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Parotid Lymphoepithelial Lesions and Squamous Cell Metaplasia in Sarcoidosis

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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Case Study

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ABSTRACT

Parotid sarcoidosis is rare. We report a case in which sarcoidosis was revealed by parotid nodules. The medical history revealed cutaneo-respiratory atopia, the blood group type was O. The ultrasound examination was suggestive of pleomorphic adenoma while the computed tomography scan of intraparotid lymph node. Histologically the parotid lesions were peculiar by the association to the non-caseating granulomas of lymphoepithelial lesions with CD3+, CD4+ and CD8+ exocytosis, of ductal squamous cell metaplasia and of calcifications.
In conclusion, lymphoepithelial lesions, squamous cell metaplasia and with T cell exocytosis may occur in parotid sarcoidosis. Parotid sarcoidosis may be misdiagnosed clinically or on imaging explorations with a pleomorphic adenoma or parotid lymph nodes while on microscopy with tuberculous, calculous or carcinoma-related duct obstruction granulomatous sialadenitis or with inflammatory pseudotumors. Associations with blood group type O, atopic disease or hypercalcemia are to be further investigated.

Keywords: Parotid; lymphoepithelial lesion; squamous cell metaplasia; granuloma; immunohisto-chemistry.

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1. INTRODUCTION AND AIMS

Parotid sarcoidosis is rare [1-4]. Women are more frequently affected. A relationship between the HLA-DRB1*0401 allele and blacks is reported [5]. The classical histological features consist in the presence of non-necrotizing/non-caseating granulomas. However, parotid sarcoidosis is rarely diagnosed at microscopic examination [3,4,6-10]. A uni- or bilateral swelling is the most frequent clinical sign, revelatory or occurring in the course of the disease. Fever may also be encountered [6]. Plain radiography may show sialoliths while sialography may suggest chronic inflammation [3,6,11]. A mass can be detected on ultrasound examination (USE), computed tomography (CT) scan or magnetic resonance imaging. The panda sign, suggestive of sarcoidosis, may be identified on the nuclear imaging with Gadolinium 67 [12]. Besides the classical thoracic involvement, a cutaneous, ophtalmic, hepatic, leptomeningeal or dural involvement is also reported [1,4,6]. The association of parotid swelling to facial palsy and uveitis, known as the Heerfordt syndrome is of particular interest. Serum angiotensin converting enzyme (ACE) may be increased while calcium is frequently normal. The main treatment options are NSAIDs and corticoids. Recurrence may occur after spontaneous or post-treatment regression [1-10].

Here we report the histological features of a case of parotid sarcoidosis and discuss relationships to main clinical characteristics.

2. PRESENTATION OF THE CASE

The patient (woman, 57 years) presented with bilateral, painful parotid tumefaction (predominant at left). There was a notion facial palsy dating months before. The medical history revealed familial hypercholesterolemia (BMI of 26.7, rosuvastatine treatment), venous insufficiency (troxerutine treatment), hysterectomy (diagnosis of adenomyoma), appendectomy and treatment with budesonide. The patient also showed eczema to latex; oedema to kiwi and peach and, allergy to dust. The blood group type (BG) was O.

The ultrasound examination showed 2 left pretragus hypoechogen nodules measuring 13- and 10-mm (with vascular pedicle for the largest). A microcyst (3-mm) was also identified. At the right pretragus level, there was a nodule of 12-mm, heterogeneous and hypoechogenous. The submaxillary glands were normal. The imaging diagnosis was suggestive of pleomorphic adenomas. The CT-scan showed multiple bilateral cervical adenopathies (bilateral / zones 1A, 1B, 2A and unilateral/right zone 3) and a left submandibular lesion (24-mm). In the left, superficial parotid there was a non-necrotic parotid lesion with regular limits (15-mm). A similar lesion (10-mm) was seen also in the right superficial lobe. The CT-scan lesions were suggestive of intraparotid lymph nodes (Fig. 1).

