FISH Technique as Additional Diagnostic Tool in Differentiating Testicular Pulmonary Metastasis from Pulmonary Congenital Cystic Adenomatoid Malformation

To the Editor:

Testicular cancers are rare, making up a small percentage (1.1%) of all malignant tumors in men with an overall mortality rate of 0.4 per 100,000 (http://eu-cancer.iarc.fr/EUCAN/CancerOne.aspx?Cancer = 30&Gender = 1).

Germ cell tumors comprise >95% of all testicular malignancies. They are the most common malignancies and, are one of the most common causes of cancer-related death in males between 15 and 35 years. Typical sites of metastases include retroperitoneal, mediastinal, and supraclavicular lymph nodes. Pulmonary metastases are the most common site of visceral organ metastases. Liver, brain and bone metastases are less common.[1]

Although testicular mixed germ cell tumors are malignant, they are curable. Important factors for clinical outcome are serum tumor marker levels, tumor stage, presence/absence of vascular invasion, and correct histologic interpretation of tumor components.[2–4] All these parameters should be taken into account for selecting the therapeutic management of a testicular germ cell tumor.

A 44-year-old patient presented with a painless gradual enlargement of the right testis during a period of several months. Physical examination was normal except for a palpable mass in the right testis. Serum α-fetoprotein was 65.41 ng/mL (normal, 0 to 15 ng/mL), β-human chorionic gonadotropin was 8.97 ng/mL (normal, 0 ng/mL). Ultrasonography of the scrotum revealed a nonhomogeneous mass in the right testis with varying echogenicity. Subsequent radical inguinal orchiectomy was performed.

Histopathology showed a mixed germ cell tumor composed of mature teratoma and embryonal carcinoma. A diagnosis of a pT2 mixed germ cell tumor of the testis with vascular invasion was made. The patient underwent 4 cycles of chemotherapy with Etoposide and Cisplatin within a period of 4 months.

A follow-up computed tomography scan of the chest, 6 weeks after surgery, revealed a middle lobe nodular-cystic density of the right lung. Histopathology of this lesion suggested a diagnosis of a pulmonary congenital cystic adenomatoid malformation (CCAM), although a fully differentiated metastasis of germ cell origin could not be ruled out by histopathology alone.

Primitive forms of testicular germ cell tumors such as seminoma and embryonal carcinoma respond well to chemotherapy, whereas mature teratoma is not chemosensitive.[5] Lung metastases of mixed germ cell tumors often show a pattern of mature teratoma, especially after chemotherapy. Typical components of teratomatous metastases are cysts lined by gastrointestinal or squamous epithelium, foci of smooth muscles, lymphoid tissue, cartilage, and striated muscles. Some metastases can be mistaken for CCAM.

By applying fluorescence in situ hybridization with TelVysion 12p Spectrum Green and CEP 12 Spectrum Orange (Vysis) on tissues taken from the lung lesion and the testicular tumor, we demonstrated the presence of polysomy 12, amplification of 12p, and isochromosome 12p in both the lesions. These are characteristic chromosomal aberrations found in testicular neoplasms.[6]

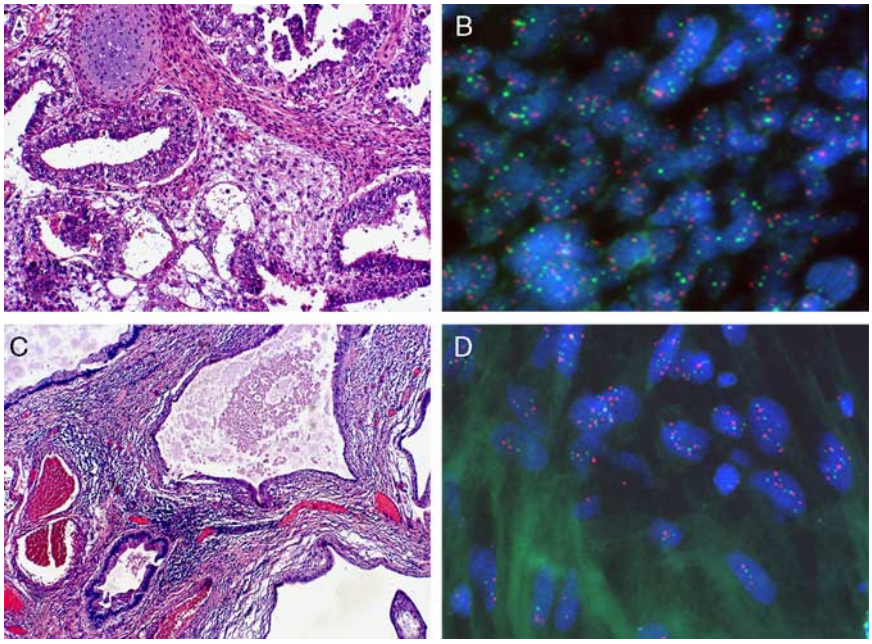

FIGURE 1. A, Testicular teratoma. C, Lung metastasis. B and D, Fluorescence in situ hybridization of the testicular tumor (B) and lung metastasis (D) with probes for the subtelomeric region of 12p (green) and the centromere region of chromosome 12 (orange) exhibiting multiple (>2) signals per interphase nucleus. This signal pattern is indicative of a chromosome 12 aberration and can be caused by polysomy 12 and amplification of 12p or the presence of one or more isochromosomes 12.

The authors declare no conflict of interest.

Finally, a definitive diagnosis of pulmonary metastasis of a testicular germ cell tumor was made, as to our knowledge CCAM does not show any chromosome 12 aberrations.[7]

Fluorescence in situ hybridization can therefore be an excellent additional diagnostic tool in identifying testicular germ cell tumor metastases (Fig. 1).

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REFERENCES

1. Rosai J. Testis. In: Rosai J, ed. *Ackermans Surgical Pathology*. 10th ed. St Louis: Mosby; 2010.
2. Kantoff P. Surgical and medical management of germ cell tumors of the chest. *Chest*. 1993;103(suppl):331S–333S.
3. Suito T, Ishihara T, Yamazaki S, et al. Endobronchial metastasis of testicular embryonal cell carcinoma—a case report. *Gan No Rinsho*. 1983;29:1340–1343.
4. Schramel FM, van Groeningen CJ, Rasker FM, et al. Pulmonary nodules in a patient with seminoma testis. *Chest*. 1996;109: 265–266.
5. Donadio AC, Motzer RJ, Bajorin DF, et al. Chemotherapy for teratoma with malignant transformation. *J Clin Oncol*. 2003;21: 4285–4291.
6. Sheikine Y, Genega E, Melamed J, et al. Molecular genetics of testicular germ cell tumors. *Am J Cancer Res*. 2012;2:153–167.
7. Vargas SO, Korpershoek E, Kozakewich HP, et al. Cytogenetic and p53 profiles in congenital cystic adenomatoid malformation: insights into its relationship with pleuropulmonary blastoma. *Pediatr Dev Pathol*. 2006;9:190–195.