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CASE REPORT

A rare association between malignant mediastinal seminoma and other malignant neoplasms

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ABSTRACT. Primary malignant mediastinal seminomas (PMMS) are rare tumors accounting for 1-6% of all mediastinal tumors. PMMS mostly affect young men, arising from primordial germ cells that abnormally migrate from the ectoderm of the yolk sac to the gonadal region. They are clinically and biologically distinct from primary testicular tumors and seem to have a worse prognosis. Due to the rarity of the disease, the choice of treatment is a matter of debate. Literature data do not show any association between this kind of tumor and malignant Schwannoma or thyroid carcinoma. In this report we describe the case of a patient affected by PMMS and 12 yr later by a malignant brachial plexus Schwannoma and papillary thyroid carcinoma (PTC). Since both mediastinal seminoma and Schwannoma were treated with surgery followed by local radiotherapy, we were not able to ascertain if either PTC or Schwannoma had been induced by radiotherapy or represented a casual neoplastic association.

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INTRODUCTION

Primary malignant mediastinal seminomas (PMMS) are rare tumors, histologically identical to their gonadal counterpart. They account for 1-6% of all mediastinal tumors (1, 4). Mediastinum is the 3rd most frequent site for malignant germ cell tumors after testes and retroperitoneum. Although uncommon, mediastinal germ cell tumors are of particular interest since they mostly affect young men aged 20 to 40 yr. Although primary mediastinal seminomas in women have also been reported (5, 8); clinically and biologically distinct from primary testicular tumors, PMMS have similar histological features (2, 3). It is widely believed that PMMS have a worse prognosis than testicular germ cells tumors and therefore require specific treatment. However, many Authors believe that the prognosis of patients with mediastinal seminomas can be very good if the tumors are diagnosed at an early stage. As only a few cases of these tumors have been reported, the therapy for this disease is still a matter of debate.

Literature data do not show any association between this kind of tumor and malignant Schwannoma or thyroid carcinoma. In this report, we describe the case of a patient affected by primary mediastinal seminoma associated with malignant Schwannoma and papillary thyroid carcinoma (PTC).

CASE REPORT

We report the case of a 48-yr-old man who underwent our evaluation for the first time in June 1974, accusing fatigue, dyspnea and dysphagia.

Chest X-ray showed a mass in the mediastinum; chest CT scan demonstrated the presence of a large tumor occupying the anterior part of the mediastinum and infiltrating the right lung with a maximum diameter of about 15 cm. Diagnosis of seminoma was obtained by exploratory thoracotomy and biopsy of the tumor.

Abdominal and cerebral CT, testicular ultrasonography (US), α-phetoprotein and β-human chorionic gonadotropin were within the normal range. The

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patient was treated with radiotherapy and 2 months later a chest CT revealed a complete disappearance of the tumor mass. In October 1986, the patient referred pain in the left superior limb. A brachial plexus CT revealed an irregular mass close to the 1st left rib, behind the succlavian artery. The patient underwent surgical resection of a tumor mass of about 6.5 cm of maximum diameter, which was histologically diagnosed as a malignant Schwannoma, located in the center of the nervous trunk. The surgical resection was followed by local radiotherapy.

One year later a clinical examination showed the presence of an anterior neck mass. A US examination demonstrated the presence of a solid nodule in the right thyroid lobe of 2.6 cm, which resulted to be "cold" at scintigraphic scan. A fine needle aspiration biopsy (FNAB) of the nodule followed by cytological evaluation indicated the presence of PTC. Serum levels of free T3 (FT_3), free T4 (FT_4), TSH and TGAb were within the normal range whereas TG serum values were above the normal range [133 ng/ml, normal values (n.v.) 0-85 ng/ml]. The patient underwent total thyroidectomy and histological examination confirmed the previous FNAB diagnosis. The primary tumor-regional lymphnodes-distant metastases (TNM) evaluation was pT2bN0Mx, G2, St.II. 131-Radioiodine ablation (50 mCi) was performed after the surgical procedure because of the evidence of locoregional residual thyroid tissue at post-operative 131-iodine whole body scan (WBS). The patient has shown no evidence of recurrence to date, although there is a persistent functional deficit of the left superior limb due to surgical damage of axillary and radial nerves.

