

Distinctive radiological aspects of bronchial carcinoid tumors

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Abstract

Learning objectives: We report in this article the various radiologic features of bronchial carcinoid tumors, as well as their specific distribution within the lung, which could help distinguishing them from other pulmonary tumors and establishing an appropriate therapeutic strategy.

Materials and methods: We reviewed the medical records of all patients with bronchial carcinoid tumors diagnosed by biopsy or surgical resection, and that underwent CT scans in the radiology department of university hospital HASSAN II in Fez, for a period of 05 years, from January 2015 up to January 2020.

Results: The study group included 24 patients of which 16 were women and eight were men. The average age was 41 years old (range: 18–64 years). The clinical presentation was dominated by hemoptysis in 16 cases. However, 04 patients were asymptomatic. Tumors were predominantly proximal (72%). The mean tumor diameter was 22 mm (range: 05–58 mm); the majority of the tumors (88%) had a lobulated outline, and they were all solid, containing partial calcifications in 26% of cases and significantly enhanced after contrast injection in 61% of cases. 17 of this tumors were typical carcinoids and the seven remaining were atypical.

Conclusion: Carcinoid bronchial tumors are known to be low-grade tumors and are classified as lung neuroendocrine tumors. There are two types of carcinoid tumors, typical and atypical, which are different in terms of aggressiveness and prognosis, although they present similar imaging features. The analysis of imaging features allows a better understanding of this type of tumor and a better management

Keywords: Bronchial tumor; Carcinoid tumor; Radiography; Computed Tomography

1. Introduction

Carcinoid bronchial tumors are known to be low-grade of malignity tumours and are classified as pulmonary neuroendocrine tumours. There are two types of carcinoid tumors, each one of them has its own aggressiveness level and prognosis, although they present similar imaging features.

Surgery is the basic treatment, with an average survival rate up to 5 years, of 90% for typical carcinoids and 75% for atypical ones.

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2. Material and methods

We reviewed the medical records of 24 patients with primary pulmonary carcinoid tumors diagnosed by biopsy or surgical resection, and that underwent CT scans in the radiology department of university hospital HASSAN II in Fez, during the last 05 years, from January 2015 up to January 2020.

A thoracic CT was done for the following reasons: location of lesions; order of the bronchi involved; size, outline and density of lesions; enhancement after contrast; the presence of peripheral atelectasis, as well as pneumonia and bronchiectasis.

3. Results

The average age in our study was 41 years old with a range going from 18 up to 64 years old, 8 of which were males and 16 were females. Only 2 patients were smokers.

The clinical presentation was dominated by hemoptysis found in 16 cases, cough was less frequent, found in 02 cases, dyspnea and chest pain were found in only 01 case each. On the other hand, 04 patients were asymptomatic and no carcinoid syndrome was revealed.

All patients underwent plain radiography and chest CT scan.

The plain radiography revealed rounded opacity with clear outlines in 11 patients (figure 1), while a blurred outlines mass was found in 5 patients, the presence of calcifications within the mass was only found in 1 patient. The indirect radiological signs were: atelectasis (n = 5), (figure 2), bronchiectasis (n = 3).

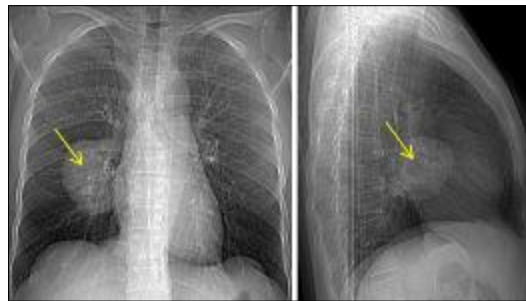


Figure 1 32 years old man, asymptomatic. He underwent a Chest X ray for a pre-therapeutic assessment for a cholecystecmy. It shows an a well-defined round para-hilary (arrow)



Figure 2 36 years old man, with a history of dyspnea for 4 months and recurrence of hemoptysis. Chest Xray shows a lower lobe atelectasis erasing the diaphragmatic dome (red arrow), a round opacity of the lower lobe poorly defined (blue arrow)

At chest CT scan, the majority of lesions had a lobulated outline. The different locations were the following:

