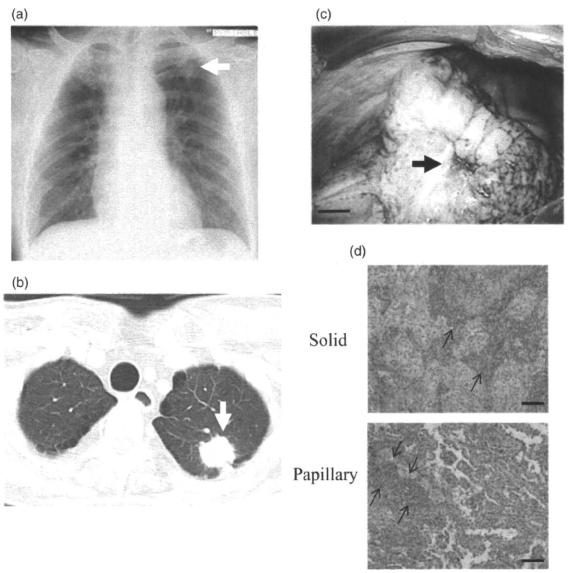

Figure 2 (a) Chest X-ray film showed an abnormal shadow in the left upper lung field, which is indicated by an arrow. (b) Computed tomography scan showed a homogenous solid tumor in the left upper lung, which is indicated by an arrow. (c). Pleural indentation without pleural effusion was observed during the surgery. Bar, 2 cm. (d) Histological specimen obtained during surgery revealed a adenocarcinoma mixed subtype; the cellular patterns were papillary and solid, with lymphocytic and plasma cell infiltration as indicated by arrows. Bar, 200 μm.

findings suggest that the WRN helicase plays an essential role in telomeric function.[6–9] The data from WRN-knockout mice indicate that the shortening and functional disability of telomeres lead to the development of osteosarcomas and soft tissue neoplasms.[10]

Lung cancer has been very rarely observed in patients with WS, probably because patients with WS have a shorter lifespan. Lung cancer develops most frequently in men who are 50 years-of-age or more.[11] Just five cases of lung cancer associated with WS have been reported so far, and all the patients were over 50 years-of-age (Table 1).[12–16]

Indeed, the recent data have shown that the lifespan of Japanese patients with WS has been significantly prolonged by approximately 10 years.[17,18] In our previous study and those of other researchers, it was reported that not only the 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase inhibitor (statins) therapy, but also a peroxisome proliferator-activated receptor-gamma agonist administration improves the prognosis of patients with WS.[19,20] Although the mechanism underlying this action is yet to be determined, statins might protect patients with WS as a result of the shortening of telomeres; thus, statins can extend the lifespan of patients with WS, not only by their antiatherosclerotic properties, but also by preventing the development of sarcomas. In this scenario, as the life expectancy of patients with WS increases, the incidence of cancer might also increase in the near future.

Regarding lung cancer, it is still unclear whether or not adenocarcinoma develops more often in WS patients compared with other pathological types of primary lung cancer. Four out of six cases (previous reports and the present case) are adenocarcinoma (including alveolar-epithelial carcinoma). There seems to be no difference in the pathological type of primary lung cancer between patients with and without WS, as half of all cases of primary lung cancer in non-WS patients are adenocarcinoma.[21] However, there are still very few reported cases of primary lung cancer in patients with WS. Therefore, more experience of primary lung cancer in WS patients is needed before definite conclusions can be drawn

WS patients characteristically develop skin ulcers in the extremities.[5] These ulcers are refractory to any conservative treatment and often require amputation of the limbs; this severely affects the quality of life of these patients.[22–24] The reduced proliferative capacity of the skin fibroblasts in patients with WS is likely to cause ulcer formation;[24] however, the molecular mechanism underlying ulcer formation has not yet been completely elucidated.

Table 1 Reported cases of lung cancer in patients with Werner syndrome

	Case 1	Case 2	Case 3	Case 4	Case 5	Present case
Age, sex	54, female	51, female	52, male	52, female	55, male	52, male
Consanguinity	None	None	First cousins	First cousins	First cousins	None
Other neoplasms	None	None	None	Osteosarcoma	None	Pharyngeal cancer
Histology	Squamous cell carcinoma	Well-differenciated adenocarcinoma	Well-differenciated	Bronchio-alveolar	Squamous cell carcinoma	Well-differenciated adenocarcinoma
Stage (TNM)	1b (T2N1M0)	1b (T2NXM0)	1a (T1NXM0)	1a (T1N0M0)	1a (T1N0M0)	1a (pT1N0m0)
Treatment	Irradiation	Local chemotherapy	Left lower lobectomy	Right upper lobectomy	Left lower lobectomy	Left upper lobectomy
Outcome	14 months, died	4 months, died	Unknown	44 months, survived	47 month, survived	24 months, died
Reference	8	9	10	11	12	

Postoperative wound healing is one of the major issues considered by surgeons before deciding on surgical management in the case of patients with WS. In our patient, despite the patient's present condition and the history of refractory skin ulcers in the extremities, the lung cancer was successfully resected, without any skin-related problems. The skin and soft tissue of the extremities tend to be atrophic and comified in WS, whereas the skin of the trunk is normal.[25] In addition, subcutaneous fat tissue in the extremities of WS patients was reported to be lipoatrophic, whereas tissue of the trunk was normal. Moreover, there are possible systemic metabolic effects of regional adiposity in a patient with WS.[26] It has also been reported that not only lung cancer, but also meningiomas[27] and pancreatic cancer[28] can be successfully operated on without any skin-related problems. Therefore, there might be no difference in the wound-healing ability of the skin of the trunk between patients with WS and the normal population of the same age group. It appears that skin ulceration might not be a potential problem of surgical treatment of the trunk, as in our case and previous reports.

In summary, we report a case of WS associated with primary lung cancer that was successfully resected. As the life expectancy of patients with WS is increasing, we need to pay attention not only to rare non-epithelial malignancies, but also to epithelial cancer. Furthermore, the shorter life expectancy of patients with WS than the general population, as well as the possibility of skin-related problems after surgery, should not be a deciding factor when considering whether to carry out surgery in the case of malignancy.

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