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A spiky issue

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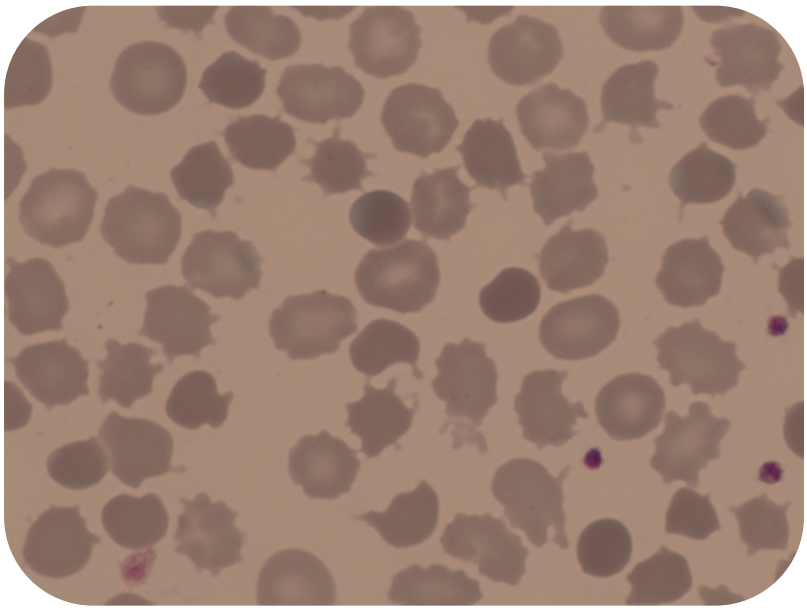

A 61-year-old man was diagnosed with metastatic adenocarcinoma of the lung. After initial treatment with carboplatin and pemetrexed, a second-line treatment with alectinib was started following the detection of an echinoderm microtubule-associated protein-like 4 (EML4) anaplastic lymphoma kinase (ALK) translocation. At the start of treatment, all peripheral blood values were within normal limits. Two months later, an occasional drop of the hemoglobin concentration was noted (nadir 126 g/L), which turned out to be related to an intermittent, mild, and well-compensated Coombs-negative hemolysis (lowest level of haptoglobin 0.21 g/L [normal range, 0.3-2]; highest levels of LDH and total bilirubin 289 U/L [<265] and 27 µmol/L [<20], respectively). A peripheral blood smear (original magnification ×630) revealed marked anisocytosis with some (micro-)spherocytes, a few fragments, and numerous acanthocytes, the latter with irregularly shaped, coarse, thorny projections of variable size.

A diagnosis of alectinib-associated hemolysis was made; however, the patient could stay on treatment without developing clinically relevant hemolysis during the follow-up of up to now 3 years. An often-marked acanthocytosis is the hallmark of alectinib-induced hemolytic anemia, which has been recognized as a side effect of this compound during post-marketing surveillance. Many patients treated with this ALK inhibitor develop hemolysis, which mostly is mild and rarely requires cessation of the drug. The exact pathophysiology is unknown, but reduced eosin-5′-maleimide (EMA) binding suggests a nonimmune drug-induced membranopathy.

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