Squamous cell carcinoma in situ of the cervix and placental site nodule: Case report

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Abstract

An asymptomatic 24-year-old woman underwent a colposcopy, cervical biopsy, and subsequently, a conization for a cervical squamous cell carcinoma in situ with glandular extension. Simultaneously, an endometrial biopsy was carried out in which, incidentally, a placental site nodule was diagnosed, a rare non-neoplastic lesion originating in the intermediate trophoblast. Given the coexistence of these two entities, it was necessary to make a differential diagnosis between them and also with other pathologies of the trophoblast such as an exaggerated placental site, placental site trophoblastic tumor, and epithelioid trophoblastic tumor.

KEY WORDS: *Placental disease. Trophoblast. Trophoblast tumor. Placental site nodule. Intermediate trophoblast. Extravillous trophoblast.*

Introduction

Placental site nodule (PSN) is a non-neoplastic infrequent lesion originating from the intermediate trophoblast, which theoretically represents a non-involuted portion of placental tissue. This lesion consists of a circumscribed nodule or plate, with abundant hyalinized stroma and trophoblastic cells of the intermediate trophoblast type[1,2]. We present the case of a patient with coexistence of squamous cell carcinoma in situ with glandular extension of the cervix and PSN.

Case report

A 24-year-old female resident of a rural area of Colombia attended the local hospital in October 2013 owing to the finding of a high-grade squamous intraepithelial lesion (HSIL) on her Pap smear. She had no relevant medical history. Pregnancies 1, deliveries 1, live births 1. Date of last delivery: September 2010. She was having birth control with subdermal implant since one year prior. Physical examination was normal.

She underwent colposcopy and cervical biopsy, with a squamous cell carcinoma in situ being found, which led to the performance of a conization that confirmed the HSIL diagnosis: severe dysplasia and squamous cell carcinoma in situ with glandular extension on six out of 16 sections, with involvement of the endocervical resection margin (Fig. 1 A and B). Simultaneously, she underwent endometrial biopsy, with proliferative endometrium fragments and a PSN being observed.

By late 2014, the subdermal implant was removed and the control Pap smear reported a low grade squamous intraepithelial lesion, with cytopathic changes consistent with human papillomavirus infection, which was classified as genotype 16. Two months later, a second colposcopy and cervical biopsy were performed, with the latter being negative for squamous

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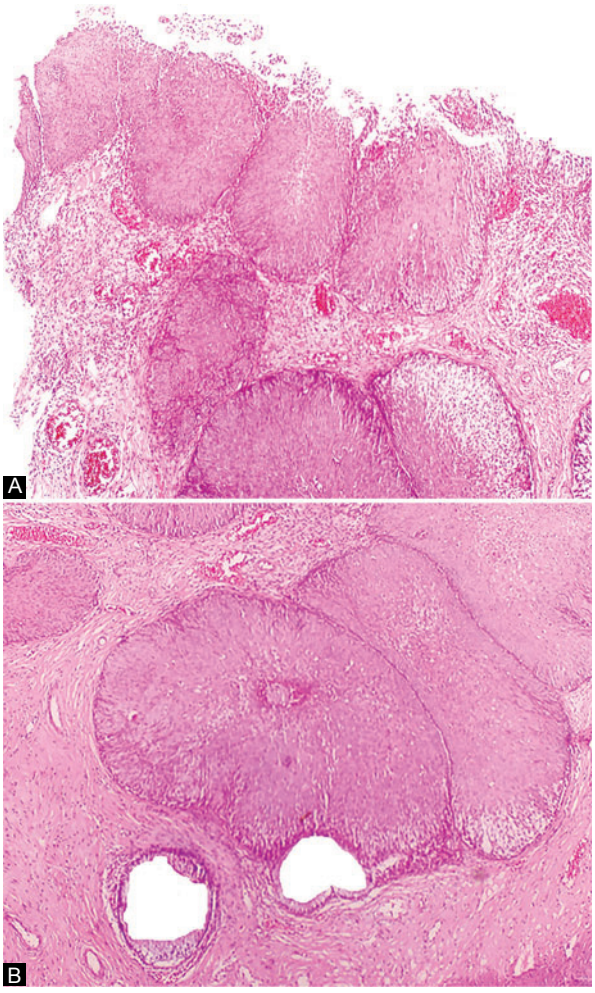

