

# Pulmonary Sclerosing Hemangioma Detected by Fluorodeoxyglucose Positron Emission Tomography in Familial Adenomatous Polyposis: Report of a Case

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We present a 53-year-old female suffering from familial adenomatous polyposis, who was found to have a positive nodus, lateral to the hilus of the left lung, on routine FDG-PET scan. This lesion was found to be a sclerosing hemangioma. We found an aberrant  $\beta$ -catenin expression on immunohistochemical staining, suggesting that sclerosing hemangioma and familial adenomatous polyposis share the same pathophysiology. It is important to be aware of the association of familial adenomatous polyposis and sclerosing hemangioma.

[Key words: Pneumocytoma; Sclerosing hemangioma; Familial adenomatosis polyposis; FDG-PET

Sclerosing hemangioma is a rare, but presumably, benign lung tumor, believed to originate from pneumocyte Type II cells,<sup>1</sup> which was first as such described by Liebow and Hubbell in 1956.<sup>2</sup> It is a rare lung tumor, probably accounting for approximately 3 to 5 percent of benign lung lesions. Case series suggest that females are mainly affected, with a reported median age of 46 years at presentation.<sup>3,4</sup> Sclerosing hemangiomas often are asymptomatic and are usually an unexpected finding on routine imaging studies. The lesions are well circumscribed and do not invade the adjacent normal lung parenchyma. The diagnosis is made on the basis of histologic examination. Sclerosing hemangiomas are composed of round cells with bland nuclei and pale to clear

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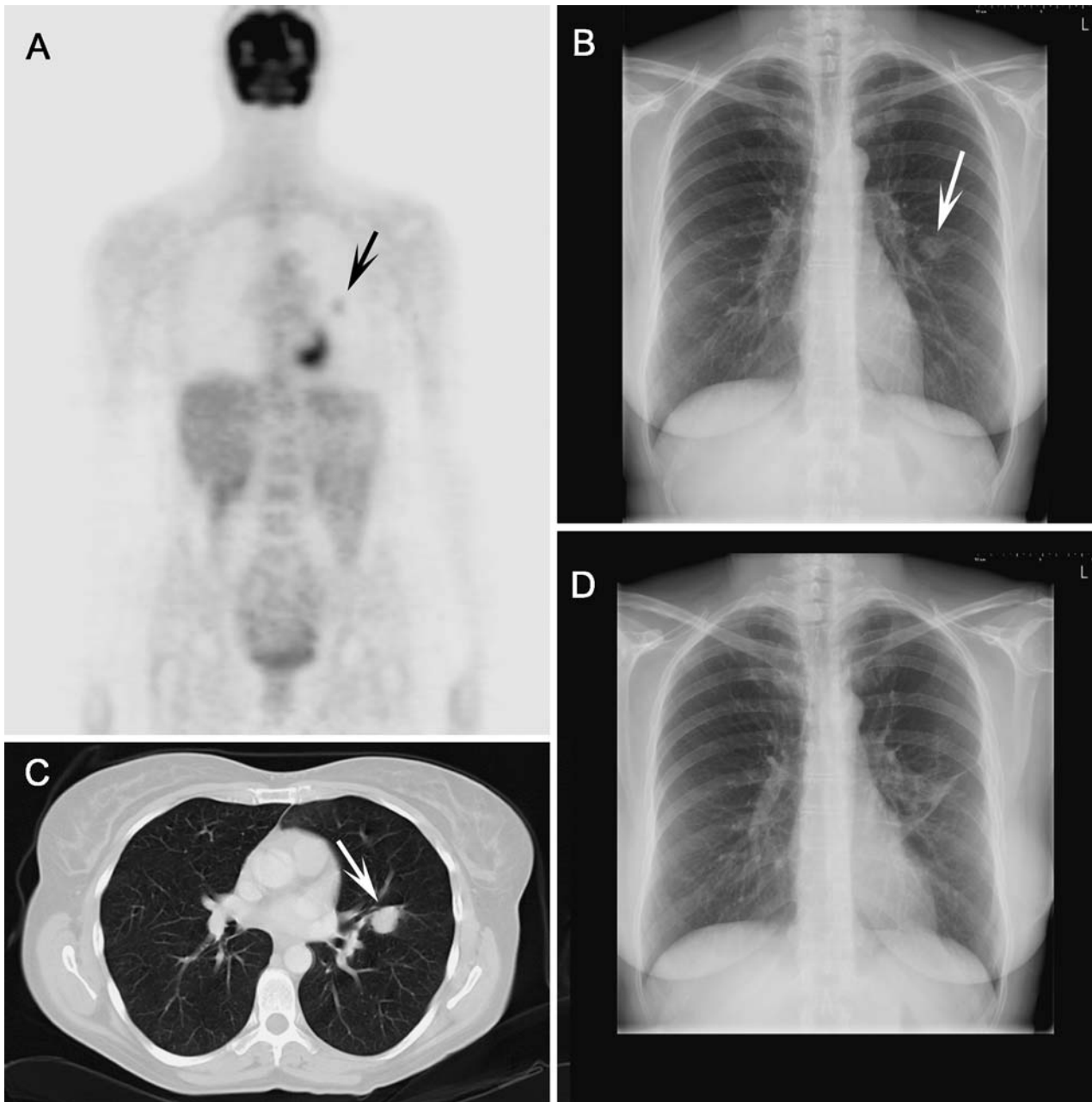
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**Figure 1.** A. Fluorodeoxyglucose on positron emission tomography (FDG-PET) showing a bright spot at the left hilum of the lung with a maximal SUV of 1.6. B. Chest x-ray showing a well-rounded hilary lesion of the left lung. There is a close lesion situated at approximately the same place as is the spot found on the FDG-PET scan. C. Contrast-enhanced CT at lung window settings, showing a sharply demarcated lesion with a diameter of 2.1 cm located in the left hemithorax. D. Chest x-ray after surgical removal of the pneumocytoma.

