Primary Mediastinal Choriocarcinoma in an Elderly Patient with Concurrent Goserelin-Treated Prostate Adenocarcinoma

Rasmus Røge,1,2 Carsten Simonsen,3 and Astrid Christine Petersen1

1Department of Pathology, Aalborg University Hospital, DK-9000 Aalborg, Denmark
2Department of Clinical Medicine, Aalborg University, 9000 Aalborg, Denmark
3Department of Cardiothoracic Surgery, Aalborg University Hospital, DK-9000 Aalborg, Denmark

Case Report

Choriocarcinoma is a rare malignant tumour that most commonly develops from the chorionic part of the placenta. In males, it is most commonly seen in the testes as part of a mixed germ cell tumour in young males. Extragonadal occurrence is rare—preferentially in axial structures, such as the mediastinum, retroperitoneum, and brain. The prognosis of mediastinal choriocarcinoma is usually poor, which underlines the necessity of rapid diagnosis [1].

We report here a rare case of primary mediastinal choriocarcinoma in an elderly patient with concurrent goserelin-treated metastasized prostate adenocarcinoma.

A 71-year-old man presented with a 5-week history of severe back pain. Five years earlier, the patient was diagnosed with metastatic prostate adenocarcinoma (Gleason score 4+4) and was treated with gonadotropin releasing hormone (GNRH) agonist implants (goserelin, 10.8 mg). After 9 months of treatment, prostate specific antigen (PSA) values returned to normal levels.

Upon admission, bone scintigraphy showed no bone metastases but a potential compression fracture of the L2 vertebra. CT-scan confirmed a lesion in L2 and revealed a 5-cm spherical tumour located in the anterior mediastinum and multiple lung metastases. The periphery of the mediastinal tumour had high levels of Fludeoxyglucose metabolism as seen on PET-CT. The lung metastases and L2 were also PET-positive. Needle biopsy from the mediastinal tumour showed necrosis but no tumour cells. Decompressive laminectomy was performed, and suspected tumour tissue was sent for histological examination. Unfortunately, the patient expired before any conclusive diagnosis could be reached and therapy instituted.

Autopsy revealed a 5.5 cm spherical tumour in the mediastinum adherent to but not invading the left lung. The lung parenchyma bilaterally contained multiple suspected metastases. The prostate was slightly enlarged but showed no macroscopic signs of adenocarcinoma. Both testes were atrophic and without signs of focal lesions.

The extensive microscopic examination of the mediastinal tumour revealed widespread necrosis and peripheral areas with two distinct tumour cell populations (syncytiotrophoblasts) (Figure 1). Morphologically, the mediastinal tumour and the metastasis in the lung and lumbar vertebra were a pure choriocarcinoma. The tumour was extensively characterized by immunohistochemistry and
Table 1: Immunohistochemical expression profile.

|                     | hCG | Inhibin | OCT3/4 | SALL4 | GLP3 | GATA3 | CD71 | CK7 | p63 |
|---------------------|-----|---------|--------|-------|------|-------|------|-----|-----|
| Syncytiotrophoblast | pos | pos     | neg    | neg   | pos  | pos   | pos  | pos | neg |
| cells               |     |         |        |       |      |       |      |     |     |
| Cytotrophoblast     | pos | neg     | neg    | pos   | neg  | pos   | pos  | pos | pos |
| cells               |     |         |        |       |      |       |      |     |     |

At time of diagnosis, the patient was 71 years old. This differs significantly from the typical epidemiology of mediastinal choriocarcinomas, which occurs primarily in younger patients [7]. One might speculate that the long-term treatment with goserelin may have stimulated development of the tumour, especially considering that GNRH receptors are expressed in choriocarcinomas [8]. On the contrary, one in vitro study found inhibitory properties of endogenous GNRH in a single choriocarcinoma cell line [9]. However, these results may only be extrapolated to goserelin with caution, since synthetic GNRH agonists are 50 to 100 times more potent than endogenous GNRH [10].

Insights into the potential carcinogenic properties of goserelin and knowledge of expression of GNRH receptors may be utilized in the diagnosis and treatment of choriocarcinomas.

3. Conclusion

Extragonadal choriocarcinomas are extremely rare germ cell tumours, and diagnosis requires advanced immunohistochemical analysis. The prognosis is usually poor, which underlines the necessity of rapid diagnosis in order to institute treatment before progression hinders treatment. In this case report, we speculate that long-term treatment with goserelin may have stimulated the development of the choriocarcinoma.

Conflicts of Interest

All authors declare that they have no conflicts of interest.

References

[1] C. A. Moran and S. Suster, “Primary mediastinal choriocarcinomas: A clinicopathologic and immunohistochemical study of eight cases,” The American Journal of Surgical Pathology, vol. 21, no. 9, pp. 1007–1012, 1997.
[2] G. Berthod, H. Bouzourene, C. Pachinger, and S. Peters, “Solitary choriocarcinoma in the lung,” Journal of Thoracic Oncology, vol. 5, no. 4, pp. 574-575, 2010.
[3] D. L. Zynger, M. J. Everton, N. D. Dimov, P. M. Chou, and X. J. Yang, “Expression of glypican 3 in ovarian and extragonadal germ cell tumors,” American Journal of Clinical Pathology, vol. 130, no. 2, pp. 224–230, 2008.
[4] D. Cao, J. Li, C. C. Guo, R. W. Allan, and P. A. Humphrey, “SALL4 is a novel diagnostic marker for testicular germ cell tumors,” The American Journal of Surgical Pathology, vol. 33, no. 7, pp. 1065–1077, 2009.
[5] M. Miettinen, P. A. McCue, M. Sarlomo-Rikala et al., "GATA3: a multispecific but potentially useful marker in surgical pathology: a systematic analysis of 2500 epithelial and nonepithelial tumors," The American Journal of Surgical Pathology, vol. 38, no. 1, pp. 1–10, 2014.

[6] S. J. Wegman, A. V. Parwani, and D. L. Zynger, "Cytokeratin 7, inhibin, and p63 in testicular germ cell tumor: superior markers of choriocarcinoma compared to $\beta$-human chorionic gonadotropin," Human Pathology, vol. 84, pp. 254–261, 2019.

[7] C. A. Moran and S. Suster, "Primary germ cell tumors of the mediastinum: I. Analysis of 322 cases with special emphasis on teratomatous lesions and a proposal for histopathologic classification and clinical staging," Cancer, vol. 80, no. 4, pp. 681–690, 1997.

[8] H. Yin, K. W. Cheng, H.-L. Hwa, C. Peng, N. Auersperg, and P. C. K. Leung, "Expression of the messenger RNA for gonadotropin-releasing hormone and its receptor in human cancer cell lines," Life Sciences, vol. 62, no. 22, pp. 2015–2023, 1998.

[9] J. Horvath, T. Ertl, Y. Qin, K. Groot, and A. Schally, "Lh-rh and its antagonist cetorelix inhibit growth of jar human choriocarcinoma cells in-vitro," International Journal of Oncology, vol. 6, no. 5, pp. 969–975, 1995.

[10] J. B. Engel and A. V. Schally, "Drug insight: Clinical use of agonists and antagonists of luteinizing-hormone-releasing hormone," Nature Clinical Practice Endocrinology & Metabolism, vol. 3, no. 2, pp. 157–167, 2007.