Figure 1. A: *squamous cel carcinoma in situ of the cervix (hematoxylin & eosin, x10).* **B:** *glandular extension (hematoxylin & eosin, x20).*

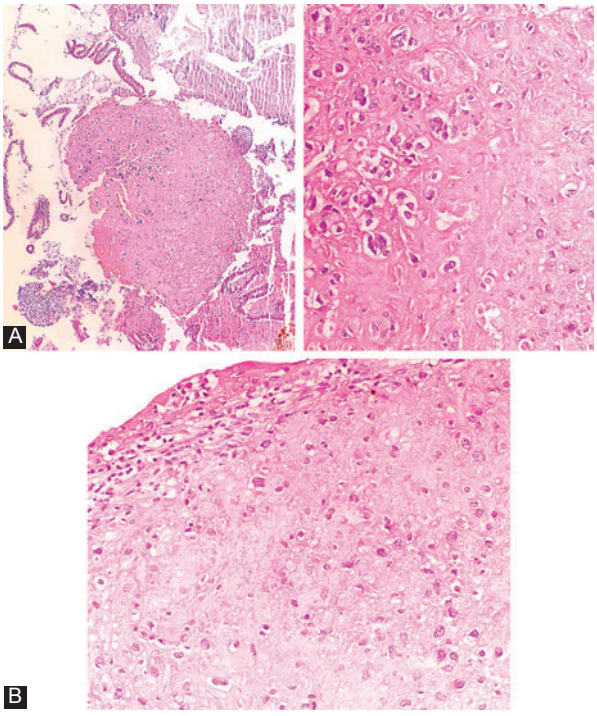

Figure 2. A: *PSN composed of intermediate type trophoblastic cells with hyperchromatic nuclei and vacuolated cytoplasms. Hyaline stroma adjacent areas (hematoxylin & eosin, x40).* **B:** *trophoblastic cells nuclei spread on large areas of hyaline stroma. Lymphocytes are appreciated at the lesion periphery (hematoxylin & eosin, x40).*

intraepithelial lesion. The patient is currently breast-feeding her second child.

Discussion

PSN occurs in childbearing age women[2,3] and, usually, it is an incidental finding of endocervical curettages, cervical and endometrial biopsy and hysterectomy[1,4,5]. It is mainly located at the endometrium or the cervix, and rarely at the uterine tube. It is usually detected several months or years after a pregnancy, with an average of 3 years[6-8].

When macroscopically visible, a yellow or hemorrhagic nodule is appreciated, with a diameter of 1 to 14 mm, although it rarely exceeds 4 mm; it can occur as multiple nodules[2,4-6]. Microscopically, a circumscribed plaque or nodule composed of hyalinized stroma with intermediate trophoblast-type cells distributed in groups or cords, or individually displayed with absence or sparse atypical mitoses. The cells vary in size; the small ones are mono- or binucleated, with a clear, glycogen-rich cytoplasm, and the large ones have broad acidophilic or amphiphilic cytoplasms, with irregular and hyperchromatic nuclei (Fig. 2 A). Multinucleated trophoblastic cells can occasionally be observed. Towards the periphery, there is a circumferential inflammatory infiltrate composed of lymphocytes and plasmocytes[2,3,5-8] (Fig. 2 B).

PSNs are positive for PLAP, p63, inhibin α and cytokeratin 18, with focal or negative expression for hPL and CD146 (Mel-CAM). They are usually negative for β-hCG and their Ki67 proliferation index ranges between 1 and 5% (Fig. 3 A and E). Given their morphology and immunohistochemical (IHC) characteristics, PSNs originate from the intermediate trophoblast of the chorionic type, and it is suggested that they are the benign counterpart of the epithelioid traphoblastic tumor (ETT)[1,2,8,9].