- Only one tumor was tracheal and was located at the junction of the upper third and middle third of the trachea.
- 17 right carcinoid tumors were found (70%): 2 in the main bronchus, (figure 3) 7 in the intermediate bronchus, 2 in the upper lobe, 3 in the middle lobe (figure 4) and 2 in the lower lobe (figure 5).
- 6 tumors have been identified in the left side (25%): 2 in the main bronchus, 1 in the upper lobe and 4 in the lower lobe.
- It should be noted that a case of synchronous bilateral typical pulmonary carcinoid tumours was found (figure 7); one was located in the intermediate bronchus and the other in the left lower lobe

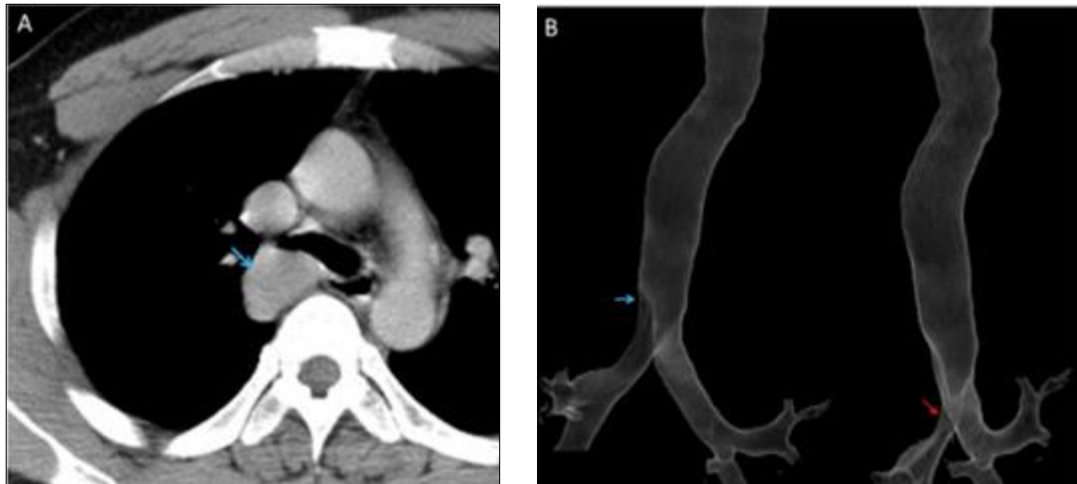


Figure 3 A- typical carcinoid in a 48-year-old man with a 3-month history of hemoptysis. Contrast enhanced chest CT with mediastinal window shows a well-defined ovoid mass close to the carina (arrow) B- Images of VR reconstruction of the trachea and bronchial tree show a narrowing of the carina (blue arrow) and the right bronchus (red arrow)

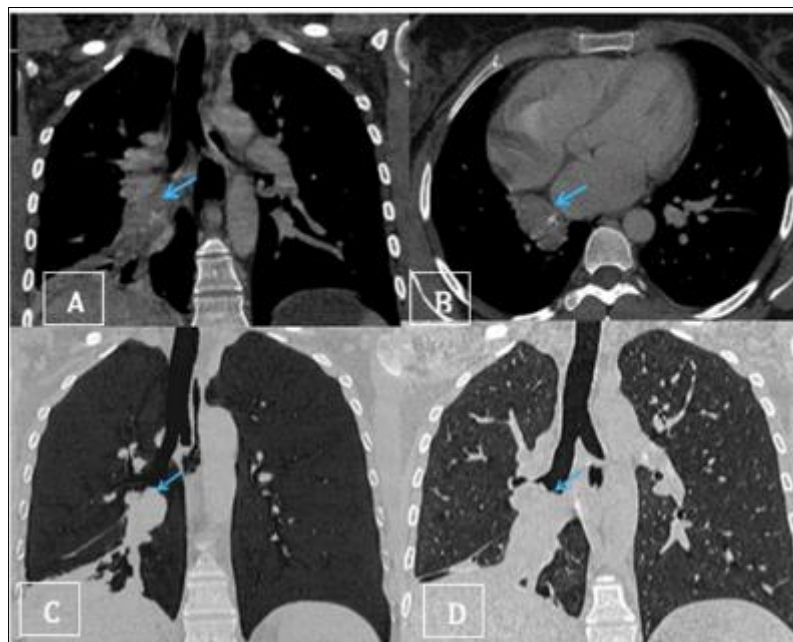


Figure 4 Typical carcinoid in a 36-year old woman with hemoptysis. A, B: Coronal and axial CT scan after contrast mediastinal window showing a well-defined ovoid, perihilar mass with narrowing of the intermediate bronchus.(arrow). C, D: Coronal view of the CT in lung window showing the mass with an atelectasis in the inferior lobe