cytoplasm, but also papillary structures, with cuboidal cells lining them, are present. Sclerosing hemangiomas can exhibit four described patterns on histologic presentation: papillary, sclerotic, hemorrhagic, and solid, and all patterns can be present or absent within lesions.<sup>4</sup>

Little is known of the natural course, prognosis, and associated risk factors of sclerosing hemangio-

ma. A recent case described the identification of a sclerosing hemangioma in a patient with attenuated familial adenomatous polyposis (FAP).<sup>5</sup> FAP is a rare genetic disease (OMIM #175100) characterized by the development of literally hundreds to thousands of adenomatous polyps in the colon, which, if left untreated, lead to cancer at a young age.<sup>6</sup> We wish to report the unexpected discovery of a sclerosing

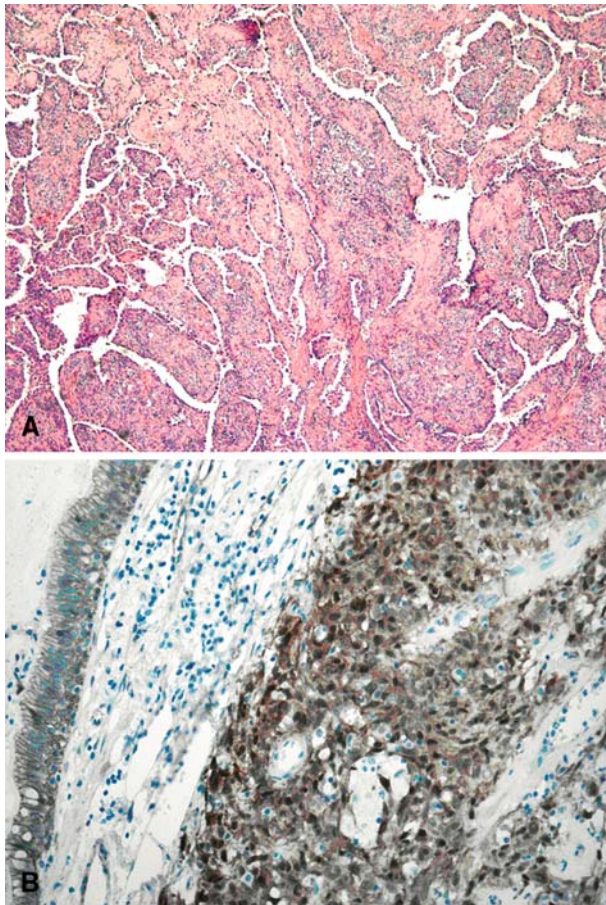
hemangioma that accumulated radiolabeled fluoro-deoxyglucose (FDG) on positron emission tomography (PET) in a patient suffering from FAP.