Most important differential diagnoses include exaggerated placental site (EPS), placental site trophobalstic tumor (PSTT), ETT and squamous cell carcinoma of the cervix[5,8-10] (Table 1). EPS is diagnosed after a normal pregnancy, an ectopic pregnancy or a

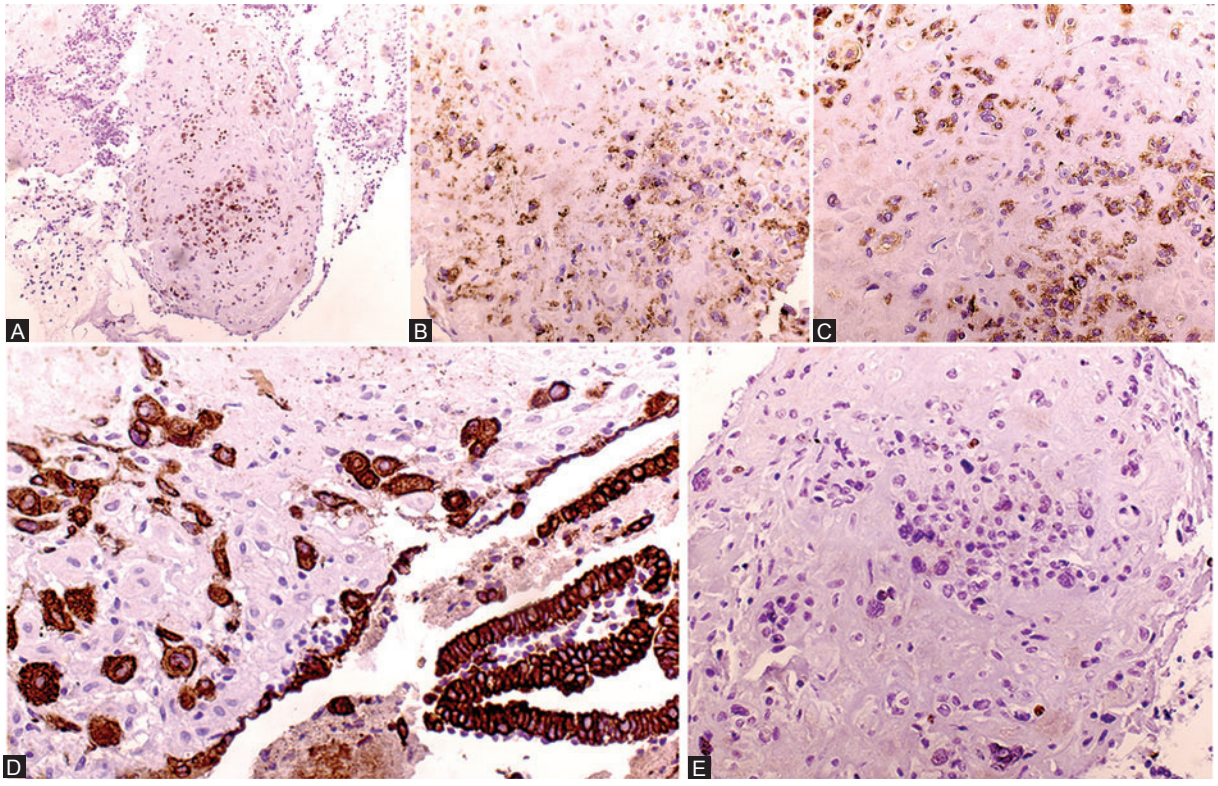

Figure 3. *PSN trophoblastic cells are positive for P63 (IHC, x20) (***A***), PLAP (IHC, x40) (***B***), inhibin (IHC, x40) (***C***) and keratin (IHC, x40) (***D***).* **E:** *Ki67proliferation index is lower than 1% (IHC, x40).*