Figure 5 34 years old woman, who presented with hemoptysis for 2 years. Axial chest CT: (parenchymal windowing) peri hilar mass of the lower lobe with regular contour and lobulated shape, classified T1NOMO, confirmed as a typical bronchial carcinoid tumor in histology

The average size of the for the 17 typical carcinoid tumors was 32 mm (range 15-80 mm) (figure 6), While it 07 was 51 mm (range: 20-110mm) for the atypical ones (figure 7 et 8).

All lesions were solid, containing partial calcifications in 26% of cases (Figure 9) and having a marked enhancement after contrast injection (figure 10). On the other hand, the tumors were associated with indirect signs including atelectasis in 06 cases, bronchiectasis in 05 cases, pneumonia (Figure 11) in 03 cases.

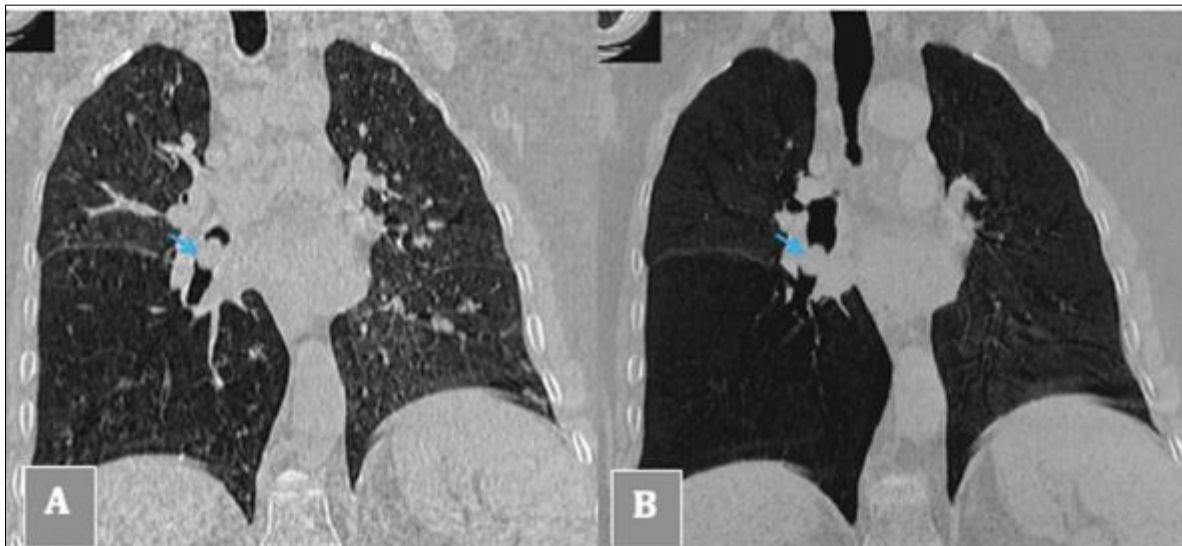


Figure 6 50 years old woman, who had a history of hemoptysis for 01 year. Chest CT: (A: lung window, B: Mini-IP) right main bronchus tumor, well circumscribed, ovoid and entirely endoluminal, T1NOMO; Histological study: typical bronchial carcinoid tumor