DISCUSSION

Primary pure seminomas represent approximately 35% of malignant mediastinal germ cell tumors. 20-30% of mediastinal seminomas are asymptomatic when discovered (9). Outcome seems to be influenced by primary mediastinal involvement by germ cell tumors (10, 11) or by initial tumor volume (12) or histology. Previous reports confirmed the good prognosis of mediastinal seminomas compared with non-seminoma germ cell tumors (13, 14). The treatment involves surgery, radiotherapy and chemotherapy in various combinations. The principal treatment of pure mediastinal seminomas is traditionally irradiation. PMMS are extremely sensitive to radiation and long-term survivors following radiotherapy have been documented (15). Thirty-five and forty Gray are the most commonly used radiation doses, although doses as low as 20 Gray have been shown to be curative. Some Authors (9, 16, 17) recommended surgical resection followed by adjuvant irradiation for small resectable tumors, but most of them believe that surgery no longer plays a role in the definitive treatment of seminomas (16, 17). Surgical debulking of large tumors did not prove to be of benefit in improving local control. Chemotherapy was previously used only in advanced extragonadal seminomas: now it can be the treatment of choice in some other circumstances (18). A study by Martini *et al.* (19) showed that 50% of patients with seminomas had a survival time of over 10 yr after resection with or without radiation therapy. Similar results were obtained by other investigators (20-22). These reports induced us to treat our patient with radiotherapy alone.

Neurilemmomas or Schwannomas are the most common tumors on the paravertebral sulcus and occur commonly in people aged 20 to 50 yr. They grow slowly and are usually smaller then 5 cm at the time of diagnosis. The malignant counterpart of Schwannomas is rare: they are commonly large, measuring more than 5 cm in diameter and present with different symptoms according to the location and the size of the tumor. They may cause superior vena cava obstruction, Horner's syndrome, dyspnea, dysphagia and hoarseness. The diagnostic criteria as to which tumors are to be designated as malignant nerve sheath tumors, like: origin from a major nerve, evidence of Schwann cells, presence of S-100 protein in tumor cells and nuclear palisading, is a matter of debate (23). Clinically, these tumors are aggressive and when resected tend to recur; their 5-yr survival is 75%. Treatment consists of surgical resection in stage I and II, adding adjuvant radiotherapy in the latter. Our patient underwent surgical treatment and subsequent radiotherapy according to international protocols.

PTC represent 80-85% of well differentiated thyroid cancers (24, 25). Exposure to radiation of the thyroid gland is the only definitively known risk factor responsible for the increase of the incidence of well-differentiated thyroid cancers (26, 27). However, only a small portion of the total annual cases of PTC is due to radiation (28); 9% of them could be related to radiation exposure, meaning that 91% of cases have no clear risk factor, the latency period after exposure is at least 3 to 5 yr and there is no apparent drop-off in the increased risk even 40 yr after the radiation exposure (29, 30). In adult patients treated with radiotherapy for malignancies, there is a drop-off of risk reflecting the importance of age at the moment of exposure (31). Recently, the Chernobyl nuclear disaster confirmed these da-

ta showing a great increase in the appearance of PTC particularly in children which was not related to the presence of RET/PTC rearrangement but strictly dependent on radiation (32-34). According to our experience, literature data reported on the association of testicular tumors with skin lesions, gastrointestinal hamartomatous polyps and a variety of non-endocrine and endocrine tumors such as thyroid gland tumors named familial lentiginoses syndromes (Carney complex, Peutz-Jeghers syndrome, Cowden disease and Bannayan-Zonana syndrome) (35-39). Nevertheless, we did not find any association in the literature between mediastinal seminoma, thyroid carcinoma and malignant Schwannoma. (35-39). In conclusion, it is difficult to verify whether thyroid carcinoma arises, in our patient, as a consequence of previous radiation exposure or could be part of a familial syndrome in association with mediastinal seminoma.

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