Table 1. PSN differential diagnoses

	EPS	PSN	PSTT	ETT	SCC
Histogenesis	Implantation site intermediate trophoblast	Chorionic type intermediate trophoblast	Implantation site intermediate trophoblast	Chorionic type intermediate trophoblast	Epithelial lesion. Non-trophoblastic
Morphological findings					
Growth pattern	Not arranged in nodules	Circumscribed nodule(s)	Poorly-defined and infiltrating mass	Falsely circumscribed mass with focal infiltration	Infiltrating mass
Cellularity	High	Low	High	High	High
Cytological atypia	Generalized	Focal/sparse	Generalized	Generalized	Generalized
Mitotic figures	Absent	Absent to rare	Common	Common	Common
Stroma	Fibrin deposit	Abundant hyalinization	Deposit of fibroid material	Deposit of hyaline material	Sparse
Necrosis	Absent	Occasional, central	Common, coagulative	Geographic and extensive	Geographic
Chorionic villi	Present	Absent	Absent	Absent	Absent
Immunohistochemistry					
CK 18	Positive. Diffuse	Positive. Diffuse	Positive. Diffuse	Positive. Diffuse	Negative
CD146 (Mel-CAM)	Positive. Diffuse	Negative/positive focal	Positive. Diffuse	Negative/positive focal	Negative

(Continue)

Table 1. PSN differential diagnoses (*Continued*)

	EPS	PSN	PSTT	ETT	SCC
PLAP	Negative	Positive. Diffuse	Negative	Positive. Diffuse	Negative
Inhibin alpha	Positive	Positive	Positive	Positive	Negative
hPL	Positive. Diffuse	Negative/positive focal	Positive. Diffuse	Negative/positive focal	Negative
P63	Negative	Positive. Diffuse	Negative	Positive. Diffuse	Positive. Diffuse
P16 (nuclear)	Negative	Negative	Negative	Negative	Positive
Ki-67	< 1%	1-5%	> 10%	10-25%	10-50%

EPS: exaggerated placental site; PSN: placental site nodule; PSTT: placental site trophoblastic tumor; ETT: epithelioid trophoblastic tumor; SCC: squamous cell carcinoma.

molar pregnancy; it doesn't arrange in nodules, it is usually associated with chorionic villi and its Ki-67 proliferation index is lower than 1%[8,10]. PSTT is macroscopically visible, and its histology is characterized by myometral infiltration, areas of coagulation necrosis, tumor cells with atypical nuclei, frequent mitosis and Ki-67 proliferation index higher than 10%[5,7,8,10]. Both EPS and PSTT are negative for p63 and diffusely positive for hPL[11]. ETT shows IHC findings similar to those of PSN; however, they are neoplasms of larger size, infiltrating growth with high cellularity, pleomorphism, atypical mitoses, geographic necrosis and high cell proliferation index (10-25%)[1,5,8,10.11].

In our case, the most important differential diagnosis is cervical squamous cell carcinoma. Some patients assessed for cervical dysplasia or carcinoma in situ with a concomitant PSN can be wrongly diagnosed with infiltrating squamous cell carcinoma. In this case, IHC is useful because antibodies against HLA-G and CK18 are diffusely positive in trophoblastic lesions and negative in squamous cell carcinoma. Inhibin alpha is positive in PSN and negative in squamous cell carcinoma[6].

PSNs are lesions that do not require treatment in addition to initial surgical resection[10].

Conclusion

PSNs are sometimes diagnosed in women with Pap smear abnormal findings[1]. In a study by Shih et al.[6], this condition was observed in 29% of patients. Although PSN is infrequent, pathologists should recognize its morphological features and obtain the necessary IHC markers to differentiate it in patients with concomitant HSIL, in order to avoid the infiltrating squamous cell carcinoma of the cervix misdiagnosis.

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Tuberculous abscess of the thoracic wall secondary to nodular tuberculosis: Atypical presentation in an older adult

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Abstract

Tuberculosis (tb) of the chest wall is uncommon and it represents less than 5% of all cases of musculoskeletal tb and only 1-2% of tb. We present the case of an elderly woman with tb of the chest wall secondary to a nodal tb with an unusual presentation. The diagnosis of this entity is difficult because the disease often mimics other diseases such as pyogenic abscess, chest wall.

KEY WORDS: *Tuberculosis. Tuberculous abscess. Nodal tuberculosis.*

Introduction

Tuberculosis (TB) remains an important global health problem. In 2013, 9 million people were estimated to have developed this disease and there were 1.5 million deaths caused by it, including 360,000 deaths of patients with HIV[1].

Over the past two decades, TB cases have decreased, especially pulmonary TB; in 2012, 0.8 million cases of extrapulmonary TB were reported worldwide[2], with tuberculous lymphadenitis being the most common form, which is responsible for 43% of peripheral lymphadenopathy in the world[3,4].

