

Case report

Pleural chondroid metaplasia in a background of IgG4 plasma cell rich chronic inflammatory infiltrate: report of a rare case with review of literature

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Summary

Mesothelial reactive and degenerative changes secondary to inflammatory conditions, toxin exposure, neoplastic and non-neoplastic disease are often encountered in routine histopathology practice. Herein, we report a very rare case of pleural chronic inflammation with features suggestive for IgG4-related disease associated with the formation of a nest of mature, benign looking cartilage in the pleura of a middle age male patient. The review of the pertinent literature reveals that to date, only few cases of chondroid metaplasia or benign tumor (choristoma) are reported in mesothelium and only occasionally in this change is found in the pleura.

Key words

Chondroid metaplasia • Pleura • Stem cells

Introduction

Mesothelium can react to different stimuli (of inflammatory, chemical, toxic, neoplastic origin) with inflammation, fibrosis necrosis and other degenerative changes. One of the most peculiar, albeit rarely seen changes is the development of mesenchymal derived tissues such as bone or cartilage. The pathogenesis of this condition is still not fully understood and further studies are needed in order to define the mechanisms at the origin of this rare form of metaplasia.

Case report

A 51-years-old male came to clinical attention for a five weeks history of breathlessness. The patient, who worked as a driver and in construction, had a significant smoking habit (30 cigarettes per day), diabetes,

hypertension and high cholesterol blood levels under treatment. Imaging showed a moderate left pleural effusion with no evidence of specific features on CT. PET showed moderately avid lymph nodes in the paratracheal and AP window regions but no evidence of activity in the pleura (Fig. 1).

The thoracentesis drained 300 ml of blood stained fluid which showed no evidence of atypical/malignant cells on cytology examination.

During the lung multidisciplinary meeting it was decided to proceed with thoroscopic pleural biopsies and talc pleurodesis.

The pleural biopsies were represented by multiple fragments of cream and yellow fat tissue with fibrotic consistency, measuring on aggregate up to 30 x 25 x 10 mm. The gross examination did not enlighten obvious pleural plaques or focal abnormalities. The tissue was entirely submitted for histological assessment.

Microscopy examination showed reactive mesothelial

How to cite this article: Spinelli M, Datta A, Montero Fenandez MA, et al. *Pleural chondroid metaplasia in a background of IgG4 plasma cell rich chronic inflammatory infiltrate: report of a rare case with review of literature.* Pathologica 2019;111:361-4. <https://doi.org/10.32074/1591-951X-1-19>.

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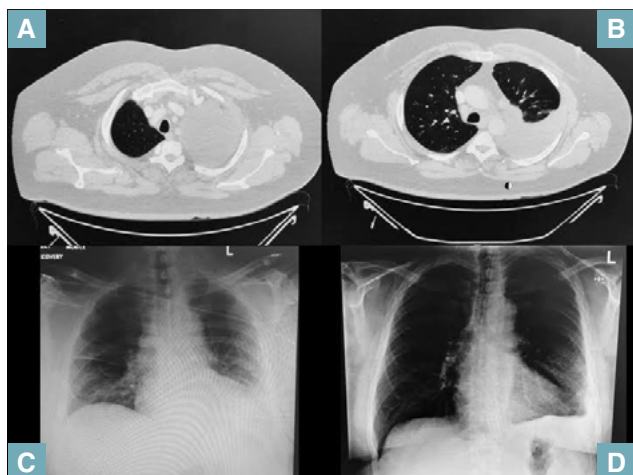


Fig. 1. A and B: CT Thorax with contrast. Large left pleural effusion with underlying compression atelectasis of the basal segment of the left lower lobe and lingual; C and D: Post op Chest X-Ray showing progressive reduction of the effusion.

tissue covering stroma and fat tissue with patchy fibrosis. The fibrotic tissue did not show storiform pattern, collagen necrosis or dysplasia. The fibrosis was associated with a moderate to severe chronic inflammation with a prominent plasma cell component and some pigment-laden histiocytes, but there was no evidence of granuloma formation. The fibrotic stroma showed areas of hyalinization and formation of cartilaginous tissue featuring bland, benign looking chondrocytes. There was no evidence of vasculitis, obliterative phlebitis, necrosis, dysplasia or malignancy.