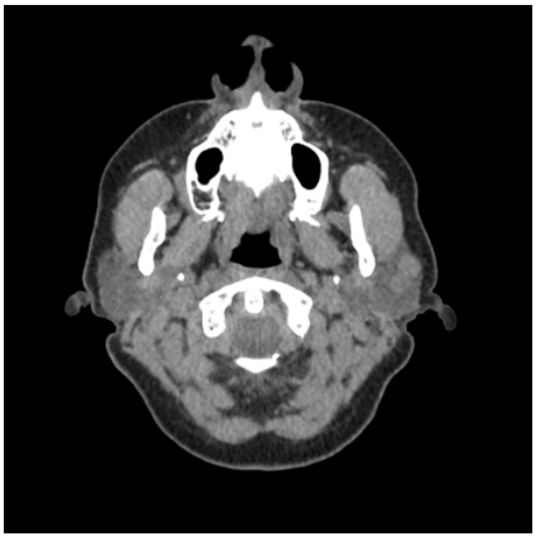

Fig. 1. On computed tomography scan, the parotids were nodular, heterogeneous

A left superficial parotidectomy was performed. Microscopy revealed multiple, confluent, non-necrotizing, non-caseating epithelioid and multinucleated giant cell granulomas (several perivascular) (Fig. 2). Fibrotic bands as well as a multifocal dense lymphocytic infiltrate was also observed along with sparse residual parotid ducts, some of them distorted. Several intra- and extracellular calcifications were also seen. The lesions were suggestive of sarcoidosis. Cytokeratin 5/6 and P63 were positive in the reactive ducts as well as in distorted, proliferative, bud-like structures some with features of squamous cell metaplasia. The lymphocytic infiltrate was CD20+ with disperse CD3+ lymphocytes. The intraepithelial lymphocytes were CD3+, the CD4+ lymphocytes outnumbering those CD8+. The immunoglobulins IgG, IgA, IgM, IgD and, IgG4 were not expressed significantly in the intraepithelial lymphocytes neither kappa or lambda chains.

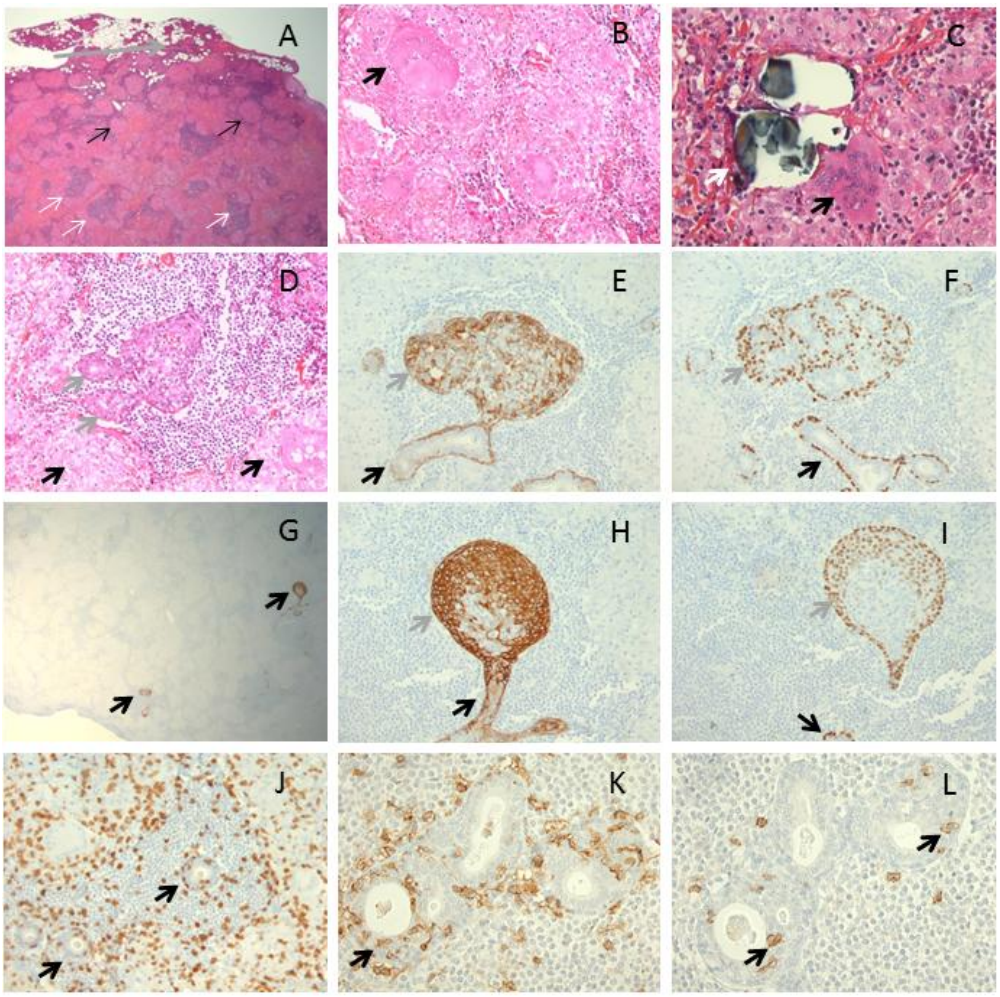

Fig. 2. On microscopy, the nodule consisted in confluent granulomas separated by lymphocytic foci (A: Black arrow for granulomas, white arrows for lymphocytic foci, grey arrow for conserved parotid; B: Black arrow for multinucleated, double horse-shoe type, giant cell). Calcifications were seen adjacent to some granulomas (C: White arrow for calcification, black arrow for multinucleated giant cell). The lymphocytic foci contained distorted ducts with lymphoepithelial lesions and squamous-type metaplasia (D: Black arrow for granulomas, grey arrow for duct). The lymphoepithelial lesion (E: Grey arrow, black arrows for granulomas) and the squamous cell metaplasia foci expressed cytokeratin 5/6 and P63 (E, G, H and F, I, respectively, black arrow for salivary duct, grey arrow for lymphoepithelial lesion/squamous cell metaplasia). CD3 was extensively expressed in granulomas and lymphocytic foci, including in exocytotic lymphocytes (J: Arrow for duct exocytosis of CD3+ lymphocytes). Exocytotic lymphocytes expressed either CD4 or CD8 (K and L, respectively, arrows for exocytotic CD4+ or CD8+ lymphocytes)

