Short Communication

Xanthomatous sialadenitis: Autoimmune- or treatment-induced lesions?

Adriana Handra-Luca

APHP GHU Avicenne, University Paris Nord Sorbonne Cite, Bobigny, France

Abstract Xanthomatous sialadenitis (XS) is rarely reported. Here we report XS in a case of HLA-B27-positive ankylosing spondylitis showing also anti-MAG-positive polyneuropathy with IgM-kappa dysimmunoglobulinemia/paraproteinemia, lung small cell carcinoma and buccal squamous cell carcinoma (SCC). The lesions were identified in submandibular and labial minor salivary glands of a neck dissection specimen (made during a buccal 1.7 cm large SCC resection procedure). The oral SCC was resected at 8 months after the diagnosis of the lung small cell carcinoma (with skull dome metastases, revealed by a superior cava syndrome) and at 2 months after radiotherapy. The microscopic XS-lesions consisted in multifocal accumulations of CD68-positive macrophages. Plasmocyte-abundant foci (CD138-positive) were extra-xanthomatous (atrophic parenchyma, zones of adipose involution). CD138 was also expressed in ductal cells and in acini (focally). In conclusion, we report XS of submandibular and labial minor salivary glands, occurring in the context of a HLA-B27-positive ankylosing spondylitis, polyneuropathy with IgM-kappa dysimmunoglobulinemia and anti-MAG antibodies in a case of small cell lung carcinoma (treated by radio-chemotherapy) and oral SCC.

Keywords: Salivary gland, sialadenitis, ankylosing spondylitis, cd138

Address for correspondence: Adriana Handra-Luca, APHP GHU Avicenne, University Paris Nord Sorbonne Cite, Bobigny, France.
E-mail: adriana.handra-luca@aphp.fr\adriana.handra-luca@hotmail.com
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Xanthomatous sialadenitis, pseudo-tumoral or not, idiopathic or secondary (Warthin's tumor), is rarely reported.[1,2]

We had encountered such lesions in the submandibular and labial minor salivary glands of a neck dissection specimen (made during a buccal 1.7-cm large squamous cell carcinoma [SCC] resection procedure). The oral SCC was resected at 8 months after the diagnosis of the lung small cell carcinoma (with skull dome metastases, revealed by a superior cava syndrome) and at 2 months after the end of the radiochemotherapy.

The medical history revealed ankylosing spondylitis human leukocyte antigen (HLA)-B27 positive (diagnosed 15 years previously) and polyneuropathy with IgM-kappa dys/para-immunoglobulinemia and anti-myelin-associated glycoprotein (MAG) antibodies (identified 4 years before the diagnosis of the lung small cell carcinoma). There was also a history of alcohol and tobacco overuse (without allergy), of radiochemotherapy (carboplatin, VP16, etoposide, neulasta), corticoid (for ankylosing spondylitis) and anti-depression (gabapentin, citalopram, valium, stilnox) treatments as well as of appendectomy and

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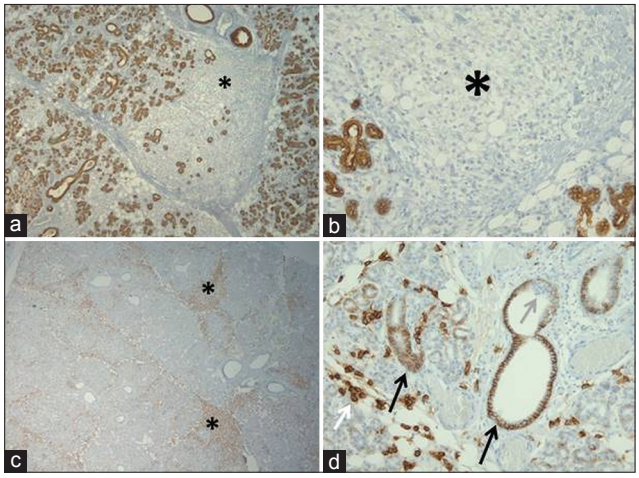

Figure 1: A multinodular xanthomatous inflammatory reaction was observed in the salivary gland connective tissue (a and b: immunohistochemistry for cytokeratin AE1/AE3, asterisk for cytokeratin-negative xanthomatous foci). The multifocal xanthomatous foci were composed of CD68-positive cells (c: asterisks). CD138 was expressed in the salivary gland duct epithelia and in plasmocytes (d: black arrow for CD138-positive ducts, white arrow for positive plasmocytes and gray arrow for ductal exocytosis). To note would be the lack of CD138-positive plasmocytes in periductal location including the exocytosis site. Original magnification ×2.5 (a and c), ×20 (b), ×10 (d)

tonsillectomy (adolescence) and of gallbladder lithiasis and pyelonephritis (dates unprecised).

The microscopic lesions consisted in a multifocal accumulation of CD68-positive macrophages intermingled with rare lymphocytes in the salivary gland lobules. Incipient lesions predominated at the periphery of the lobules, along the interlobular connective tissue septa [Figure 1]. Periductal and parenchymal fibrosis were mild and focal. Glandular acini were focally absent/atrophic while the ducts were conserved. Several ducts showed basal cell hyperplasia and focal exocytosis. There were no intraluminal stones or calcified secretions. CD138-positive plasmocyte-abundant foci were seen in the atrophic parenchyma and zones of adipose involution, outside the xanthomatous foci. CD138 was also expressed in ductal cells with a membrane pattern (intralobular, interlobular and extralobular) and focally in acinar cells.

Here, we report xanthomatous sialadenitis in a case of HLA-B27-positive ankylosing spondylitis showing also anti-MAG-positive polyneuropathy with IgM-kappa dys/para-immunoglobulinemia, lung small cell carcinoma and buccal SCC.

The histogenesis of the multifocal and multiglandular (both major and minor salivary glands) xanthomatous sialadenitis lesions is difficult to precise. A peculiar immune background may be incriminated although the CD138-positive plasmocytes were mainly seen outside the xanthomatous foci. However, recurrent submandibular sialadenitis as diagnosed by sialendoscopy is reported in cases of HLA-B27 seropositivity.[3]

To note would be the expression of CD138 in the salivary gland duct epithelia, from acini to extralobular duct level, these observations in human submandibular and labial minor salivary glands being in agreement with data on syndecan-1 and submandibular gland branching and acinar development.[4,5] Interestingly, foci of exocytosis in the CD138-positive epithelia were encountered, consistent with the known CD138-related transepithelial efflux of inflammatory cells.[6]

The potential impact of the radiotherapy treatment given for the lung tumor, on the salivary gland lesions, remains difficult to evaluate as well as that of the chemotherapeutic and/or antidepressive drugs and of the alcohol and smoking overuse.[7-9] A paraneoplasia-type background in relationship either with the lung small cell carcinoma or with the oral SCC, of quasi-synchronous development, cannot be excluded both for the polyneuropathy with anti-MAG antibodies and IgM-kappa dys/para-immunoglobulinemia and for the multifocal sialadenitis lesions.

In conclusion, we report xanthomatous sialadenitis of the submandibular and labial minor salivary glands, occurring in the context of a HLA-B27-positive ankylosing spondylitis, polyneuropathy with IgM-kappa dys/para-immunoglobulinemia and anti-MAG antibodies in a case of small cell lung carcinoma (treated by radiochemotherapy) and oral SCC. Further investigations may be required to elucidate the precise histogenesis of such lesions.

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