Immunohistochemistry and special stains confirmed the presence of reactive mesothelial cells (Calretinin and CKAE1/AE3 +), polytypic benign plasma cells (Kappa and Lambda chains stains +) and the absence of amyloid (Congo Red -). The presence of patchy areas of increased, polyclonal plasma cells associated with fibrosis raised the concern of a possible IgG4-related disease. The presence of the chondroid metaplasia itself did not influence this suspect as no data are available in literature to support a relationship between chondroid metaplasia and this entity. The stain for IgG4 showed an increased number of IgG4 + plasma cells focally up to 50 cells/HPF. In these fields the IgG4+/IgG ratio was occasionally more than 40% (Figg. 2-3). The overall appearance, together with the special stains and immunohistochemical features was compatible with moderate to severe chronic inflammation with features suggestive, but not entirely diagnostic for IgG4-related disease. However, the absence of diffuse fibrosis

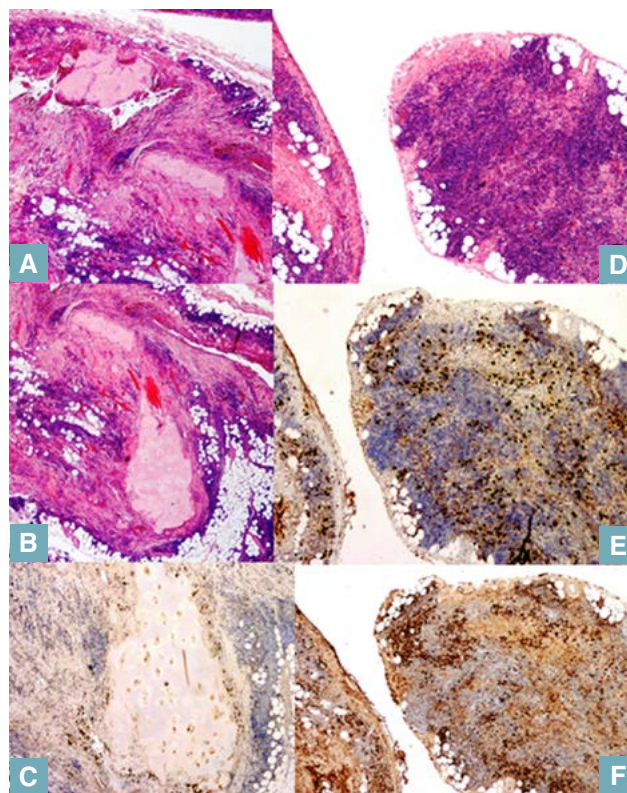


Fig. 2. A and B: Islands of chondroid metaplasia in the pleural tissue (H&E 2X); C: Chondroid tissue highlighted by S100 (IHC 4X); D: Lymphoplasmacellular infiltrate (H&E 2X); E and F: Inflammatory infiltrate IgG and IgG4 staining (2X).

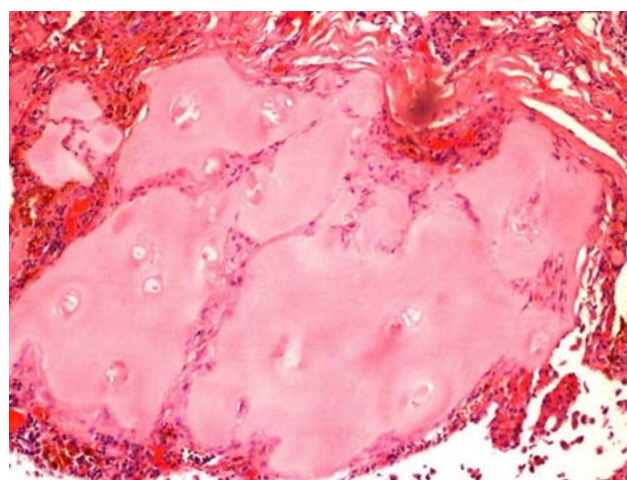


Fig. 3. Magnification of the mature chondroid metaplastic tissue (H&E 10X).

and phlebitis was not entirely supportive for a diagnosis of IgG4 related disease and serology levels were re-

quested for confirmation. Serum IgG4 resulted within normal limits, thus excluding the diagnosis of IgG4-RD.