## REPORT OF A CASE

### Clinical Evaluation

A 53-year-old female was seen at our outpatient clinic because of follow-up of FAP. Her medical history revealed a total colectomy and insertion of an ileostoma in 1986 because of FAP. The germline mutation was localized on exon 13 of the APC gene (C1660 T; Arg 554 X). Routine endoscopy of duodenum revealed a number of adenomatous polyps, mainly located around the ampulla of Vater. Her

father had died at age 60 years because of lung cancer. She complained of a persistent, dry cough, but denied smoking. No abnormalities were found on physical examination. Because of a protocol for the follow-up of duodenal adenomas, a FDG-PET scan was made. Whole-body PET, 30 minutes after the intravenous injection of 250 MBq Fluor-18-FDG, revealed a small hot spot located at the hilus of the left lung (Fig. 1A). Although the uptake of the entire mass was little over background uptake (standard uptake value (SUV) 1.6), this did not rule out a malignancy. A chest x-ray and contrast-enhanced CT revealed a single circumscriptive lesion, with a diameter of 2.1 cm, situated in the left lung close to the hilus (Fig. 1B and C). There were no enlarged lymph nodes. Because a malignant lung tumor could not be excluded on basis of the available imaging data and because of her underlying FAP, we proceeded to a left-sided thoracotomy with excision of the tumor followed.



**Figure 2.** A. Histology of sclerosing hemangioma, papillary pattern with sclerotic areas (hematoxylin and eosin stain;  $\times 5$ ). B. Immunohistochemical stain for  $\beta$ -catenin ( $\times 20$ ). A normal expression at cell membrane was displayed in the adjacent bronchusepithelium (most left in photo), whereas an aberrant expression was seen in nucleus and cytoplasm of both the surface and round cells in sclerosing hemangioma.

### Pathologic Examination

On gross examination, a well-circumscribed, solid, subpleural tumor was found with a greatest dimension of 2 cm. Histologically, the lesion had a mixed papillary, solid and sclerotic pattern of two cell types: cuboidal surface cells, and round stromal cells. Focal clusters of foamy macrophages and cholesterol clefts were seen. Immunohistochemical studies showed expression of cytokeratin 7 in the surface cells (Fig. 2A). Thyroid transcription factor 1 was positive in both surface cells as well as in stromal cells. The tumor was classified as a sclerosing hemangioma. Additional immunohistochemical staining for  $\beta$ -catenin showed an aberrant expression in the cytoplasm and in the nucleus of both the surface and round cells (Fig. 2B).

## DISCUSSION

This is a case report of a solitary pulmonary lesion discovered by FDG-PET in a patient with FAP and found to be a sclerosing hemangioma on pathologic examination. Most manifestations of FAP are restricted to the gastrointestinal tract and include duodenal and colonic cancer as well as fundic gland polyposis. In a variant of FAP, Gardner's syndrome, patients not only have colonic polyps, but also extracolonic manifestations, such as desmoid tumors, osteomas, epidermoid cysts, various soft tissue tumors, and a

predisposition to thyroid cancers.<sup>7</sup> Our patient did not have any extraintestinal manifestations of her FAP until she presented with a sclerosing hemangioma. We were able to identify a single, comparable case from the literature. This 54-year-old, asymptomatic female affected with attenuated familial adenomatous polyposis (AFAP) presented with a left lower lobe mass on chest x-ray examination on a routine health checkup. CT and magnetic resonance imaging studies revealed a sharply demarcated lesion with a maximal diameter of 3.6 cm without evidence for metastases. The lesion had a slightly increased FDG uptake ratio of 1.8 on PET. A surgical enucleation followed and pathologic examination was compatible for sclerosing hemangioma.<sup>8</sup>