TB presentation on the chest wall is uncommon, and it is often secondary to a history of pulmonary, pleural or lymph node TB, as in the case we next present[5].

Case presentation

This is the case of an 81-year-old woman with no relevant personal history or chronic-degenerative conditions such as diabetes mellitus. On the directed interrogatory she denied a history of cohabitation with people with TB. Her symptoms had started 2 weeks prior to her admission with volume increase at the left infraclavicular region, with no change of temperature or color at said region; 1 week later, pain in the area was added, as well as malaise, diaphoresis and non-quantified hyperthermia of nocturnal predominance that required physical measures and acetaminophen to be controlled. These symptoms persisted on subsequent days and she therefore attended our hospital. At her admission, during physical examination, a left infraclavicular tumor was found of 8 x 6 cm in size at fixed tension, with burning pain on superficial palpation, and no changes of color or temperature; in addition, ipsilateral axillary chain lymphadenitis was found, the largest size of which was approximately 1.5 cm (Fig. 1). The rest of examination was normal. Laboratory data indicated the presence of leukocytosis of 16,900/mL at the expense of 15,717/µL neutrophilia; a chest X-ray was also performed (Fig. 2 A).

Continuing with the protocol, a chest computed tomography (CT) was performed, where a lesion was observed occupying the left hemithorax, posterior and inferior to the pectoralis minor muscle, with

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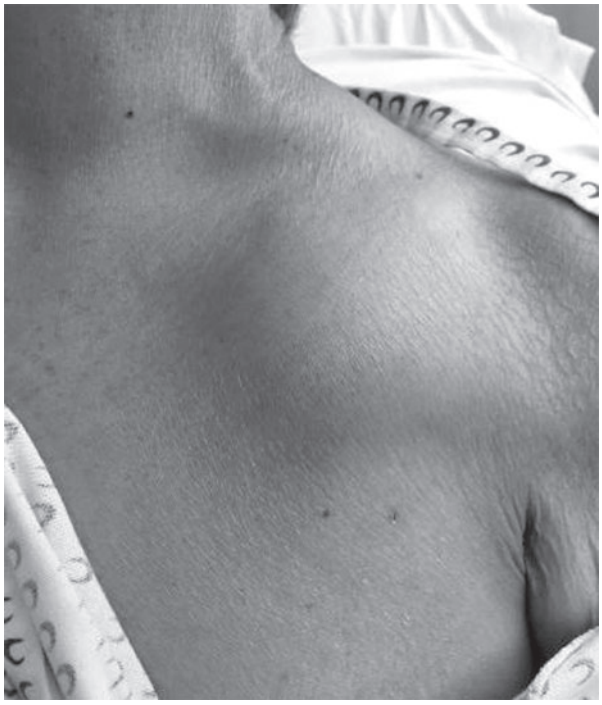

Figure 1. *Clinical photograph showing the volume increase located at the left pectoral infraclavicular region, without hyperemia or skin alterations.*

4.3 x 5.3 mm in diameter, heterogeneous density, multiple adenopathies of the ipsilateral axillary chain and a left supraclavicular lymph node mass associated with cutaneous and fatty involvement, with diffuse interstitial thickening and presence of isolated pulmonary bullae (Fig. 2 B-D).

A pyogenic abscess was suspected and empiric management was started with moxifloxacin for 6 days with a decrease of the mass volume, and the patient was therefore discharged owing to clinical improvement. One month after the discharge, she started with 38 °C fever of nocturnal predominance; she self-medicated with acetaminophen and the temperature decreased. This clinical picture was repeated for the 3 subsequent days and she attended the hospital again. On physical examination, an 11 x 6 cm lesion was found on the left sternocleidomastoid muscle with the same characteristics of the previous one and with ipsilateral cervical lymph nodes present. The rest of the examination was normal.

Plain and contrasted chest CT revealed a 100 x 50 mm hypodense image located below the left sternocleidomastoid muscle extending to the midline, pushing the trachea to the right and compressing the vascular structures of the left cervical region. The contrast revealed peripheral enhancement, which indicated the diagnosis of an abscess at this level. No abdominal or renal lymph nodes were found.