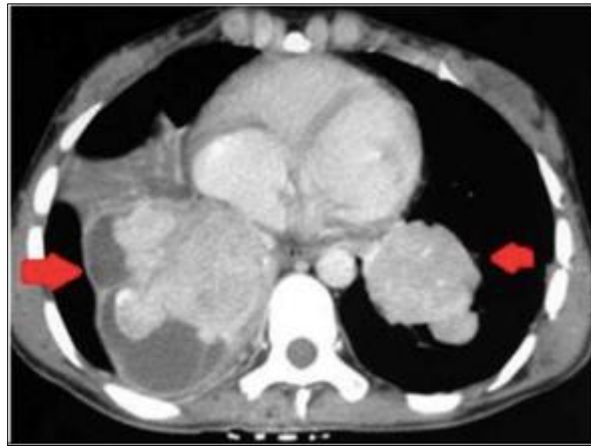


Figure 7 31 years old woman with 4 months history of dyspnea and recurrent hemoptysis. Thoracic CT scan after contrast enhancement (axial reconstruction mediastina window) shows 02 bilateral parenchymal masses of both inferior lobes (arrows). Histological study: Atypical carcinoid tumor



Figure 8 53 years old woman with a 3 years history of coughing and recurrent pneumonia. CT scan with A: axial, B: Coronal and C: sagittal reconstructions (lung and mediastinal window) showing a well circumscribed lobular mass with a low contrast enhance ment in the lung parenchyma around complicated by a complete atelectasis in the inferior lobe (arrow). Histological study: atypical carcinoid tumor

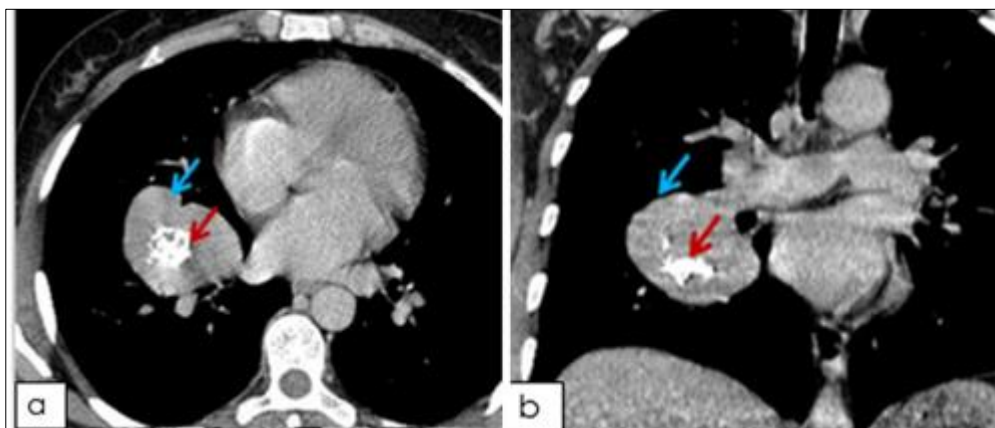


Figure 9 46 years old man with a history of chronic coughing. Axial (a) & coronal (b) CT scan (mediastinal windowing) shows a right perihilar mass with regular contour (blue arrow) and foci of macrocalcifications (red arrow). Histological study: Typical carcinoid tumor

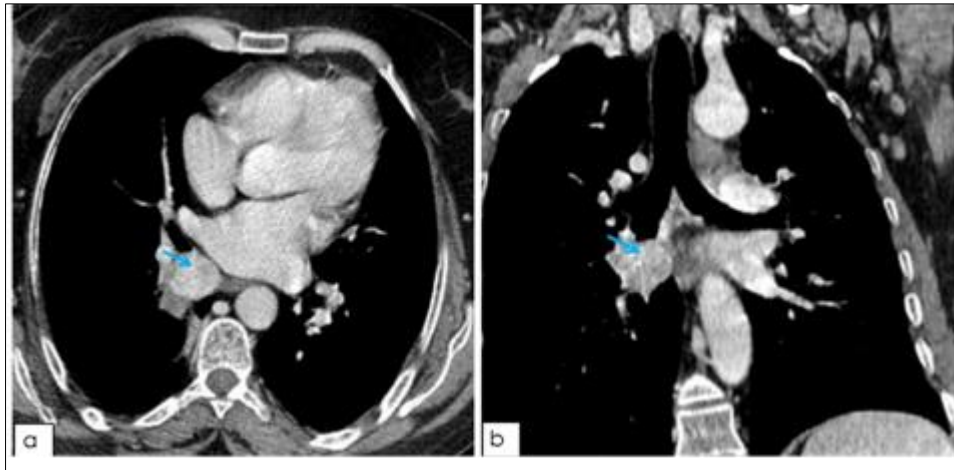


Figure 10 46 years old man, who presented with hemoptysis. Contrast enhanced CT scan: (a: axial, b: coronal reconstruction mediastinal windowing) showing a proximal mass with marked homogeneous contrast enhancement (arrow)



