado a implantes mamarios. Actas Dermosifiliogr. 2021;112:928–930.

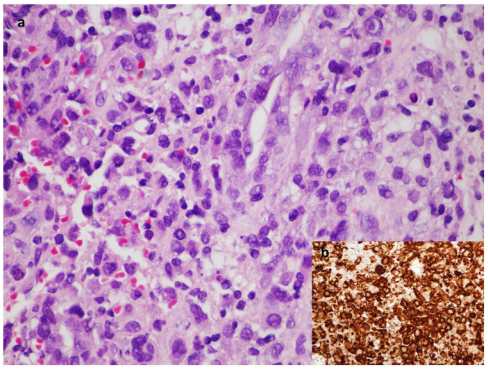

Figure 3 A, Microscopic image of the cell block preparation from the periprosthetic fluid (hematoxylin-eosin, original magnification ×60) showing large loose and small discohesive clusters of pleomorphic tumor cells against a background of inflammatory granulation tissue. B, Strong immunohistochemical expression of CD30.

The mean age at diagnosis is 52.5 years and the mean time from breast implantation to diagnosis is 9 years.[2] BIA-ALCL presents as periprosthetic seroma in 86% of cases,[2] although it can also manifest as a mass, nodule, or lymph node enlargement. Skin lesions are very rare.[1]

Just 2 cases of BIA-ALCL with skin lesions as the presenting manifestation have been reported.[1,3]Elswick and Nguyen[1] described the case of a woman who presented with a breast mass, erythema, and breast swelling in addition to elevated acute phase reactants in the blood work-up. The skin biopsy was negative for malignancy, suggesting to the authors that the skin lesions were due to a periprosthetic infection concurrent with the lymphoma. In the case published by Alcalá et al.,[3] however, the detection of $CD30^{+}$ tumor cells during histologic examination of the skin nodules was key to establishing a diagnosis of BIA-ALCL rather than breast cancer recurrence. Nineteen of the 186 patients in the PROFILE (Patient Registry and Outcomes for Breast Implants and Anaplastic Large Cell Lymphoma Etiology and Epidemiology[2]) registry developed skin lesions in addition to other systemic manifestations, and 12 of these lesions were described as redness on the skin. Type of skin lesion was not specified in the other cases, and none of the lesions were analyzed histologically.

Neither our case nor the cases in the literature (with the exception of that described by Alcalá et al.[3]) exhibited specific clinical or microscopic changes. BIA-ALCL should be suspected in patients with breast implants who develop skin lesions, in particular erythema, and breast swelling.

It has been hypothesized that the etiology of BIA-ALCL is multifactorial and is influenced by type of implant, genetic predisposition, and possible chronic periprosthetic superinfection associated with a bacterial biofilm.[4]

The Spanish Ministry of Health recently published a clinical protocol for the detection of BIA-ALCL that recommends an initial ultrasound assessment with aspiration and cytologic and microbiologic analysis of periprosthetic fluid.[5] BIA-ALCL is histologically characterized by a proliferation of highly pleomorphic lymphoid cells with abundant cytoplasm and an irregular nucleus.[3] Diagnosis must be confirmed by immunohistochemistry, which characteristically shows CD30 positivity and ALK negativity in all tumor cells.[3,6]

BIA-ALCL is generally localized at diagnosis and the prognosis is excellent following surgical excision.[7] Extracapsular spread is very uncommon. In their review of 173 cases of BIA-ALCL, Brody et al.[8] reported just 18 cases of extracapsular spread and 9 of these had a fatal outcome.

We have described a new case of advanced-stage BIA-ALCL in a woman who, in addition to increased breast volume, presented with skin lesions and constitutional syndrome. She required chemotherapy prior to surgery.

Although BIA-ALCL is rare, the number of cases in recent years has increased exponentially.[8] It is crucial thus to be familiar with this condition, as early diagnosis together with detection of localized disease is associated with a favorable prognosis following surgical explantation and capsulectomy.

Conflicts of interest

The authors declare that they have no conflicts of interest.

References

1. Elswick SM, Nguyen MT. Breast erythema in a patient with breast implant-associated anaplastic large cell lymphoma: a case report discussing cutaneous manifestations. Aesthet Surg J. 2018;38:N47–52, http://dx.doi.org/10.1093/asj/sjx209.
2. McCarthy CM, Loyo-Berríos N, Qureshi A, Mullen E, Gordillo G, Pusic A, et al. Patient Registry and Outcomes for Breast Implants and Anaplastic Large Cell Lymphoma Etiology and Epidemiology (PROFILE): Initial Report of Findings, 2012–2018. Plast Reconstr Surg. 2019;143(3S):65s–73s, http://dx.doi.org/10.1097/PRS.0000000000005571.
3. Alcalá R, Llombart B, Lavernia J, Traves V, Guillén C, Sanmartín O. Skin involvement as the first manifestation of breast implant-associated anaplastic large cell lymphoma. J Cutan Pathol. 2016;43:602–8, http://dx.doi.org/10.1111/cup.12697.
4. Hu H, Johani K, Almatroudi A, Vickery K, Van Natta B, Kadin ME, et al. Bacterial Biofilm Infection Detected in Breast Implant–Associated Anaplastic Large-Cell Lymphoma. Plast Reconstr Surg. 2016;137:1659–69, http://dx.doi.org/10.1097/PRS.0000000000002010.
5. AEMPS, Agencia española de medicamentos y productos sanitarios [Internet]. Protocolo clínico para la detección de LACG asociado a implantes de mama 6, de febrero de 2019. AEMPS; 2019 [actualized 6 Feb 2019; accessed 8 Jul 2019]. Available from: https://www.aemps.gob.es/vigilancia/productosSanitarios/linfomaanaplasicoLACG/docs/Protocolo_Clinico_ALCL_implantes_mamarios.pdf.
6. Ramos-Gallardo G, Cuenca-Pardo J, Rodríguez-Olivares E, Iribarren-Moreno R, Contreras-Bulnes L, Vallarta-Rodríguez A, et al. Breast implant and anaplastic large cell lymphoma meta-analysis. J Invest Surg. 2017;30:56–65, http://dx.doi.org/10.1080/08941939.2016.1215576.
7. Clemens MW, Horwitz SM. NCCN consensus guidelines for the diagnosis and management of breast implant-associated anaplastic large cell lymphoma. Aesthet Surg J. 2017;37:285–9, http://dx.doi.org/10.1093/asj/sjy331.
8. Brody GS, Deapen D, Taylor CR, Pinter-Brown L, House-Lightner SR, Andersen JS, et al. Anaplastic large cell lymphoma