The abscess was drained under fluoroscopy guidance, with 90 cc of purulent material being obtained; Ziehl-Neelsen staining revealed the presence of acid-alcohol-resistant bacilli (AARB) and the sample was sent for culture (Fig. 3 A).

Two days after the puncture, an increase of the abscess volume was found and surgical drainage was carried out, as well as left jugular lymph node resection, with histological report of tuberculous granulomatous lymphadenitis (Fig. 3 C, D). Purified Protein Derived test (PPD) was positive; three bacilloscopies were negative, and the Quanti-FERON-TB assay for TB had an indeterminate result. At 8 weeks of the drainage, *Mycobacterium tuberculosis* growth was reported in Löwenstein-Jensen culture medium (Fig. 3 B), and treatment was therefore started with rifampicin (RIF), isoniazid (INH), pyrazinamide (PZA) and ethambutol (EMB). The patient is currently on follow-up as an outpatient with report of clinical improvement and no relapse of the abscess so far.

Discussion

Tuberculous involvement of the chest wall, as the presented case, is infrequent and accounts for less than 5% of musculoskeletal TB cases and only 1-2% of TB overall; usually, it is 8-fold more common in males than in females and more than half the patients has a previous history of pulmonary TB, unlike the presented case, where there was no history of pulmonary involvement[5,6].

In a series of 181 cases of tuberculous lymphadenitis, Smaoui et al. demonstrated that 55.2% (n = 100) had extended lymphadenopathy and that most common localizations were cervical (83.4%), axillary (6.6%) and unilateral (78.4%). In addition, they found concomitant extrapulmonary TB in 13 patients: miliary in 5, pleural in 2 and abdominal, skin and others only in 1[7].

TB involvement in soft tissues is generally associated with an underlying condition, such as collagenopathies, immunosuppressive therapy or local lesions; however, our patient had none, and reaching a diagnosis was therefore difficult right from the start[8].

Some tissues, such as bone marrow, liver and spleen tissues, are almost always invaded, but rarely allow replication, while others promote growth (pulmonary apices, kidney, brain and bone)[9]. Chest wall TB abscesses are more commonly found at the sternum margins, along the rib axes and also can be located at the costochondral and costovertebral joints. The low incidence of chest TB may be due to the fact that