Figure 11 27 years old woman, who presented with recurrent pneumonitis associated with hemoptysis. Contrast enhanced CT scan: (a: axial, b and d: coronal, c: sagittal; reconstructions mediastinal windowing) showing a proximal mass with marked homogeneous contrast enhancement (arrow) The staging was done using a chest-abdomen-pelvis CT scan and no further metastasis was found

All patients underwent a flexible bronchial fibroscopy except one case of peripheral tumor location. The fibroscopies have shown an endobronchial or endotracheal bud, with a pinkish red color (**figure 10**), bleeding spontaneously or by contact. It was totally obstructive in 65% of cases (n = 15). Biopsy could be performed in only 26% of cases (n = 6) and allowed the diagnosis in 5 cases (2 typical carcinoids and 3 atypical forms). In the sixth case, the diagnosis was rectified on the surgical specimen (first typical then atypical carcinoid).

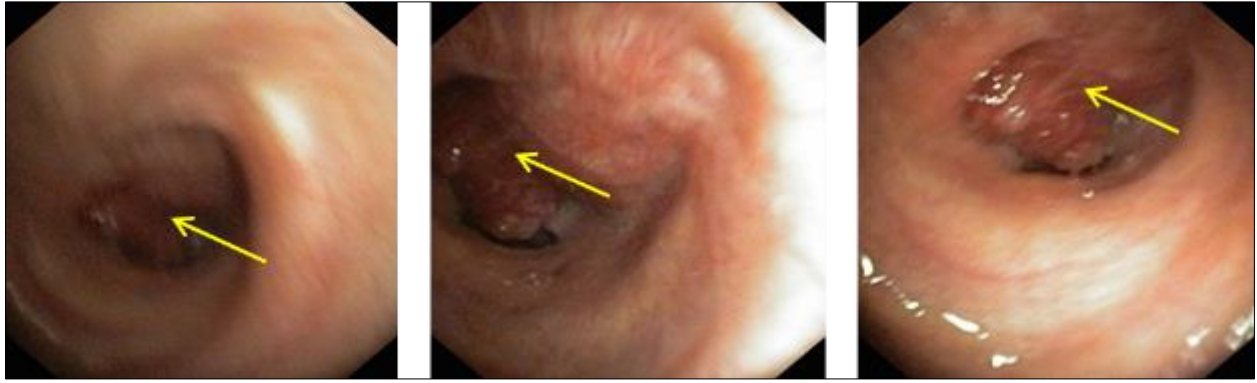


Figure 12 Endoscopy of the intermediate trunk showing an endobronchial bud with a smooth, highly vascularized surface extending over its posterior wall

Spirometry was performed in all patients except the case with a peripheral tumor localization. The forced expiratory volume in seconds (FEV) ranged from 1.40 L to 3.70 L and 3 cases of non-reversible obstructive disorders were identified.

All patients were operated, with a posterolateral thoracotomy conserving the dorsalis major muscle except the one with the tracheal location where a cervico-manubriotomy was performed. In addition, the patient with a synchronous bilateral tumor benefited from a deferred bilateral surgery, after a multidisciplinary consultation, starting with the largest tumor on the right side.

The procedures performed were lobectomy in 9 cases.

Concerning the tracheal localization, a terminal anastomosis resection was performed. Radical mediastinal lymph node dissection was performed in 91% of cases ($n = 21$). It was not performed in the case of the tracheal tumor and the peripheral tumor. The surgery was hemorrhagic in 3 cases, requiring transfusion.

All surgical specimens (Figure 11) were sent for pathological examination. Macroscopically, they were well-limited, encapsulated tumors with a beige or whitish color. The size ranged from 1.5 cm to 11 cm long axis with a mean of 3.9 cm.