In the majority of cases, a sclerosing hemangioma is asymptomatic and is usually found only after routine imaging studies for other unrelated reasons. In a clinical series, 11 percent of patients presented with hemoptysis and 9 percent with cough.<sup>3</sup> In a retrospective series of 100 cases, there was no evidence for bilateral tumors or widespread metastasized disease, corroborating with the benign nature of the tumor.<sup>3</sup> On the other hand, there was one patient with regional lymph node metastases, and there have been reports with multiple sclerosing hemangioma lesions and lymph node metastases implying a more malignant potential.<sup>9,10</sup> This might corroborate with the monoclonality of the cells within the lesion.<sup>11</sup> This finding suggests a neoplastic growth pattern, but invasion of normal lung parenchyma has not been described.<sup>12</sup> The prognosis after surgical resection is excellent, although performing a second surgical procedure because of local recurrence is necessary in a small percentage of cases.<sup>3,4</sup>

The actual prevalence of sclerosing hemangiomas among FAP patients is unknown, and this is most likely caused by the relatively asymptomatic nature of the disease. Although the co-occurrence may have arisen by chance, a recent report reiterates its association and demonstrated an aberrant nuclear and cytoplasmic expression of  $\beta$ -catenin in the sclerosing hemangioma.<sup>5</sup>  $\beta$ -catenin is an extracellular circulating protein that activates the Wnt-pathway. Uncontrolled activation of the Wnt-pathway leads to uncontrolled cell growth and finally to malignancy. The aberrant staining of  $\beta$ -catenin of the sclerosing hemangioma in FAP suggests that it is a part of the clinical phenotype of FAP.<sup>5</sup> When abundantly available in the cell cytosol,  $\beta$ -catenin can induce transcription of a number of genes, primarily in-

involved in regulating cell growth, which are thought to play a critical role in tumorigenesis. Positive staining for  $\beta$ -catenin, thus demonstrating accumulation of the protein in the cell cytosol, is described in a number of tumors, especially colorectal cancers. In colorectal cancer,  $\beta$ -catenin accumulation emerges as a result of mutation of the APC gene, which encodes for a product that is critical for  $\beta$ -catenin degradation. FAP probably arises because a dominant-negative effect of APC gene protein products, which suggest that it acts as a tumor-suppressor gene. APC gene mutations have been described almost exclusively in colorectal cancer. It is possible that somatic APC mutations underlie the sclerosing hemangioma, which would imply sclerosing hemangioma and FAP share the same pathophysiology. We did not pursue this possibility, but we found aberrant  $\beta$ -catenin staining, which has not been described in sclerosing hemangioma so far, with the exception of one other FAP case. The aberrant  $\beta$ -catenin is similar to those found in other FAP-associated tumors.<sup>13,14</sup>

FDG-PET is well positioned to distinguish benign from malignant lesions in the evaluation of a solitary pulmonary nodule. A recent meta-analysis indicated that FDG-PET has an overall median sensitivity of 97 percent and a specificity of 78 percent in the evaluation of a solitary pulmonary nodule.<sup>15</sup> In this respect, this diagnostic approach has been shown to be more accurate than CT. The relatively low SUV in our patient with FAP (1.6) and another recent FAP case from the literature (1.8) suggest that the biologic behavior of sclerosing hemangioma in FAP may be benign because malignant lesions are characterized by higher SUV values.<sup>5</sup> We used FDG as radiopharmakon, but C-11-choline might be an alternative for identification of a sclerosing hemangioma with PET.<sup>16</sup>

## CONCLUSIONS

We described the first sclerosing hemangioma associated with true FAP, a lesion that may become increasingly more important when more patients with FAP are screened with modern imaging modalities.

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