Possible Tx N2 M0 atypical bronchial carcinoid associated with Cushing syndrome

To the Editor:

Although bronchial carcinoids (BCs) account for only 1% of cases of Cushing syndrome (CS),1 in many cases the ectopic adrenocorticotropic hormone production has a source within the thorax. Usually typical BCs are the cause of ectopic CS, but rarely atypical ones have been described. BCs associated with CS appear more aggressive than others, with high tendency to metastasize.2

The article of Sugawara and colleagues,3 “Successful Localization and Treatment for Ectopic Adrenocorticotropic Hormone Secretion in a Rare Case of Possible Tx N2 M0 Carcinoid Tumor With Cushing Syndrome,” is interesting and highlights the importance of a correct management of a patient with ectopic CS. I have some questions for the authors:

1. Why did they not perform a mediastinoscopy before 2001, rather than video-assisted thoracoscopic lymph nodal resection?
2. Why was scintigraphy with indium In-111 pentetreotide (OctreoScan) performed only in 2001 and not earlier?
3. Why was the surgical resection was performed by thoracoscopy and not by thoracotomy?
4. Was the patient subjected to any adjuvant therapy?
5. Was OctreoScan scintigraphic follow-up planned or not?

I think that any pulmonary or mediastinal masses should be investigated in case of suspected ectopic adrenocorticotropic hormone production, and OctreoScan scintigraphy represents the most effective diagnostic tool and should be performed early. I think that thoracotomy should have been preferred for mediastinal lymphadenectomy because of the possibility of achieving a radical resection of the nodes and the possibility of an accurate lung palpation to detect possible small pulmonary nodules.

Shrager and associates2 confirm that the use of video-assisted thoracoscopic resection in BC with CS would be inappropriate. In cases of N2 atypical BC, adjuvant therapy is mandatory because of the risk of local relapses or distant metastases. Marty-Ané and coworkers4 suggest chemotherapy, but medical therapy with octreotide could be considered too. Octreotide, in fact, binds with high affinity to subtype 2 somatostatin receptors that are present in neuroendocrine cells surface, exerting a growth inhibitory effect in neuroendocrine tumors. Octreotide could be considered as an effective biologic postoperative therapy, generally well-tolerated and without important side effects. Using the long-acting form of this drug, only a single administration every 28 days is required. Finally OctreoScan scintigraphy is mandatory for the follow-up, because it has been demonstrated to be effective in detecting recurrences earlier than traditional radiologic procedures.5

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References

Reply to the Editor:
We read with interest the letter by Filosso from the University of Torino. When the patient came to our department, we had questions similar to those that Filosso posed.

In Japan, scintigraphy with indium In-111 pentetreotide (OctreoScan) is still only available for research purposes, not for clinical use. This is one of the reasons why we did not perform the scan before 2001, nor did we after the operation.

As Filosso mentioned, it is thought that bronchial carcinoid producing adrenocorticotropic hormone is aggressive. However, our patient showed a different clinical course, as we reported. More than 5 years passed between the onset of symptoms and her operation. Despite her long follow-up duration, no change in the size of mediastinal nodes was de
dected by serial examination until 2001. This may be the reason that her physician hesitated to consult us. In addition, the levels of adrenocorticotropic hormone and cortisol had not become worse during her course.

With regard to the use of a mediastinoscope, we also believe that this procedure is a useful method to localize and diagnose a tumor. However, with this procedure, it is sometimes difficult to perform en bloc removal of the whole tumor. We were also afraid that piece by piece removal might cause an intraoperative crisis of Cushing syndrome. In addition, our previous studies showed that removal of lymph nodes could be completed under thorascopic surgery. Our data revealed that only 2% of lymph nodes in weight could not be removed when performing sequential thoracotomy just after thorascopic surgery. Regarding the region of prerachal and paratracheal lymph nodes, no residual lymph nodes were detected in our studies. So in our case, we chose thorascopic surgery.

As mentioned by Filosso, we also believe that any pulmonary masses should be investigated in case of suspected ectopic adrenocorticotropic hormone production. However, we did not detect any tiny lesions in either lung on thin-sliced computed tomographic images. In such case, should we perform bilateral thoracotomy? We informed our patient, and she chose thorascopic resection. We also told her and her family about the possible need for further surgery should a new lung mass shadow develop.

Octreotide is also a good alternative option for adjuvant therapy in cases of stage III carcinoid tumor after surgery to prevent recurrence. Before our patient’s operation, she received octreotide treatment for about 1 year. She refused to continue the treatment, however, because of pain caused by subcutaneous injection. Now 2 years have passed since her operation. She is doing well without any signs of recurrence; the values of hormones are within normal ranges, and no abnormal mass has been detected by whole-body screening.

Finally, we appreciate Filosso’s advice. He advised us to implement a follow-up plan including OctreoScan scintigraphy and possible octreotide treatment. Considering his advice, we will discuss her adjuvant therapy and follow-up plan with her physicians and perform careful and intensive follow-up.

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Spiral pattern: Universe, normal heart, and complex congenital defects

To the Editor:
In the fascinating article “Basic Science Review: The Helix and the Heart” in a recent issue of Journal, Gerald Buckberg, supported by the anatomic studies of Torrent-Guasp and colleagues, illustrated the spiral anatomy of the muscle bands and the helicoid shape of the myocardium. On the basis of recent observations on embryology and genetics, we have reached similar conclusions regarding the spiral pattern of the heart morphology in complex congenital defects.

The normal heart has a clockwise spiral pattern of the outflow tracts and of the great arteries. The helicoid 3-dimensional movement driving to this condition, genetically determined in subjects with situs solitus, appears with the dextroventricular loop (right ventricle to the right, left ventricle to the left), progresses with the looping (anterior rotation of the right ventricle, posterior rotation of the left ventricle), and finishes with the spiral septations of the outflow tracts and the great arteries. Because the dextroventricular loop is the first recognized sign of asymmetry and lateralization of the body organs, the clockwise spiralization of the heart should be considered a specific pattern of chirality in vertebrates. In subjects with situs inversus, an incompletely understood genetic mechanism is responsible for a “mirror image” anatomy of the heart, with counterclockwise shape of the outflow tracts and great arteries. This condition appears with a