The postsurgical CT-scan showed axillary, hilar and superior lung adenopathies. The serum CPK, LDH and GGT were increased as well as the ACE, osseous PAL and calcium. The 25-hydroxycholecalciferol D3 was decreased. TSH and PTH were normal as well as osteocalcin and testosterone. The tuberculin intradermal reaction and sputum cultures for Koch bacillus were negative. The findings were consistent with the diagnosis of sarcoidosis. At 15 months after the initial diagnosis a corticoid treatment (Cortancyl 30 mg/day) was begun as related to a transformation to stage 2 sarcoidosis suggested by the CT-scan aspects, the increased ACE and hypergammaglobuliemia. The corticoid treatment was taken for 26 months. Two months after the

stopping of this treatment, the patient presented with dyspnea, cough and parotid swelling. These findings suggested a sarcoidosis recurrence.

3. DISCUSSION AND CONCLUSION

Here we report a case of parotid non-caseating granulomatous inflammation with lymphoepithelial lesions (LEL) and squamous cell metaplasia revealing sarcoidosis. The inflammatory lesions consisted in a pseudolymphoid/MALT-type lymphocytic reaction surrounding the epithelioid- and multinucleated giant cell granulomas. CD3, CD4 and/or CD8-positive epithelial exocytosis was identified in intralesion epithelial ducts, either conserved or of LEL-type with squamous cell metaplasia. The histogenesis of these proliferative epi-myoepithelial sialadenitis lesions also described in tuberculosis and in Sjogren syndrome (including in cases with associated inflammatory pseudotumors), showing T-lymphocyte exocytosis, is matter of debate, since the investigation in the present case for acid-fast bacilli and dry eye and mouth syndrome were negative [9,13,14].

The main clinical differential diagnosis was that of a pleomorphic adenoma as suggested by the ultrasound examination, a similar clinical, presurgical diagnosis being reported also by van der Walt et al. [9]. Other differential diagnoses were those of intraparotid lymph nodes as suggested in the present case by the CT-scan or lymphoma, unsustained by the microscopy findings. Other diagnoses which can be outruled as based on microscopy are granulomatous sialadenitis related to calculous or carcinomatous duct obstruction [9]. The diagnosis of parotid inflammatory pseudotumor has also to be included in the list of differential diagnoses. This term defines parotid reactive pseudoneoplastic phenomena, reported in many parts of the body. This diagnosis may be ruled out as the predominant fibroblastic/myofibroblastic component lacked in the present case [14,15].

Similarly to parotid inflammatory pseudotumors, calcifications are observed in sarcoidosis, related to the HLA-DRB1*1101 allele in whites [5]. In the present case, calcifications were at contact to the granulomas. Their precise histogenesis, whether corresponding to sialoliths or extraskeletal multiorgan calcifications associated to the sarcoidosis-related hypercalcemia, remains difficult to determine [3,16].

Of interest would be the presence of atopia of eczema and oedema-type and of allergy in the case we report, previously related disorders in sarcoidosis being urticaria and asthma [17]. Interestingly no uveitis was present although more frequent in sarcoidosis patients with atopia/eczema [18]. A putative relationship to the BG-type O, seen in the present case, has to be mentioned as BG-type O patients are known to be at higher risk to develop atopic disease, however of respiratory type [19,20].

Pain and facial palsy in sarcoidosis are also rarely reported. However, facial nerve involvement is reported in 15% of parotid sarcoidosis cases [3]. Although possibly spurious, the similarities with the case reported by McCormick et al. in 2016 [8], consisting in an altered lipid metabolism and endometrial dystopia (hyperlipemia and endometriosis in the reported case) should not be outlooked.

In conclusion, lymphoepithelial lesions, squamous cell metaplasia and T-cell exocytosis may occur in parotid sarcoidosis. Parotid sarcoidosis may be misdiagnosed clinically or on imaging explorations with a pleomorphic adenoma or lymph nodes while on microscopy with tuberculous, calculous or carcinoma-related duct obstruction granulomatous sialadenitis or with inflammatory pseudotumors. Associations with BG-type O, atopic and allergic disease, hypercalcemia are to be further investigated.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The study is performed in agreement with national and international ethics legislation.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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