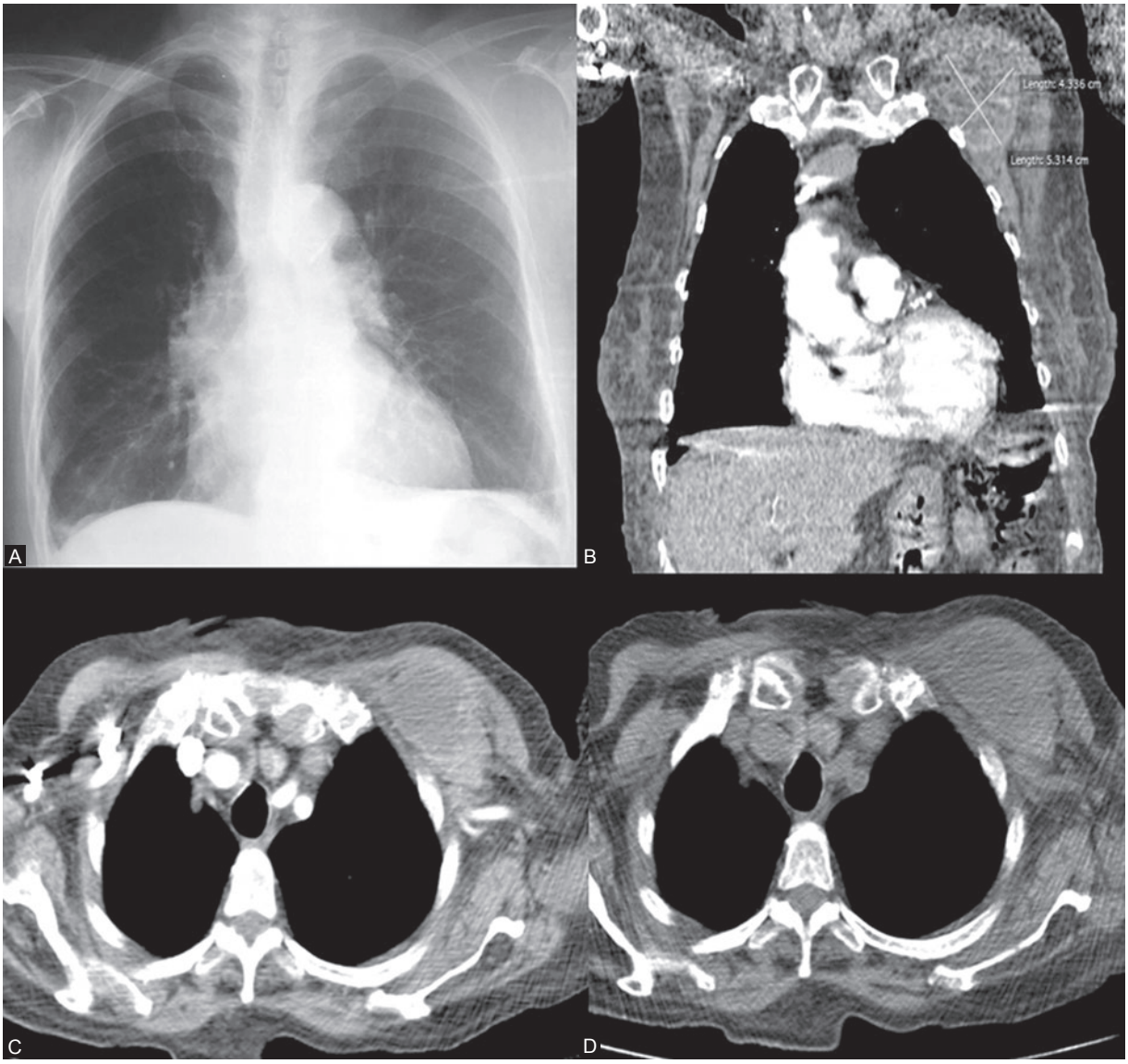

Figure 2. A: *Chest X-ray with evident asymmetry between both infraclavicular regions and left clavicle upward shift. Note the increased density of the ipsilateral hemithorax upper portion.* **B:** *computerized axial tomography (CAT) coronal reconstruction showing the left infraclavicular region tuberculous abscess. CAT sections at simple (***C***) and contrasted (***D***) phases showing a left subpectoral collection with thick capsule that enhances in an annular shape after intravenous administration of non-ionic iodized contrast, of semi-liquid content.*

breast and musculoskeletal tissues appear to be relatively resistant to TB[6].

Clinically, it occurs as a painful, thick, soft or firm tumor, as in the case of our patient[6]. Other of the described systemic clinical manifestations are weight loss, fever, asthenia and nocturnal diaphoresis[7].

Sometimes, abscesses can form fistulae towards the pleural cavity with underlying destruction of bone and cartilage. There are three mechanisms in the pathogenesis of a chest wall tuberculous abscess: 1) direct extension of underlying pleural or pulmonary TB, 2) direct extension of chest wall lymphadenitis and 3) hematogenous dissemination owing to the presence of latent TB[10].

There is one classification by location and level of involvement on CAT scan: 1) lesion confined to the chest wall, 2) lesion confined to the interior chest wall below the ribs and also protruding at the pleural space and 3) lesion that compromises most part of the chest wall and that also protrudes at the pleural space[10].

Diagnosis of the disease is complicated, since TB is known as “the great pretender” and its clinical manifestations occur according to the affected organ. Owing to this, the possibilities of abscess versus neoplasm were the two main probable diagnoses[11]. Nonaka et al. reported AARB positivity only in 35% of cases and positive cultures only in 60% of patients with chest wall TB[12].