Discussion and review of literature

The most important features of this biopsy were the plasma cell rich chronic inflammation and the formation of ectopic chondroid tissue. Chondroid metaplasia is a relatively uncommon finding which has been described in different anatomical sites and conditions (both neoplastic and non-neoplastic), but is rarely reported in mesothelium¹ and even more occasionally in pleura. Chondroid metaplasia has been reported in tongue², head and neck³⁻⁵, breast^{6,7}, lung⁸ and brain⁹. Formation of ectopic, metaplastic cartilage in the mesothelium is rare and only a few cases are reported in the literature¹⁰⁻¹⁵.

The pathogenesis of benign-looking cartilaginous tissue in mesothelium covered anatomic sites is still not fully understood. Some authors speculate that a population of sub-mesothelial pluripotent stem cells could differentiate towards mesenchymal and chondroid phenotypes^{11,13}. Other factors such as previous surgery, trauma, hemorrhage, abortion, ectopic pregnancies, teratomas or other neoplasms (both benign and malignant) have been considered as pathogenetic factors¹⁰⁻¹².

As shown in the Table the presence of metaplastic cartilaginous tissue is rare in pleura: in 1931 Klemperer et al. reported chondroid metaplasia in a series of pleural tumors¹³ (although it was not possible to identify the exact number of metaplasia cases in this study), and in 2014 Walsh et al. reported a case of chondroid metaplasia within a rare pleural lipoma¹⁴.

The present case is peculiar for its rarity and the lack of association with neoplasia. It presented itself as a focal area of well defined, mature and S-100 + cartilage on the background patchy, non storiform fibrosis and prominent lymphoplasmacellular inflammatory in-

filtrate. One of the most relevant features of our case is the association with several, polytypic active plasma cells which, in areas, were expressing the IgG4 phenotype. The presence of this specific plasma cellular phenotype raised the possibility of a systemic IgG4-related disease, thus clinical and serological correlation was strongly recommended in the histopathology report. The serology results came back as negative for pathologic IgG4 levels in blood, and thus a diagnosis of IgG4-Related disease was excluded.

Our case showed only one of three histopathological criteria, but clinical and serological results were negative. The review of the pertinent literature¹⁵⁻¹⁷ did not enlighten the development of chondroid metaplasia in the specific settings of IgG4-RD. However, it is possible that inflammatory-related molecules produced by activated plasma cells, or the specific micro-environment favored by the chronic inflammation may lead to a local increased expression of matrix and osteo-cartilaginous molecules (such as osteopontin, osteonectin, CD68, different cytokines and interleukins) which could promote the differentiation of fibroblasts and mesenchymal stem cells into the chondroid phenotype^{10,11,15,18,19}. A similar pathway is known in the development of heterotopic ossification in several organs (thyroid, soft tissue, gastro-intestinal and genito-urinary tracts) as a reactive/dystrophic reaction to many different neoplastic and non-neoplastic disorders including ischemia, necrosis, hemorrhage and fibrosis¹⁹.

Conclusions

We report here a rare case of pleural cartilaginous metaplasia on the background of a chronic inflammation rich in IgG4+ plasma cells. Our case can be considered of interest for the rarity of the chondroid metaplasia itself and for its possible association with a chronic systemic inflammatory disease such as IgG4-

Tab. I. Chondroid metaplasia in mesothelium: review of literature.

Author	Year	Site	Surgery/trauma	No. of cases
Jacobowitz et al.	1930	Peritoneum	Not known	Not known
Klemperer et al.	1931	Pleura	Not known	Not known
Roth et al.	1966	Uterine serosa	Not reported	2
Fadare et al.	2002	Peritoneum	Not reported	2
Houang et al.	2010	Pelvic peritoneum	Yes	1
Walsh et al.	2014	Pleura (within pleural lipoma)	No	1
Kaur et al.	2017	Pelvic peritoneum, broad ligament	Yes	1
Nwanze et al.	2018	Peritoneum surface at porta hepatis	No	1
Franceschi et al.	2018	Peritoneum	Not reported	2
Present case	2018	Pleura	No	1

RD. Only occasional cases of pleural chondroid metaplasia have been reported in the literature to the best of our knowledge and none was related with such a peculiar background.

CONFLICT OF INTEREST STATEMENT

None declared.

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