Lung Fibrosis, Premature Graying, and Macrocytosis

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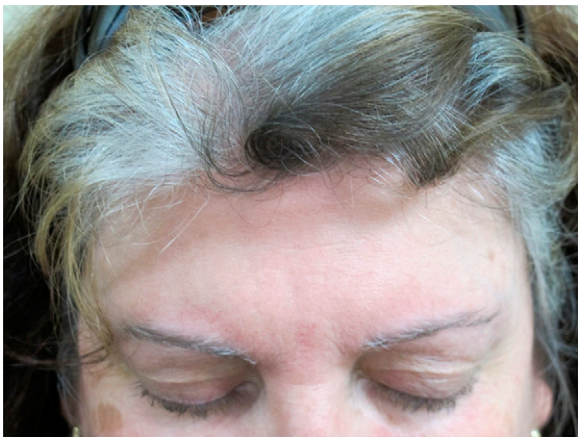

Figure 1.

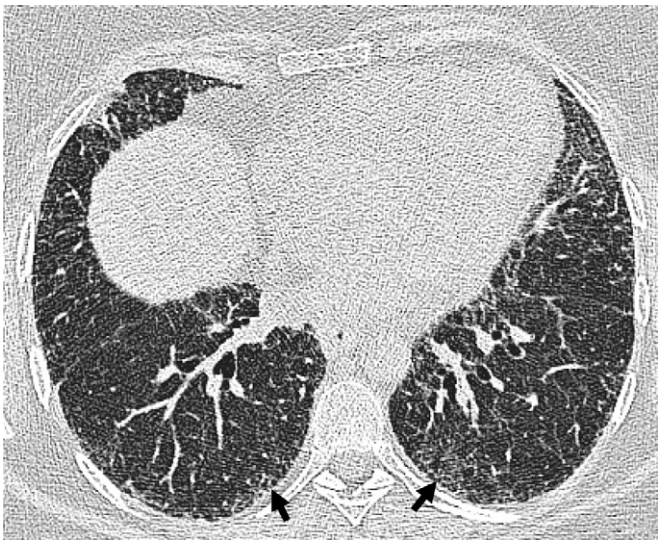

Figure 2.

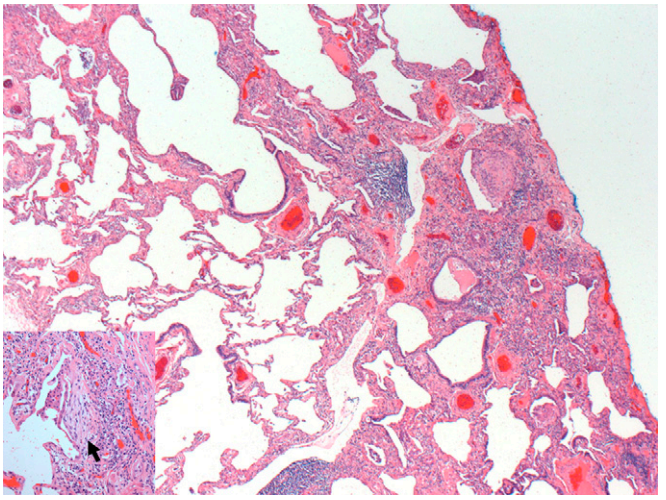

Figure 3.

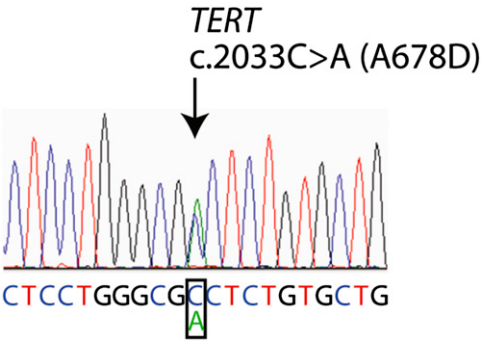

Figure 4.

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A 42-year-old woman with an 8-year history of unexplained macrocytosis (MCV 114) and mild thrombocytopaenia (105) presented with dry cough and dyspnea. She was noted to have fine inspiratory crepitations on auscultation of the chest and gray eyebrows and hair roots (Figure 1). The patient admitted to coloring her hair since she went completely gray at the age of 17. A thin section computed tomography scan of the chest demonstrated subpleural and basal predominant reticular changes and early honeycombing (Figure 2, *arrowheads*), and open lung biopsy confirmed usual interstitial pneumonia (Figure 3, hematoxylin and eosin, ×20) with fibroblastic foci (*arrow*, *inset* ×100) and early honeycomb change. Her peripheral blood mononuclear cell telomere length was well below the 1st percentile for her age, and Sanger sequencing confirmed a novel mutation resulting in a change from alanine to aspartic acid at position 678 in the *TERT* gene (Figure 4). There was no family history of lung disease; however, details were limited because the patient was adopted. Telomerase deficiency leads to progressive shortening of telomere length and premature cellular senescence, and is a recently identified cause of familial and sporadic pulmonary fibrosis, with which premature graying and hematologic abnormalities are often associated (1–4).

Author disclosures are available with the text of this article at www.atsjournals.org.

References

1. Diaz de Leon A, Cronkhite JT, Katzenstein AL, Godwin JD, Raghu G, Glazer CS, Rosenblatt RL, Girod CE, Garrity ER, Xing C, *et al*. Telomere lengths, pulmonary fibrosis and telomerase (TERT) mutations. *PLoS ONE* 2010;5:e10680.
2. Diaz de Leon A, Cronkhite JT, Yilmaz C, Brewington C, Wang R, Xing C, Hsia CC, Garcia CK. Subclinical lung disease, macrocytosis, and premature graying in kindreds with telomerase (TERT) mutations. *Chest* 2011;140:753–763.
3. Tsakiri KD, Cronkhite JT, Kuan PJ, Xing C, Raghu G, Weissler JC, Rosenblatt RL, Shay JW, Garcia CK. Adult-onset pulmonary fibrosis caused by mutations in telomerase. *Proc Natl Acad Sci USA* 2007;104:7552–7557.
4. Armanios MY, Chen JJ, Cogan JD, Alder JK, Ingersoll RG, Markin C, Lawson WE, Xie M, Vulto I, Phillips JA 3rd, *et al*. Telomerase mutations in families with idiopathic pulmonary fibrosis. *N Engl J Med* 2007;356:1317–1326.