Thus, a typical carcinoid tumor was found in 61% of cases ($n = 14$) and an atypical tumor in 39% of cases ($n = 9$). The tracheal and bronchial cuttings were healthy in 95.6% of cases. In one case, a bronchial cut was tumorous. Node dissection was negative in 95.6% of cases, positive in one case.



Figure 13 Surgical specimen showing the tumor process obstructing $\frac{3}{4}$ of the bronchial lumen (white arrow) with a completely hepatic right upper lobe (black arrow)

The duration of hospitalization varied between one to six days with an average of three days. All patients stayed in the intensive care unit immediately after surgery. Morbidity was 13% (n = 3).

There were

- Two cases of bronchial congestion after bronchial anastomosis resection (BAR) rapidly resolved by fibroaspiration;
- One case of hemopneumothorax on the sixth postoperative day for which the patient benefited from thoracic drainage with a satisfactory outcome.

Adjuvant chemotherapy was chosen in 17% of cases (n = 4) as decided in the multidisciplinary consultation meeting.

In all these patients, the main indication for chemotherapy was the risk of local recurrence and distant extension. All the 4 cases were atypical carcinoid tumors, thus presenting potential regional aggressiveness similar to that of non-small cell bronchial cancers. On the other hand, they were large tumors, with lymph node extension for some cases and the lack of R0 resection margin.

Mortality was 9% (n = 2). The first case was a patient who benefited from a left lower lobectomy for aspergilloma and then anastomotic resection for tracheal tumor; he died the 4th day after the surgery with a cataclysmic hemothorax following a broncho-arterial fistula complicating the left lower lobectomy. The second case was a patient with an altered general condition (WHO at 2) who died the 18th day after the surgery in the intensive care unit with a profound cachexia.

The evolution was favorable in 91% of cases, without any regional recurrence nor distant metastasis after a mean follow-up of 38 months. No radiotherapy was administered.

4. Discussion

Bronchial carcinoids are rare tumors. According to the American SEER database, this group represent 1 to 2% of primary bronchial tumors [1].

In our study, lesions occurred preferentially in young adults (average age of 41 years), in agreement with literature data where the peak incidence is between 40 and 50 years for carcinoids [4].

The sex ratio is controversial, in fact while some studies are in favor of a balanced distribution, others have shown a preponderance of atypical carcinoids in men and a clear predominance, in typical carcinoids, in women. This was demonstrated in our study where almost all patients were women in the case of typical carcinoids (16/17) against a slight male predominance for the atypical carcinoid group (5 men versus 3 women) [3, 4, 5, 6, 7].

According to the studies, neither the environmental factors nor smoking were retained for typical carcinoids. Nevertheless, several surveys assume that smoking might be a risk factor for the development of atypical carcinoids [8]. In our series, the 02 smoking patients had atypical carcinoids.

It has been noted in the literature that patients with bronchial carcinoids are often symptomatic and the most common symptoms include cough, hemoptysis, wheezing, and pneumonia as a result of central airway involvement [9]. Rare associations of pulmonary carcinoid tumors include carcinoid syndrome, Cushing disease from ectopic adrenocorticotrophic hormone (ACTH) production, and acromegaly from ectopic production of growth hormone [10].

However, about 19-51% of the patients are asymptomatic and bronchial carcinoid is diagnosed because of their abnormal findings on chest radiographs [11].

4.1. Imaging findings

4.1.1. Contribution of plain radiography

Carcinoid tumors generally present as an isolated, well-defined opacities, sometimes lobulated. Partial calcifications or even excavations are possible [12]. Tumor localization can be hilar or perihilar in 80% of cases, or distal in 20% [13]. The intra-bronchial character is hardly detectable by standard radiography [14].

The lesions are exceptionally multifocal or bilateral.

The findings of the tumor in a chest X ray are not always obvious and can sometimes only be shown by the indirect signs due to the bronchial obstruction caused by the tumor, such as atelectasis, air trapping, obstructive pneumonitis, bronchocele or bronchial dilatation.

On the other hand, chest X ray can be normal in 20% of cases in pure and non-obstructive endobronchial forms [15], hence the need to complete the radiological assessment with a chest CT scan in the event of suggestive carcinoid syndrome, or obstructive parenchymal involvement resistant to treatment, especially in a young patients [16].