occurring in women with breast implants: analysis of 173 cases. Plast Reconstr Surg. 2015;135:695, http://dx.doi.org/10.1097/PRS.0000000000001033.

I. Gracia-Darder*, N. Izquierdo, J. Boix-Vilanova, D. Ramos

Departamento de Dermatología, Hospital Universitario Son Espases, Palma de Mallorca, Baleares, Spain

* Corresponding author.
E-mail address: ines.gracia@ssib.es (I. Gracia-Darder).

https://doi.org/10.1016/j.ad.2020.03.017

Contact allergy to aluminum following vaccination: A report of 3 cases☆

Alergia de contacto a aluminio tras vacunación: presentación de tres casos

Dear Editor:

Vaccination is an essential measure in preventive medicine. However, it is not free from complications, since it can lead to adverse reactions, although these are mainly mild, transient, and self-limiting[1]. The reactions are rarely persistent, with most cases involving a hypersensitivity reaction to aluminum[2,3].

We report the cases of 2 girls (age, 2 and 3 years) and a boy (8 years) who experienced persistent cutaneous reactions after vaccination (Table 1). All 3 patients developed nodules at the injection site, and in 1 case, the reaction was accompanied by eczema and hypertrichosis, which had first appeared more than 1 year previously (Fig. 1)[4]. The vaccinations had been administered according to the corresponding schedule, and the clinical picture was associated with the vaccines included in the schedule. Given that the clinical suspicion included other conditions in 2 cases, diagnosis was based on skin biopsy, which revealed findings typical of this type of reaction (histiocytes with granular cytoplasm) (Fig. 2). All 3 patients underwent patch testing with aluminum chloride 2% in petrolatum (Chemotechnique), which yielded positive readings at 72 and 168 hours (Fig. 3).

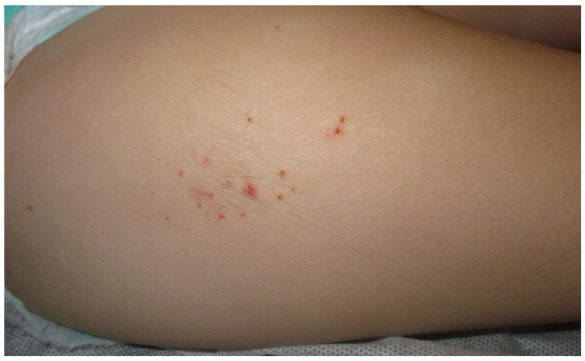

Figure 1 Lesions on the right thigh in the form of excoriated erythematous macules clustered over a nodular lesion with hypertrichosis on the surface.

Aluminum compounds have been used as adjuvants in vaccines for more than 80 years to boost the immune response to the antigen. Administration of vaccines can lead to cutaneous lesions, mostly in the form of pruritus or subcutaneous nodules; areas of hypertrichosis or eczema are less common. The reactions persist in 0.5%–6% of cases, mainly because of a type IV hypersensitivity reaction to aluminum hydroxide. Patch testing with aluminium hydroxide 2% is positive in 77%–95% of children with persistent reactions, thus demonstrating the presence of contact allergy to the metal[5].

Various histologic patterns have been described (panniculitis, pseudolymphomatous, granuloma annulare–like), although the characteristic finding is histiocytes with a granular cytoplasm. Nevertheless, given the high sensitivity of patch testing, skin biopsy is not considered essential for diagnosis[5,6].

Table 1 Summary of Cases of Contact Allergy to Aluminum.

Case	Age, y	Sex	Cutaneous Symptoms	Associated Vaccine	No. of Aluminum-Containing vaccines	Duration of Symptoms at the First Evaluation, mo
1	2	Female	Nodules, eczema, and hypertrichosis	PCV13	4	12
2	3	Female	Nodules	DTP, Hib	5	18
3	8	Male	Nodules	DTP	6	24

Abbreviations: DPT, diphtheria, pertussis, tetanus; Hib: *Haemophilus influenzae* b; PCV, pneumococcal conjugate vaccine.

☆ Please cite this article as: Tous Romero F, Palencia Pérez SI, Rodríguez Peralto JL, Ortiz de Frutos FJ. Alergia de contacto a aluminio tras vacunación: presentación de tres casos. Actas Dermosifiliogr. 2021;112:930–932.