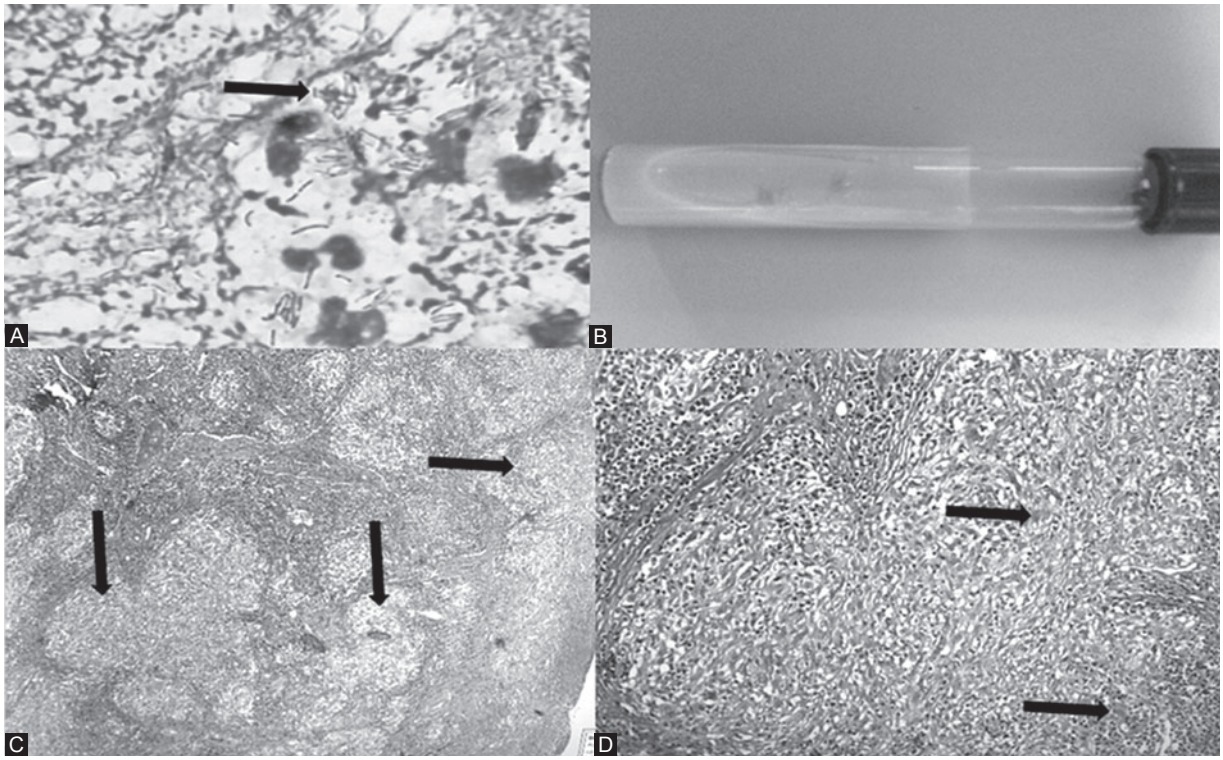

Figure 3. A: *Ziehl-Neelsen staining with abundant AARB (100X lens with immersion oil).* **B:** *positive Löwenstein-Jensen culture.* **C:** *lymph node with architectural distortion caused by the multifocal granulomatous lesion (lens 5X).* **D:** *granulomatous lesion with giant multinucleated and epithelioid cells (lens 25X).*

The treatment of chest wall tuberculous abscess is controversial, but the combination of medical and surgical treatment is the best approach with a recommended duration of 6 to 12 months of medical treatment with 2 months of daily quadruple antitubercular medications (INH, RIF, EMB and PZA) and 4 months of daily dual therapy with INH and RIF or thrice-weekly with at least two of the main antitubercular drugs prescribed during the course of treatment. There is currently no clear global consensus for treatment, including its duration[5,7].

Surgical treatment methods are controversial. The literature refers that this disease is best treated with antibiotics, drainage and debridement, and excision is reserved for most extended cases. Optimal surgical approach consists in extirpating the abscess with wounds primary closure, but the resection extent is not defined. However, extirpation and medical treatment with antitubercular drugs during the postoperative period are mandatory to achieve an acceptable cure rate and the prognosis is generally good if detection is opportunely made[10].

Conclusion

Chest TB diagnosis is always difficult, since its clinical presentation often mimics pyogenic abscess or chest wall tumors, but its likelihood should always be suspected even in the absence of a history of TB disease.

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