4.1.2. Contribution of chest CT

It is more efficient for studying the characteristics of the tumor, it allows to specify the exact location, size, morphology and enhancement of the tumor. Furthermore, it determines the extent of the primary tumor, involvement of mediastinal lymph nodes, and presence of distant metastases.

The main contribution of CT compared to fibroscopy is to show tumors with external-bronchial development, to explore the state of the bronchi and pulmonary complications downstream from obstructive tumors as well as the study of the loco-regional extension. Significant differences in radiological presentation exist between typical and atypical carcinoid tumors, but the diagnosis of certainty remains anatomopathological.

Location

Some authors find a predominance of lesions in the right lobes (55-75%) [17]. This agrees with our series where 14 cases (66%), were of right localization.

The predominance of lesions in the proximal bronchial tree is recognized by all [18], despite a central topographic versus peripheral differentiation varying from one author to another. Also in our study, all 24 patients presented with central tumors (upstream of a segmental bronchus).

- Hilar or Perihilar masses

Central bronchial carcinoids most frequently manifest as a hilar or perihilar mass

Despite the primarily endoluminal origin, it is typically observed on CT that most of the mass extends to the adjacent parenchyma, and the endoluminal component may be minimal. This finding is what is called the “tip of the iceberg” sign [19][21].

- Endobronchial nodules

Approximately 20% of carcinoid tumors present as endobronchial polyp-like lesion without involvement of lung parenchyma [1].

- Peripheral bronchial carcinoids

None of our patients had a peripheral tumor (downstream of a segmental bronchus). The peripheral topography does not allow the distinction between typical or atypical carcinoid tumor [22]. Finally, if the peripheral lesion is a solitary pulmonary nodule, the differential diagnosis of the lesions may include many disorders.

- Tracheal localization

This location is rare. Indeed, in the series of Ayadi-kaddour [23], Kyriass [24], Federico [25] and Fink [26], no tracheal localization was found.

Whereas, in our series one patient presented with tracheal localization.

- Bilateral localization

Bilateral localization is very rare, indeed, it was found in the Fink series [21] (n = 8 or 5.7%), in our series (n = 1 or 5%) and in the Ayadi-kaddour series [18], where 2 cases of bifocal tumors were noted as well as a case of multifocal tumors on the left.

Tumor morphology

According to the literature concerning the size of the carcinoid tumor, atypical carcinoids are larger in volume than typical carcinoids. This was confirmed in our series, where the average size of atypical carcinoids was 5.1 cm, significantly larger than typical carcinoids whose average was 3.2 cm.

According to Zwiebel, oval tumors with a long axis parallel to the bronchus are in favor of a slow and minimally invasive form of tumor progression [27]. He describes this particular radiological sign under the name of the “parallelism sign”. In fact, this radiological sign is rare and not very sensitive, but very specific of a carcinoid tumor, moreover, it does not allow the distinction between the two histological forms.

Commonly, the lesion is made of solid tissue, with a round shape, sometimes polylobulate, with regular contours, never infiltrating or spiculated edges.

Tumor calcifications are better appreciated by CT. They can be diffuse or localized and are more common in proximal tumors. [28] Moreover, we noted, a predominance of punctiform eccentric calcifications compared to macrocalcifications, which explains the low yield of plain radiography.

Endobronchial calcifications can be confused with broncholithiasis or hamartochondroma [29].

The strong enhancement after contrast injection is explained by the significant stroma characterizing carcinoid tumors. [22] However, it can't differentiate carcinoid bronchial tumors from any other malignant lung lesions. Intense enhancement is mostly seen in typical carcinoid tumors but may be misled for a vascular malformation.

Associated signs related to bronchial obstruction

The presence of atelectasis or post obstructive pulmonary pneumonitis on a chest X ray, is usually associated with proximal lesion on CT scan [32].

The presence of dilation of the bronchi or bronchocele reflects a chronic obstructive nature [22].

Lymph node extension

Adenomegaly can be associated with carcinoid tumors: they are related to recurrent infections or to metastatic invasion. Lymph node invasion is more frequent in cases of atypical carcinoid [30, 31].

4.2. Bronchoscopic examination

Bronchial carcinoids are usually redish-brown to bluish-taned endobronchial masses with a smooth surface. They are often very vascularised and might cause bleeding when biopsied. Therefore, cauterisation must be available at all times. [33]

4.3. Histology

Bronchial carcinoids arise in the bronchial and bronchiolar epithelium and may derive from existing Kulchitsky cells, neuroepithelial bodies or pluripotential bronchial epithelial stem cells [34]

They are categorized into two major groups: About 90% are typical carcinoid (TC) tumors. The remaining 10% of the lesions are atypical carcinoid (AC) tumors, which tend to have a higher rate of metastasis and are larger at the time of diagnosis [35].

The WHO diagnostic criteria for TC are: a tumor with carcinoid morphology and <2 mitoses/ 2 mm^2 (10 HPH), lacking necrosis, and tumor of 0.5 cm or larger. An AC is defined as a tumor with carcinoid morphology with 2 to 10 mitoses/ 2 mm^2 and/or necrosis [36].

Our study shows typical and atypical carcinoids in respectively 85% and 15% of the patients.

4.4. Surgical treatment

Surgery can be performed by conventional open or minimally invasive approaches.

The posterolateral thoracotomy, which conserves the dorsalis major muscle, was the preferred approach in our series. This approach was the one adopted in almost 99% of the patients in the multicenter study conducted by Filosso et al. on a series of 260 patients with atypical carcinoid tumor and large cell neuroendocrine carcinoma [37]. Video-assisted thoracoscopic surgery (VATS) was performed in his series in only 3 cases, one reason being the central location of these tumors. In addition, these resections sometimes involve parenchymal sparing procedures that can only be performed by thoracotomy. These procedures involve sleeve lobectomies and bronchoplasties with or without parenchymal

resection. In our series, these BARs were performed in 3 patients. In a multicenter series, Fink et al. found 56% of lobectomies. Machuca et al. also found that lobectomy was the most common parenchymal resection [39]. However, in typical carcinoids, wedge resections and segmentectomies can be performed. Thus, in a large series, Fox et al. found no difference in survival between lobectomy and infralobar resection in typical sectionwedge carcinoids [40]. Similarly, Yendamuri et al. concluded that a lobectomy was not mandatory in typical carcinoid tumors, provided that a mediastinal lymph node dissection was performed [41]. In our practice, the latter is systematically performed for any central tumor and only one case of lymph node extension was found. This lymph node extension was found in 12% of typical carcinoids and 37.5% of atypical carcinoids in the series by Fox et al [40]. Some authors propose a mediastinal sampling only for tumor staging while others propose a radical mediastinal lymph node curage in case of central tumor even N0 staging sampling [42]. However, lymph node involvement has a prognostic value. Cardillo et al. concluded that prognosis was more related to lymph node involvement than to histological type, N2 involvement being associated with a worse prognosis [43]. Thus, the 5- and 10-year survival for N1 and N2 involvement is 90% and 75%, respectively, for typical carcinoids and 60% and 50% for atypical carcinoids [42]. In our series, the prognosis was favorable with a recurrence-free survival at 29 months of 91%; we therefore recommend a systematic mediastinal lymph node dissection in case of central tumor [44].

5. Conclusion

Carcinoid bronchial tumors are known to be low-grade tumors and are classified as pulmonary neuroendocrine tumors. There are two types of carcinoid tumours, each one of them has its own aggressiveness level and prognosis, although they present similar imaging features.

In a young or a non-smoking patient who has a central lesion, that is well defined and deforms or obstructs a bronchus, the diagnosis of a bronchial carcinoid tumour should be mentioned.

Imaging techniques particularly the CT scan helps differentiate between the typical and atypical carcinoid from its localization, enhancement, size and associated signs, however the diagnosis of certainty is made by anatomopathology.

Moreover, the presence of calcifications (usually eccentric) or a recurrent history of pulmonary infections concerning the same topography in the same patient should warn us to this specific tumor. The couple thoracic CT scan and bronchial fibroscopy is undoubtedly the best means for the diagnosis.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no competing interest.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors'.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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